

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**FORM S-1**

REGISTRATION STATEMENT  
UNDER

THE SECURITIES ACT OF 1933

**TRANSCODE THERAPEUTICS, INC.**

(Exact name of Registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**2834**  
(Primary Standard Industrial  
Classification Code Number)

**81-1065054**  
(I.R.S. Employer  
Identification No.)

**6 Liberty Square, #2382  
Boston, MA 02109  
(857) 837-3099**

(Address, including zip code and telephone number, including area code, of Registrant's principal executive offices)

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**Approximate date of commencement of proposed sale to the public:** As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer   
Non-accelerated filer

Accelerated filer   
Smaller reporting company   
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

**The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.**

**PRELIMINARY PROSPECTUS      SUBJECT TO COMPLETION      DATED FEBRUARY 1, 2023**

**12,000,000 Shares of Common Stock  
Up to 12,000,000 Pre-Funded Warrants to Purchase Common Stock**

**T R A N S C O D E**

T H E R A P E U T I C S <sup>TM</sup>

**TransCode Therapeutics, Inc.**

We are offering 12,000,000 shares of our common stock on a firm commitment basis.

Our common stock is listed on the Nasdaq Capital Market under the symbol “RNAZ.” The last reported sale price of our common stock on the Nasdaq Capital Market on January 31, 2023, was \$0.75 per share. The final public offering price will be determined through negotiation between us and the underwriter; the recent market price used throughout this prospectus may not be indicative of the actual offering price.

We are also offering to each purchaser whose purchase of shares of our common stock in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% (or, at the election of the holder, 9.99%) of our outstanding shares of common stock immediately following the consummation of this offering, the opportunity to purchase, if the purchaser so chooses, pre-funded warrants to purchase shares of common stock, or the pre-funded warrants, in lieu of shares of common stock. Each pre-funded warrant will be exercisable for one share of our common stock. The purchase price of each pre-funded warrant will equal the price per share of common stock being sold to the public in this offering, minus \$0.01, and the exercise price of each pre-funded warrant will be \$0.01 per share. For each pre-funded warrant that we sell, the number of shares of our common stock that we are offering will be decreased on a one-for-one basis. The pre-funded warrants will not be listed on the Nasdaq Capital Market and are not expected to trade in any market, however the shares of our common stock to be issued upon exercise of the pre-funded warrants will trade on the Nasdaq Capital Market.

We are an “emerging growth company” and a “smaller reporting company” as defined under federal securities law and, as such, we have elected to comply with certain reduced public company reporting requirements. See the section titled “Prospectus Summary—Implications of Being an Emerging Growth Company and a Smaller Reporting Company.”

**Investing in our common stock involves a high degree of risks. See “Risk Factors” beginning on page 15. Neither the U.S. Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.**

	Per Share	Per Pre-Funded Warrant	Total
Public offering price	\$ —	\$ —	\$ —
Underwriting discounts and commissions <sup>(1)</sup>	\$ —	\$ —	\$ —
Proceeds to us, before expenses	\$ —	\$ —	\$ —

(1) We refer you to “Underwriting” beginning on page 169 for additional information regarding underwriter’s compensation.

We have granted a 45-day option to the underwriter to purchase up to an additional 1,800,000 shares of our common stock (and/or pre-funded warrants in lieu thereof), representing 15% of the shares of common stock and pre-funded warrants sold in the offering solely to cover over-allotments, if any.

The underwriter expects to deliver the shares on or about February           , 2023.

**EF HUTTON**

division of Benchmark Investments, LLC

The date of this prospectus is           , 2023

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

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Neither we nor the underwriter have authorized anyone to provide you with information other than that contained in this prospectus or any free writing prospectus prepared by or on our behalf or to which we have referred you. We and the underwriter take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriter are offering to sell, and seeking offers to buy, securities only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date on the front cover page of this prospectus, or other earlier date stated in this prospectus, regardless of the time of delivery of this prospectus or of any sale of our securities. Our business, financial condition, results of operations and future prospects may have changed since that date.

No action is being taken in any jurisdiction outside the United States to permit a public offering of our securities or possession or distribution of this prospectus in that jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus applicable to that jurisdiction.

We and the underwriter are offering to sell, and seeking offers to buy, our shares of common stock and pre-funded warrants only in jurisdictions where offers and sales are permitted. Neither we nor any of the underwriter have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of our shares of common stock and pre-funded warrants and the distribution of this prospectus outside of the United States.

## TRADEMARKS, SERVICE MARKS AND TRADE NAMES

We own, have applied for or have rights to use one or more registered and common law trademarks, service marks and/or trade names in connection with our business in the United States and/or in certain foreign jurisdictions.

This prospectus and our other public filings may contain trademarks, service marks and trade names of third-parties which are the property of their respective owners. Our use or display of third-parties' trademarks, service marks, trade names or products in this prospectus and our other public filings is not intended to, and does not imply a relationship with, or endorsement or sponsorship by us. Solely for convenience, the trademarks, service marks, logos and trade names referred to in this prospectus and our other public filings may appear without the ®, ™ or SM symbols, but the omission of such references is not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable owner of or licensor to these trademarks, service marks and trade names.

This prospectus contains additional trademarks, service marks and trade names of others, which are the property of their respective owners. All trademarks, service marks and trade names appearing in this prospectus are, to our knowledge, the property of their respective owners. We do not intend our use or display of other companies' trademarks, service marks, copyrights or trade names to imply a relationship with, or endorsement or sponsorship of us by, any other company.

On October 20, 2021, TransCode Therapeutics, Inc. applied to the United States Commissioner of Trademarks to register TRANSCODE THERAPEUTICS as a trademark under International Class 005, pharmaceutical preparations for the treatment of cancer, diagnostic preparations for medical purposes, having Serial Number 97/083236. For the purpose of this prospectus, TransCode Therapeutics® is referred to as TransCode. Additionally, "we", "our", "us" and "the company" will refer to TransCode.

## WHERE YOU CAN OBTAIN MORE INFORMATION

We have filed with the Securities and Exchange Commission, or SEC, a registration statement on Form S-1 under the Securities Act of 1933, as amended, or the Securities Act, with respect to the securities offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all the information set forth in the registration statement, some of which is contained in exhibits to the registration statement as permitted by the rules and regulations of the SEC. For further information with respect to us and our securities, we refer you to the registration statement, including the exhibits filed as a part of the registration statement of which this prospectus forms a part. Statements contained in this prospectus concerning the contents of any contract or any other documents are not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding issuers, like us, that file electronically with the SEC. The address of that website is [www.sec.gov](http://www.sec.gov).

We are subject to the information reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and we file reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address is [www.sec.gov](http://www.sec.gov). We also maintain a website at [www.transcodetherapeutics.com](http://www.transcodetherapeutics.com). You may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC.

Information contained in, or accessible through, our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is only as an inactive textual reference.

Our code of conduct, corporate governance guidelines and the charters of our Audit Committee, Compensation Committee and Nomination and Corporate Governance Committee are available through the “Governance” portion of our website.

## PROSPECTUS SUMMARY

**This summary highlights information contained elsewhere in this prospectus. This summary provides an overview of selected information and does not contain all of the information you should consider before investing in our securities. You should read the entire prospectus carefully, especially the “Risk Factors,” as well as “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements included in this prospectus, including the accompanying notes to those statements, before making an investment decision. If any of the risks materialize or other events or conditions arise that we cannot predict, our business, financial condition, operating results and prospects could be materially and adversely affected. As a result, the price of our common stock could decline, and you could lose part or all of your investment. Some of the statements in this prospectus constitute forward-looking statements that involve risks and uncertainties. See “Cautionary Note Regarding Forward-Looking Statements.” Our actual results could differ materially from those anticipated in such forward-looking statements as a result of certain factors, including those discussed in “Risk Factors” and other sections of this prospectus.**

### Overview

TransCode is an RNA oncology company created on the belief that cancer can be defeated through the intelligent design and effective delivery of RNA therapeutics. Our lead therapeutic candidate, TTX-MC138, targets microRNA-10b, or miRNA-10b, a master regulator of metastatic cell viability in a range of cancers, including breast, pancreatic, ovarian, colon cancer, glioblastomas, and several others. TransCode submitted to the U.S. Food and Drug Administration, or FDA, an exploratory investigational new drug application, or eIND, on November 30, 2022, to conduct a Phase 0 clinical trial intended to demonstrate quantitative delivery of TTX-MC138 to metastatic lesions in subjects with advanced solid tumors. In parallel, we are conducting investigational new drug, or IND, enabling studies with TTX-MC138 in support of our planned IND application for a Phase I/II clinical trial with TTX-MC138. On December 23, 2022, we received written authorization from the FDA allowing us to proceed with the Phase 0 trial.

Our other preclinical programs include two solid tumor programs, TTX-siPDL1, an siRNA-based modulator of programmed death-ligand 1, or PD-L1, and TTX-siLIN28B, an siRNA-based inhibitor of RNA-binding protein LIN28B. TransCode also has three cancer agnostic programs, TTX-RIGA, an RNA-based agonist of the retinoic acid-inducible gene I, or RIG-I, targeting activation of innate immunity in the tumor microenvironment; TTX-CRISPR, a CRISPR/Cas9-based therapy platform for the repair or elimination of cancer-causing genes inside tumor cells; and TTX-mRNA, an mRNA-based platform for the development of cancer vaccines that activate cytotoxic immune responses against tumor cells.

For decades, ribonucleic acid, or RNA, has been a topic of investigation by the scientific community as a potentially attractive therapeutic modality because it can target any gene and it lends itself to rational and straightforward drug design. RNA-based therapeutics are highly selective to their targets, potentially making available a broad array of previously undruggable targets in the human genome.

TransCode has created a design engine to customize the development of RNA therapeutics that is modular, both at the levels of the core nanoparticle and therapeutic loading. The size, charge, and surface chemistry of the core iron oxide nanoparticle can be tuned to optimize the particles for the intended genetic target and therapeutic load. The therapeutic load consisting of synthetic oligonucleotides can also be adapted to the specific approach being developed. The approach can range from RNA interference, RNAi, including small interfering RNAs, antisense oligonucleotides, and non-coding RNA mimics to mRNA-based cancer vaccines and CRISPR-based gene repair and replacement platforms as well as Pattern Recognition Receptors such as RIG-I. The platform can further be used for developing RNA-targeted radiolabeled therapeutics and diagnostics and other custom products targeting known and novel biomarkers and other genetic elements as they are discovered and validated. The TTX platform, which is described below in more detail, is intended to overcome delivery issues of stability, efficiency, and immunogenicity faced by existing lipid and liposomal nanoparticle platforms while optimizing targeting of and accumulation in tumor cells and metastatic sites.

The ability to deliver RNA therapeutics inside tumors and metastases gives us the potential to target genes of importance for cancer treatment that have remained undruggable up until now using an RNA approach.

### *Delivery System*

The therapeutic potential of RNA in oncology remains an unrealized promise due to the difficulty in safely and effectively delivering oligonucleotides to tumors. TransCode believes it is now closer to solving this challenge by means of a proprietary oligonucleotide delivery platform, our TTX platform, which leverages an iron oxide nanoparticle, approved for clinical use as a cancer imaging agent and in treating iron deficiency anemia, as the physical carrier.

Due to its small size, the TTX delivery system is expected to minimize early kidney and liver clearance, translating into a long circulation half-life that allows for efficient accumulation in tumor cells and metastatic sites. Nanoparticles similar in formulation to ours have an excellent clinical safety record of low toxicity and immunogenicity, and their built-in imaging capabilities have the bonus of enabling quantification of the particles' delivery to target organs. The nanoparticles are functionalized with amino groups to provide stable links through disulfide bonds to the therapeutic oligonucleotides of interest. The nanoparticles are coated with dextran, a glucose polymer, to protect the oligonucleotides from degradation and to provide overall stability to the particle.

The small hydrodynamic size and the charge of the resulting nanoparticles should allow them to infiltrate the tumor microvasculature, extravasate into the interstitium of tumors and metastases, and be readily taken up by tumor cells. The physicochemical properties of the nanoparticles are expected to further facilitate their rapid uptake by tumor cells by exploiting the high metabolic activity of cancer cells, a process analogous to the mechanism behind the systemic loading of metastatic cancer cells with fluorodeoxyglucose for diagnostic Positron Emission Tomography. The combined result of a hydrodynamically-favored distribution and a metabolically triggered uptake should result in the enhanced ability of TransCode's nanoparticles to access genetic targets inside tumor cells.

The Lancet Oncology Commission on Medical Imaging and Nuclear Medicine published an assessment of imaging and nuclear medicine resources, finding that scale-up of imaging, treatment and care would avert 9.5 million deaths in 11 million cancers globally (Lancet Oncol. 2021 April; 22(4), 136-172). It has been estimated by Guggenheim Securities in a 2022 report that targeted radiopharmaceuticals will grow to a \$22 billion global opportunity by 2026.

The intended therapeutic use of TransCode's TTX delivery system is based in part on the repurposing of the clinically validated imaging agents iron-oxide nanoparticles (combidex) and glucose (fluorodeoxyglucose), and now radiation. The concept of nuclear medicine has an 80-year clinical history, starting with Phosphorus-32 for leukemia in 1941. Exemplified by the recent filing of U.S. provisional application 63/356,449, TransCode has initiated research and development efforts designed to introduce radiotherapy into the delivery of TTX-carrying RNA therapeutic payloads. Two of TransCode's programs TTX-MC138 and TTX-RIGA are being investigated for radio integration in either a systemically or locally delivered manner for both the treatment and diagnosis of solid tumors.

### *Our Lead Therapeutic Candidate*

Our scientific co-founders developed TransCode's initial therapeutic candidate at The General Hospital Corporation, d/b/a Massachusetts General Hospital, or MGH, to target microRNA-10b, a well-validated biomarker linked to metastatic cancer. In contrast, most anti-cancer therapies target primary tumors and do not address metastatic disease specifically. MicroRNA-10b has been shown to be the master regulator of metastatic disease in multiple tumor types. Effective therapeutics have not been developed targeting microRNA-10b because of challenges in delivering therapeutics to tumors despite microRNA-10b's strong association with cancer metastasis, as documented in over 200 peer-reviewed scientific publications over the last ten years.

TTX-MC138 comprises proprietary iron-oxide nanoparticles and oligonucleotides which are synthetic LNA/DNA molecules that specifically target microRNA-10b, a regulatory RNA. The nanoparticles serve as a vehicle to deliver oligonucleotides to metastatic tumor cells. The magnetic properties of these nanoparticles allow for monitoring of their delivery using non-invasive imaging, which we believe adds value for clinical implementation of this therapeutic approach.

## Preclinical Study Results

Our scientific co-founders conducted a variety of preclinical animal studies involving human metastatic breast cancer models. In these studies, TTX-MC138 was successfully delivered to existing metastatic lesions in the lymph nodes, lungs, and bones as shown by non-invasive imaging performed 24 hours after injection. In five separate studies involving over 125 mice, TTX-MC138 was injected into mice in which human models of metastatic breast cancer tumors had been implanted. These mouse models included the rodent 4T1-luc2 orthotopic allograft, which is a very aggressive model of stage IV metastatic breast cancer, the human MDA-MB-231-luc-D3H2LN xenograft, which is a stage II/III cancer model, and the human MDA-MB-231-BrM2-831 xenograft, which is a model of breast cancer metastatic to the brain. Tumors in mice implanted with MDA-MB-231 cells typically progress from localized disease to lymph node metastases within 21 days of implantation. Tumors in mice implanted with 4T1-luc2 cells typically progress to distant sites in the animals within 10 days of implantation.

To test TTX-MC138 in the model of lymph node metastatic breast cancer, mice had their primary tumors surgically removed four to five weeks after tumor inoculation, following confirmation of lymph node metastases via imaging. This was done to better simulate a clinical scenario, since the current standard of care involves surgical removal of the primary tumor in patients with lymph node metastatic breast cancer. Treatment with TTX-MC138 was then initiated during the week of tumor removal. Because tumors in mice replicate more rapidly than is typical in humans, we combined low-dose doxorubicin with the TTX-MC138 because doxorubicin slows metastatic cell replication specific to these tumor models. Doing so allowed the TTX-MC138 to reach and inhibit the targeted RNA (miR-10b) inside the tumor cells more efficiently.

After four weeks of therapy, metastases in mice treated with TTX-MC138 regressed. By contrast, in the control groups, there was metastatic progression (Within-Subjects ANOVA:  $p < 0.05$ ). Treatment was discontinued once complete metastatic regression was observed. By the end of the study at 12 weeks, there was no recurrence and 100% survival in treated subjects having this cancer model.

In similar studies involving mice implanted with 4T1-luc2 breast tumors, we observed regression of distant metastases by week six, at which point treatment was stopped (Within-Subjects ANOVA:  $p < 0.05$ ). Despite stopping treatment, the animals remained metastasis-free and by the end of the study, no recurrence of disease had been observed. There was evidence of complete regression without recurrence in 65% of treated subjects while 35% progressed due to insufficient inhibition of miR-10b in this group. We believe this was due to the high rate of tumor cell replication in this model resulting in dilution of the therapeutic. We do not expect this to be the case in humans with metastatic disease, in whom tumor cell replication is dramatically slower than in mice.

### Positive Preclinical Results with TTX-MC138 in Pancreatic Adenocarcinoma

We recently evaluated the efficacy of TTX-MC138 applied as monotherapy in a murine model of pancreatic adenocarcinoma. In this study, we treated mice bearing human pancreatic tumors implanted in their pancreata with TTX-MC138 once weekly for eight weeks. The candidate demonstrated a pharmacodynamic response by successfully inhibiting its target, microRNA-10b (miR-10b). Serum miR-10b was down-regulated by TTX-MC138 and was shown to be a potential surrogate biomarker of therapeutic efficacy, opening up the possibility of noninvasive monitoring of therapeutic response in human patients. Forty percent (40%) of animals treated with TTX-MC138 had complete responses, defined as complete regression of disease and long-term survival without recurrence.

These new findings expand the potential therapeutic relevance of TTX-MC138 beyond breast cancer, in which activity had previously been shown in preclinical studies, to include pancreatic adenocarcinoma. However, there is no assurance that these preclinical results will be duplicated in further preclinical studies or in cancer patients suffering from pancreatic cancer.



## Planned Clinical Trials

We submitted an eIND application to the FDA on November 30, 2022, to conduct a First-in-Human, or FIH, clinical trial with TTX-MC138-NODAGA-Cu<sup>64</sup> and received written authorization from the agency on December 23, 2022, allowing us to proceed with the clinical trial. This FIH, Phase 0, clinical trial involves injecting a single microdose of radiolabeled TTX-MC138, termed TTX-MC138-NODAGA-Cu<sup>64</sup>, into subjects with advanced solid tumors. Injections are to be followed by imaging using integrated positron emission tomography-magnetic resonance imaging, or PET- MRI. The Phase 0 trial is intended to quantify the amount of radiolabeled TTX-MC138 delivered to metastatic lesions and the pharmacokinetics and biodistribution of the therapeutic candidate in cancer patients. The Phase 0 trial could yield critical data regarding therapeutic dose, timing, and potential safety that could inform our later clinical trials. We believe that demonstrating our ability to overcome the challenge of RNA delivery to genetic targets outside the liver, and specifically to tumors and metastases, would represent a major step forward in unlocking therapeutic access to genetic targets involved in a range of cancers. Assuming the completion of this offering and approval by the institution's institutional review board, or IRB, we expect to commence enrollment of the Phase 0 trial during the first half of 2023 and we expect to announce preliminary, topline data from this trial as soon as practical thereafter. Concurrent with the Phase 0 trial, we expect to continue additional IND-enabling studies to support filing an IND for a Phase I/II clinical trial with TTX-MC138.

## Modular Design Toolbox

We employ a design engine to enable development of therapeutic candidates that we believe can be efficiently delivered to genetic targets inside tumor cells. This approach is based on four complementary elements that together address the challenges of RNA drug development in oncology:

**Genetic Code** — Our approach to drug development takes advantage of our rapidly expanding knowledge about the human genome and the annotation of the genome — the knowledge about what different genes are responsible for especially in cancer. Armed with this knowledge, we can take advantage of the coded nature of the genome to design specific oligos that correspond to genetic targets of interest. Once we determine the code of the cancer target, we can develop therapeutic candidates using specific oligos that are harmonized to that target and potentially rewrite the story on cancer. This is what TransCode means — to change the code. After determining the genetic target of interest, we may be able to choose from a variety of RNA approaches best suited for that target. Those approaches will likely range from RNAi, which include siRNAs, antisense oligonucleotides, and non-coding RNA mimics; messenger RNA-based cancer vaccines; CRISPR-based gene repair and replacement platforms; or Pattern Recognition Receptors like RIG-I.

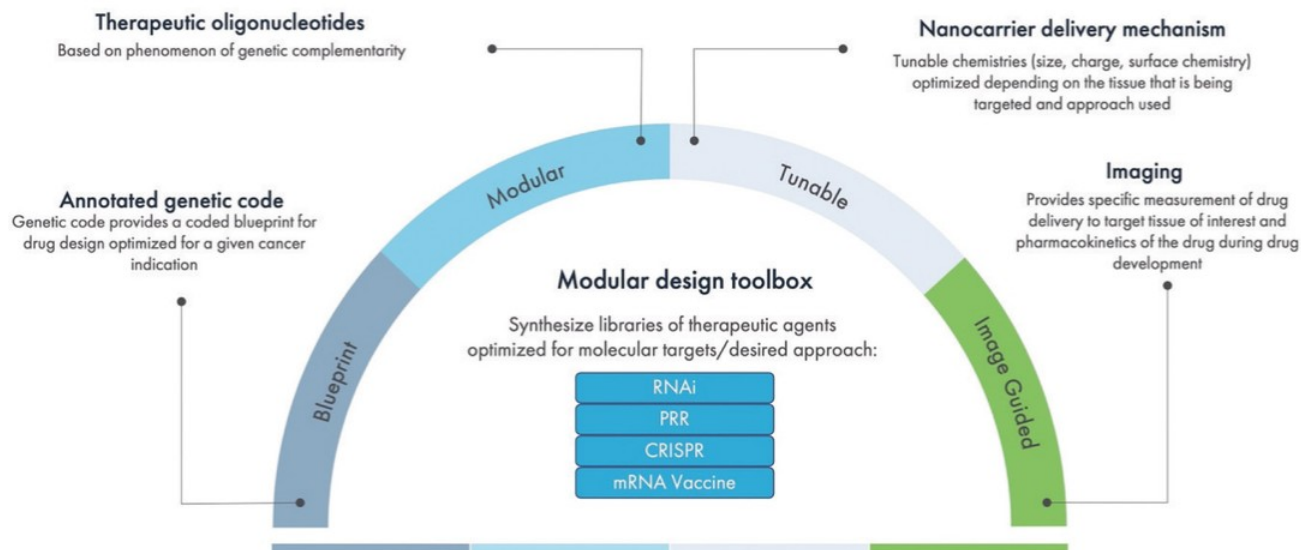
**Modular Design for Therapeutic Development** — Our discovery platform consists of a modular 'toolbox' for developing therapeutic candidates designed to attack specific disease-causing RNA targets based on the phenomenon of genetic complementarity. These therapeutic candidates incorporate synthetic oligonucleotides, or oligos, that can be designed as antagomirs, mimics, miRNA sponges, siRNA duplexes, ribozymes, and others depending on the desired therapeutic strategy. In addition to the varied oligo design approach, we can also synthesize nanocarriers with tunable chemistry properties. Combined, the modularity and tunability of these oligonucleotides and nanocarrier components may enable the potential to synthesize libraries of therapeutic agents designed for a given indication or a given patient in terms of therapeutic oligonucleotide design, size, surface coating and charge, hydrophilicity and hydrophobicity, and antigen- targeting through incorporation of targeting peptides.

**Nanocarrier Delivery Mechanism** — Our strategy seeks to leverage a nanoparticle that has been extensively used in humans for imaging by repurposing it to deliver oligonucleotides to cancer cells. The nanocarrier is tunable to pre-designed specifications to deliver therapeutic oligonucleotides to an RNA target in tumors and metastases without compromising its integrity. These nanocarriers differentiate us from competitive delivery approaches, many of which rely on lipid particles or chemical structures, such as GalNAc. Competitive delivery approaches effectively target sites in the liver but not sites in tumors and metastases. Our nanocarrier is derived from, and is chemically similar to, nanoparticles extensively used in imaging (Feridex, from Advanced Magnetics) or for treating iron deficiency anemia (Feraheme, also from Advanced Magnetics).

We believe that our competitive advantages include effectively reaching tumors and metastases, achieving robust target engagement in tumor cells, and an anticipated wide therapeutic window based on prior experience in preclinical models and clinical experience of others with similar iron oxide nanoparticles.

**Image Guided** — Because our therapeutic candidates are innately detectable using non-invasive imaging, we can monitor their delivery to the tissue of interest and measure their bioavailability. The ability to monitor delivery using Magnetic Resonance Imaging, or MRI, can be instrumental in assessing and controlling the amount of oligonucleotide that reaches the targeted tissues. MRI use during the design phase of the therapeutic candidate could guide drug design, delivery schedule, route, and dose and could suggest alternatives should treatment with the therapeutic candidate fail in a given patient. This is critical during drug development because it should allow us to optimize drug design to maximize therapeutic effect.

The following graphic summarizes our modular design approach:



## Recent Developments

### NIH SBIR Award

On May 26, 2022, we received a Notice of Award from the National Institutes of Health confirming the availability of the second tranche of funding under the award we received in April 2021. The award is for a total of approximately \$2.3 million; we received approximately \$309 thousand in the first tranche and have been authorized to withdraw approximately \$1.1 million in the second tranche. The balance of the award is expected to be available in 2023. There is no guarantee that funds awarded for the third year of the SBIR grant will be received or not reduced in the sole discretion of the funding agency.

### TTX-MC138 eIND-enabling studies

We completed our TTX-MC138 eIND-enabling studies, scale-up and analytical work with the TTX- MC138-NODAGA precursor to be radiolabeled with  $\text{Cu}^{64}$  for detection by PET-MRI. Final chemistry, manufacturing and controls, or CMC, development of the radiolabeled TTX-MC138-NODAGA- $\text{Cu}^{64}$  and a nonhuman primate dosimetry study were also completed. The results of these activities were incorporated in our eIND application, which we submitted to the FDA on November 30, 2022. We subsequently received written authorization from the agency on December 23, 2022, allowing us to proceed with the clinical trial.

### TTX-MC138 IND-enabling studies

As discussed above, in addition to conducting eIND-enabling studies for our planned Phase 0 clinical trial with TTX-MC138, we are also preparing for and conducting IND-enabling studies for TTX-MC138. Upon completion of these studies and our FDA briefing book, we plan to file an IND with FDA as soon as practical to conduct a Phase 1 clinical trial with TTX-MC138.

### *MDACC Alliance Program*

On July 22, 2022, we were chosen as a strategic research alliance partner by MD Anderson Cancer Center, a world-leading cancer research center, to advance preclinical and clinical development of our RNA therapeutic candidates for oncology applications. Leading the collaboration for MD Anderson are George Calin, MD, PhD, Professor in the Department of Translational Molecular Pathology of Pathology/Lab Medicine, and Co-Director, The RNA Interference and non-coding RNA Center, and a member of our Science Advisory Board, and Vivek Subbiah, MD, Medical Director of the Clinical Center for Targeted Therapy. We believe that being chosen as a strategic research alliance partner by MD Anderson to advance the clinical development of RNA therapeutics is an important step forward for our oncology programs.

Under the five-year strategic collaboration agreement with MD Anderson, we have committed to fund up to \$10 million over the term of the collaboration, with \$500,000 of such amount payable within the first year. Subsequent payments are \$2 million on the first anniversary of the effective date of the agreement and \$2.5 million on each of the second, third and fourth anniversaries thereof. This funding is in line with amounts already budgeted for preclinical and clinical development, so does not represent additional spending.

The alliance is expected to result in applied research regarding the role of regulatory RNAs in cancer, and the results then translated into the identification of biomarkers and the development of a clinical pathway to serve as a foundation for Phase I/II clinical trials and beyond.

### *Case Study*

To test the applicability of our therapeutic strategy in a larger animal, our scientific co-founders conducted a case study with a feline that had developed spontaneous mammary carcinoma, or FMC, the third most common cancer in cats and highly metastatic. FMC has high resemblance to human breast cancer compared to mammary carcinomas of other companion animals in terms of relative age at onset, incidence, risk factors, prognostic aspects, histopathology, biological behavior, metastatic pattern and response to therapy.

In the case study, a feline patient that previously had failed multiple rounds of standard-of-care treatment for advanced metastatic FMC and was at the end of its life expectancy, was dosed with TTX-MC138. Delivery of TTX-MC138 to the metastatic lesions was demonstrated using noninvasive magnetic resonance imaging, or MRI. Dosing with TTX-MC138 resulted in durable inhibition of the miR-10b target and induction of the downstream metastasis suppressor, HOXD10, lasting as long as three months after injection. The patient tolerated the injection well with no adverse effects and vital signs remained within the normal range.

Additionally, seven weeks after the first dose, the feline patient was dosed a second time and tolerated the injection well.

The patient survived for approximately five months compared to its life expectancy prior to dosing. Notwithstanding the need for additional therapeutic and toxicology studies, we believe that in combination with our other preclinical findings, this case study suggests the robustness and tolerability of a novel first-in-class therapeutic approach.

### *Positive Preclinical Results with TTX-MC138 in Pancreatic Adenocarcinoma*

We recently evaluated the efficacy of TTX-MC138 applied as monotherapy in a murine model of pancreatic adenocarcinoma. In this study, we treated mice bearing human pancreatic tumors implanted in their pancreata with TTX-MC138 once weekly for eight weeks. The candidate demonstrated a pharmacodynamic response by successfully inhibiting its target, microRNA-10b (miR-10b). Serum miR-10b was down-regulated by TTX-MC138 and was shown to be a potential surrogate biomarker of therapeutic efficacy, opening up the possibility of noninvasive monitoring of therapeutic response in human patients. Forty percent (40%) of animals treated with TTX-MC138 had complete responses, defined as complete regression of disease and long-term survival without recurrence.

These new findings expand the potential therapeutic relevance of TTX-MC138 beyond breast cancer, in which activity had previously been shown in preclinical studies, to include pancreatic adenocarcinoma. However, there is no assurance that these preclinical results will be duplicated in further preclinical studies or in cancer patients suffering from pancreatic cancer.

### *Orphan Drug Designation*

In June 2022, we received Orphan Drug Designation from the FDA for our magnetic nanocarrier- conjugated small interfering RNA against PD-L1 for treatment of pancreatic cancer. The designation was granted based on positive results achieved in *in vivo* studies treating human pancreatic tumors implanted in animals. We recently conducted preclinical *in vivo* studies with TTX-MC138 in a pancreatic cancer model and submitted data to the FDA requesting orphan drug designation status on December 5, 2022. We intend to conduct additional *in vivo* studies to support filings of other TTX-based therapeutic candidates in other orphan disease indications including osteosarcoma, glioblastoma, and small cell lung cancer. There is no assurance that we will receive any additional designations.

### *Recent Publications*

In collaboration with scientists from MGH, Harvard Medical School and Michigan State University, we have published three manuscripts as listed below. The publication by Smith et al. reviews recent progress towards translating short non-coding RNAs into the clinic. The manuscript by Le Fur et al. describes a method for radiolabeling our lead therapeutic candidate, TTX-MC138, and employing PET-MRI to assess the tissue biodistribution of the therapeutic candidate. This manuscript serves as the basis for our eIND study. The publication by Chen et al. reviews key microRNA targets, including miR-10b in glioblastoma.

*Clinical Applications of Short Non-Coding RNA-Based Therapies in the Era of Precision Medicine. Smith ES, Whitty E, Yoo B, Moore A, Sempere LF, Medarova Z. Cancers (Basel). 2022 Mar 21;14(6):1588.*

*Radiolabeling and PET-MRI microdosing of the experimental cancer therapeutic, MN-anti-miR10b, demonstrates delivery to metastatic lesions in a murine model of metastatic breast cancer. Le Fur M, Ross A, Pantazopoulos P, Rotile N, Zhou I, Caravan P, Medarova Z, Yoo B. Cancer Nanotechnol. 2021;12(1):16.*

*Role of microRNAs in glioblastoma.*

*Chen M, Medarova Z, Moore A. Oncotarget. 2021 Aug 17;12(17):1707-1723.*

In addition to these three publications and the Case Study described above which was published in *Frontiers in Oncology*, we have submitted a manuscript describing the feasibility of our RIG-I targeting approach using our TTX-RIGA candidate. This manuscript was recently published in BioRxiv.

### *New Patent Applications*

TransCode filed provisional application 63/356,449 on June 28, 2022. This filing discloses the use of nucleic acid-based agonists of RIG-I singly or in combination with a radiolabeled nanoparticle for activation of the immune system that we anticipate will lead to tumor cell death. This technology potentially enables development of therapeutic candidates to treat advanced cancer patients and may have applicability outside of oncology in immune-related indications such as infectious disease.

### *Licensing Option*

On May 9, 2022, TransCode executed an option agreement with MGH giving TransCode the right to negotiate an exclusive, worldwide, royalty-bearing license related to a radiotheranostic technology disclosed in patent application PCT/US2021/057912 entitled THERAPEUTIC, RADIOLABLED NANOPARTICLES AND METHODS OF USE THEREOF.

### **Preliminary Financial Information**

We had cash of approximately \$5.0 million, as of December 31, 2022. However, this estimate is preliminary and subject to the completion of our financial statements as of and for the year ended December 31, 2022. The actual amount that we report will be subject to the completion of our financial closing procedures and any final adjustments that may be made prior to the time our results for the year ended December 31, 2022, are finalized and filed with the SEC. Our independent registered public accounting firm has not audited, reviewed, compiled, or performed any procedures with respect to our cash and, accordingly, does not express an opinion or any other form of assurance on it. This estimate should not be viewed as a substitute for financial statements prepared in accordance

with accounting principles generally accepted in the United States and is not necessarily indicative of the results to be achieved in any future period. We assume no duty to update this preliminary estimate except as required by law.

### **Summary of Risks**

Our business is subject to numerous material and other risks and uncertainties that you should be aware of in evaluating our business. These risks are described more fully elsewhere in this prospectus, including in the section entitled “*Risk Factors*”, and include, but are not limited to, the following:

- Our independent public accounting firm has expressed substantial doubt about our ability to continue as a going concern.
- We have incurred significant losses since inception, and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future.
- We have never generated any revenue from product sales and may never be profitable.
- We will need to raise substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, scale back or discontinue some of our therapeutic candidate development programs or commercialization efforts.
- The amount of our future losses is uncertain, and our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.
- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- Because our therapeutic candidates are in an early stage of development, there is a high risk of failure, and we may never succeed in developing marketable products or generating product revenues.
- Our business is highly dependent on the success of TTX-MC138, our lead therapeutic candidate which is at the early stages of development. All of our therapeutic and diagnostic candidates require significant additional preclinical and clinical development before we may be able to seek regulatory approval for and launch a product commercially.
- Clinical development involves a lengthy, complex and expensive process, with an uncertain outcome, and the results of preclinical studies and early-stage clinical trials of our therapeutic candidates may not be predictive of the results of later-stage clinical trials.
- We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of TTX-MC138 or any of our other therapeutic candidates.
- Quality problems could delay or prevent delivery of our materials for clinical trials or to the market.
- Changes in methods of therapeutic candidate manufacturing or formulation may result in additional costs or delays.
- If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- If product liability lawsuits are brought against us, we may incur substantial financial or other liabilities and may be required to limit commercialization of our therapeutic candidates.

- Our therapeutic candidates may cause undesirable side effects or death or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.
- We are very early in our development efforts. All of our therapeutic candidates are still in preclinical development. If we are unable to advance our therapeutic candidates to clinical development, obtain regulatory approval and ultimately commercialize our therapeutic candidates or experience significant delays in doing so, our business will be materially harmed.
- Even if we receive regulatory approval of TTX-MC138 or any of our other therapeutic candidates, we will be subject to ongoing regulatory requirements and continued regulatory review, which may result in significant additional expense. We may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our therapeutic candidates.
- We expect to rely on third-parties to manufacture and supply materials we require for research and development, preclinical studies and clinical trials which could result in supplies that are limited or interrupted or which may not be of satisfactory quantity or quality or other delays or disruptions.
- We rely on third-parties to conduct certain aspects of our preclinical studies and clinical trials. If these third-parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any therapeutic candidates.
- Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.
- We are subject to geopolitical risks, economic volatility, anti-corruption laws, export and import restrictions, local regulatory authorities and the laws and medical practices in foreign jurisdictions.
- Obtaining and maintaining regulatory approval for our therapeutic candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval for that or of any of our other therapeutic candidates in other jurisdictions.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- The global pandemic of the novel coronavirus disease, COVID-19, has, and may continue to, adversely impact our business, including our preclinical studies and clinical trials. Dislocations related to the pandemic and the development of vaccines and other treatments for COVID-19 has led to a shortage of animals available for preclinical toxicology and other forms of required testing which could cause delays to our IND-enabling studies or other required testing.
- Our future success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.
- The patents covering our lead therapeutic candidate, TTX-MC138, are currently issued only in the U.S. and there are no foreign applications pending for this invention at this time. We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.
- The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.
- We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

- Investors may incur dilution in the net tangible book value of the shares purchased in the offering, assuming no sale of any pre-funded warrants in lieu of common stock.
- We have identified material weaknesses in our internal control over financial reporting. If we are unable to remediate these material weaknesses, or if we identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business and the trading price of our common stock.
- We could lose our listing on the Nasdaq Capital Market if the closing bid price of our common stock does not return to above \$1.00 for ten consecutive days during the 180 days ending July 7, 2023. The loss of the Nasdaq listing would make our common stock significantly less liquid and would affect its value.

### **Corporate Information**

We were incorporated in the State of Delaware in January 2016. The address of our principal executive office is 6 Liberty Square, #2382, Boston, Massachusetts 02109; our telephone number is (857) 837-3099. Our website is [www.transcodetherapeutics.com](http://www.transcodetherapeutics.com). Information contained in, or that can be accessed through, our website is not incorporated by reference into this prospectus, and you should not consider information on our website to be part of this prospectus. Our design logo and our other registered and common law trade names, trademarks and service marks are the property of TransCode.

### **Implications of being an Emerging Growth Company and a Smaller Reporting Company**

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include those that allow us to:

- provide only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- make reduced disclosure about our executive compensation arrangements;
- hold no non-binding advisory votes on executive compensation or golden parachute arrangements; and
- exempt us from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.235 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the completion of our initial public offering (i.e., December 31, 2026); (iii) the date on which we have issued more than \$1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. Additionally, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, therefore, while we are an emerging growth company, and we will not be subject to new or revised accounting standards at the same time that they become applicable to other public companies that are not emerging growth companies.

We are also a “smaller reporting company” as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies (i) until the fiscal year following the determination that the market value of our voting and non-voting common stock held by non-affiliates is more than \$250 million measured on the last business day of our second fiscal quarter, or (ii) if our annual revenues are less than \$100 million during the most recently completed fiscal year, until the fiscal year following the determination that the market value of our voting and non-voting common stock held by non-affiliates is more than \$700 million measured on the last business day of our second fiscal quarter.



## THE OFFERING

Common Stock offered by us	12,000,000 shares of our common stock (13,800,000 shares if the underwriter exercises its over-allotment option in full).
Pre-funded warrants offered by us	<p>We are also offering to those purchasers, if any, whose purchase of the common stock in this offering would result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% (or at the election of the purchaser, 9.99%) of our outstanding common stock immediately following the consummation of this offering, the opportunity to purchase, if they so choose, pre-funded warrants in lieu of the common stock that would otherwise result in ownership in excess of 4.99% (or 9.99%, as applicable) of our outstanding common stock.</p> <p>The purchase price of each pre-funded warrants will equal the price per share of common stock being sold to the public in this offering, minus \$0.01, and the exercise price of each pre-funded warrant will be \$0.01 per share.</p> <p>For each pre-funded warrant we sell, the number of shares of common stock we are offering will be decreased on a one-for-one basis.</p> <p>Each pre-funded warrant will be immediately exercisable and may be exercised at any time, subject to ownership limitations. The pre-funded warrants do not expire. To better understand the terms of the pre-funded warrants, you should carefully read the “Description of Capital Stock” section of this prospectus. You should also read the form of pre-funded warrant, which is filed as an exhibit to the registration statement that includes this prospectus.</p>
Common Stock to be outstanding after this offering <sup>(1)</sup>	24,977,234 shares of common stock (26,777,234 shares if the underwriter exercises its over-allotment option in full), assuming no sale of any pre-funded warrants. To the extent pre-funded warrants are sold, the number of shares of common stock sold in this offering will be reduced on a one-for-one basis.
Over-Allotment Option	<p>The underwriter has an option for a period of 45 days to purchase up to 1,800,000 additional shares of our common stock and/or pre-funded warrants to cover over-allotments, if any.</p> <p>The purchase price to be paid by the underwriter per additional share of common stock or pre-funded warrant shall be equal to the public offering price of one share of common stock or pre-funded warrant, as applicable, less the underwriting discount.</p>
Use of Proceeds	We intend to use the net proceeds of this offering (i) to fund one or more clinical trials of TTX-MC138, our lead therapeutic candidate, including related IND enabling studies; (ii) to fund further research and development of our other therapeutic candidates; and (iii) for working capital and general corporate purposes. See “ <i>Use of Proceeds</i> ” for more information.

Nasdaq Capital Market Symbol

RNAZ

We do not intend to apply to list the pre-funded warrants on any national securities exchange or other trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited.

Lock-up Agreements

The company and our directors, officers and certain of our stockholders have agreed with the underwriter, subject to certain exceptions, not to sell, transfer or dispose of, directly or indirectly, any of our common stock or securities convertible into or exercisable or exchangeable for our common stock for a period of 90 days with respect to the company, and for a period of 180 days with respect to our directors, officers and certain of our stockholders after the date of this prospectus. See “*Underwriting*” for more information.

Risk Factors

Investing in our securities involves a high degree of risk. See “*Risk Factors*” beginning on page 15 for important information.

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(1) The number of shares of common stock to be outstanding after the offering is based on 12,977,234 shares of common stock outstanding as of December 31, 2022, and excludes, as of that date, the following:

- 3,017,033 shares of common stock issuable upon exercise of outstanding stock options at a weighted average exercise price of \$0.74 per share;
- 312,500 shares of common stock issuable upon the exercise of outstanding common stock purchase warrants at an exercise price of \$5.00 per share;
- 2,450,351 shares of common stock reserved for future issuance under our 2021 Stock Option and Equity Incentive Plan, or the 2021 Plan; and
- 330,000 shares of common stock reserved for future issuance under our 2021 Employee Stock Purchase Plan, or our 2021 ESPP.

Except as otherwise indicated herein, all information in this prospectus assumes the following:

- no exercise by the underwriter of the over-allotment option to purchase additional shares (or pre-funded warrants in lieu thereof);
- no exercise of outstanding options or warrants; and
- no sale of any pre-funded warrants in lieu of common stock in this offering.

## SUMMARY FINANCIAL DATA

You should read the following summary financial data together with the section entitled “*Management’s Discussion and Analysis of Financial Condition and Results of Operations*” and our financial statements and related notes for the year ended December 31, 2021, and for the quarter ended September 30, 2022 appearing elsewhere in this prospectus. The following summary statement of operations data for the years ended December 31, 2021 and 2020, are derived from our audited financial statements appearing elsewhere in this prospectus. We have derived the summary statements of operations data for the nine months ended September 30, 2022 and 2021, and balance sheet data as of September 30, 2022, from our unaudited interim financial statements appearing elsewhere in this prospectus. We have prepared the unaudited interim financial statements on the same basis as the audited financial statements and have included all adjustments, consisting only of normal recurring adjustments that, in management’s opinion, are necessary to state fairly the information set forth in those financial statements. Our historical results are not necessarily indicative of the results that may be expected in the future and our results for the nine months ended September 30, 2022, are not necessarily indicative of the results that may be expected for the full year ending December 31, 2022, or any other period. The summary financial data in this section are not intended to replace our financial statements and related notes and are qualified in their entirety by the financial statements and related notes included elsewhere in this prospectus.

	<u>Nine Months Ended September 30,</u>		<u>Years Ended December 31,</u>	
	<u>2022</u>	<u>2021</u>	<u>2021</u>	<u>2020</u>
<b>Unaudited</b>				
<b>Statement of Operations Data</b>				
Operating expenses				
Research and development	\$ 7,545,628	\$ 1,468,457	\$ 2,753,966	\$ 284,459
General and administrative	5,592,727	1,696,444	3,397,169	442,145
Total operating expenses	<u>13,138,355</u>	<u>3,164,901</u>	<u>6,151,135</u>	<u>726,604</u>
Operating loss	(13,138,355)	(3,164,901)	(6,151,135)	(726,604)
Other income (expense)				
Change in fair value of derivative liabilities	—	(867,000)	(867,000)	(1,208,000)
Change in fair value of warranty liability	—	(6,109)	(6,109)	(14,852)
Grant income	696,669	88,786	278,333	—
Loss on sale of equipment	—	—	(3,082)	—
Interest expense	—	(95,070)	(95,070)	(394,573)
Interest income	10,774	154	664	136
Total other income (expense)	<u>707,443</u>	<u>(879,239)</u>	<u>(692,264)</u>	<u>(1,617,289)</u>
Loss before income taxes	(12,430,912)	(4,044,140)	(6,843,399)	(2,343,893)
Income tax expense (benefit)	—	—	—	—
Net loss	<u>\$ (12,430,912)</u>	<u>\$ (4,044,140)</u>	<u>\$ (6,843,399)</u>	<u>\$ (2,343,893)</u>
Basic and diluted loss per common share <sup>(1)</sup>	<u>\$ (0.96)</u>	<u>\$ (0.58)</u>	<u>\$ (0.81)</u>	<u>\$ (0.51)</u>
Weighted average number of common shares outstanding, basic and diluted <sup>(1)</sup>	<u>12,977,234</u>	<u>6,932,982</u>	<u>8,425,880</u>	<u>4,636,216</u>
<b>Unaudited</b>				
<b>Balance Sheet Data</b>				
Current assets	\$ 11,569,885	\$ 22,732,175	\$ 831,215	
Total assets	12,015,573	22,938,443	1,055,368	
Current liabilities	3,771,376	2,534,097	404,862	
Total liabilities	3,771,376	2,534,097	4,463,600	
Total stockholders’ equity (deficit)	8,244,197	20,404,346	(3,408,232)	

(1) See note 13 to our audited financial statements and our unaudited interim financial statements for further details on the calculation of basic and diluted net loss per common share.

## RISK FACTORS

*Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below, as well as the other information in this prospectus. Our business, prospects, financial condition, or operating results could be harmed by any of these risks, as well as other risks not currently known to us or that we currently consider immaterial. If any such risks or uncertainties actually occur, our business, prospects, financial condition or operating results could differ materially from the plans, projections and other forward-looking statements included in the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” The trading price of our common stock could decline significantly due to any of these risks or other factors, and as a result, you may lose all or part of your investment.*

### **Risks related to our financial position and need for additional capital**

***Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern.***

As of December 31, 2022, we had estimated cash totaling approximately \$5.0 million. We do not believe that our cash as of December 31, 2022, will enable us to fund our operating expenses and capital requirements beyond the first quarter of 2023. We will need to raise additional capital to continue as a going concern. Our recurring losses from operations and negative cash flow raise substantial doubt about our ability to continue as a going concern without sufficient capital resources. Our independent registered public accounting firm included an explanatory paragraph in its report on our financial statements for the years ended December 31, 2021, and 2020, with respect to this uncertainty. Our ability to continue as a going concern is dependent on both our available cash and how well we manage that cash and our operating requirements. We believe that the net proceeds from this offering, together with our existing cash and funds we expect to receive under our SBIR award, will be sufficient to fund our current operating plans into the third quarter 2023. We have based these estimates, however, on assumptions that may prove to be wrong, and we could spend our available financial resources much faster than we currently expect and need to raise additional funds sooner than we anticipate. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our research and development programs and commercialization efforts.

***We have incurred significant losses since inception, and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future.***

Investment in oncology product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risk that any potential therapeutic candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval or become commercially viable. We are still in the early stages of development of our therapeutic candidates. Our lead therapeutic candidate, TTX-MC138, has not yet entered clinical trials. We submitted to FDA an eIND application on November 30, 2022, to conduct a First-in-Human clinical trial with TTX-MC138-NODAGA-Cu<sup>64</sup> and received written authorization from the agency on December 23, 2022, allowing us to proceed with the clinical trial. We intend to initiate a Phase 0 trial in up to 12 cancer patients with advanced solid tumors after approval by the IRB, where we expect to conduct the trial. We expect IRB approval in the first half of 2023. We have no products licensed for commercial sale and have not generated any revenue from product sales or otherwise to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. We finance our current operations with funds obtained primarily through our initial public offering and from our SBIR Award.

We have incurred significant annual net losses in each period since inception. For the years ended December 31, 2021, and 2020, our net losses were approximately \$6.8 million and approximately \$2.3 million, respectively. As of September 30, 2022, our accumulated deficit was approximately \$22.7 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if and as we:

- conduct preclinical studies and clinical trials for our current and future therapeutic candidates;
- continue our research and development efforts and submit INDs for future therapeutic candidates;
- seek marketing approvals for any therapeutic candidates that successfully complete clinical trials;

- build infrastructure to support sales and marketing for any approved therapeutic candidates;
- scale up external manufacturing and distribution capabilities for clinical and, if approved, commercial supply of our therapeutic candidates;
- expand, maintain and attempt to protect our intellectual property portfolio;
- hire additional clinical, regulatory, scientific and other personnel; and
- operate as a public company.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even if we succeed in eventually commercializing one or more of our therapeutic candidates, we will continue to incur substantial research and development and other expenditures to develop, seek approval for, and market therapeutic candidates. We may never succeed in these activities and, even if we succeed in commercializing one or more of our current therapeutic candidates and any future therapeutic candidates, we may never generate revenues that are significant or large enough to achieve profitability. In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on stockholders' equity (deficit).

***We have never generated any revenue from product sales and may never be profitable.***

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from any product sales. We have no products approved for commercial sale, and do not anticipate generating any revenue from product sales until after we have received marketing approval for the commercial sale of a therapeutic candidate, if ever. Our ability to generate revenue and achieve profitability depends significantly on our success in achieving a number of goals, including:

- initiating and completing research regarding preclinical and clinical development of, TTX-MC138 and any future therapeutic candidates;
- developing a sustainable and scalable manufacturing process for TTX-MC138 or our other therapeutic candidates and any future therapeutic candidates, including establishing and maintaining commercially viable supply and manufacturing relationships with third-parties;
- launching and commercializing TTX-MC138, our other therapeutic candidates and any future therapeutic candidates for which we obtain marketing approvals, either directly or with a collaborator or distributor;
- obtaining market acceptance of TTX-MC138, our other therapeutic candidates and any future therapeutic candidates as viable treatment options;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and developing new therapeutic candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- obtaining, maintaining, attempting protection of, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and

- attracting, hiring, and retaining qualified personnel.

Even if our current therapeutic candidates or any future therapeutic candidates that we develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any such therapeutic candidate. Our expenses could increase beyond expectations if we are required by the FDA or comparable foreign regulatory authorities to change our manufacturing processes or assays, or to perform clinical, nonclinical, or other types of studies in addition to those that we currently anticipate.

If we are successful in the future in obtaining regulatory approvals to market TTX-MC138 or any future therapeutic candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain marketing approval, the price for the product we obtain, the ability to obtain reimbursement at any price and whether we own the commercial rights for that territory. If the number of addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, the labels for our current therapeutic candidates and any future therapeutic candidates contain significant safety warnings, regulatory authorities impose burdensome or restrictive distribution requirements, or the reasonably accepted patient population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. If we are not able to generate sufficient revenue from the sale of any approved products, we could be prevented from or significantly delayed in achieving profitability.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our development efforts, obtain product approvals, diversify our product offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

***Even if we consummate this offering, we will need to raise substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, scale back or discontinue some of our therapeutic candidate development programs or commercialization efforts.***

The development of pharmaceutical drugs is capital intensive. We are currently advancing TTX-MC138 through preclinical development. Our current cash resources are insufficient to fund our planned operations or development plans beyond the first quarter of 2023. We may not be able to complete our planned FIH trial. If we are able to complete the trial, we may only be able to complete the trial in a small subset of patients and in only one tumor type. Even if completed, we will require additional funds to advance further. If we are capital constrained, we may not be able to meet our obligations. If we are unable to meet our obligations, or we experience a disruption in our cash flows, it could limit or halt our ability to continue to develop our therapeutic candidates or even to continue operations, either of which occurrence would have a material adverse effect on us.

We expect our expenses to continue to increase in connection with our ongoing activities, particularly as we continue the research and development of, advance the preclinical and clinical activities of, and seek marketing approval for, our current or future therapeutic candidates. In addition, if we obtain marketing approval for any of our current or future therapeutic candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution to the extent that such sales, marketing, product manufacturing and distribution are not the responsibility of our collaborators. We may also need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our current or future therapeutic candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we expect to continue to incur significant costs associated with operating as a public company. If we are unable to raise capital when needed, we would be forced to delay, scale back or discontinue the development and commercialization of one or more of our therapeutic candidates, delay our pursuit of potential licenses or acquisitions, or significantly reduce our operations.

We expect that the net proceeds from this offering, together with our existing cash and funds we expect to receive under our SBIR Award, will be sufficient to fund our operations into the third quarter 2023. Our future capital requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our current or future therapeutic candidates;

- the potential additional expenses attributable to adjusting our development plans (including any supply-related matters) to the COVID-19 pandemic;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our current or future therapeutic candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or are entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or license other current or future therapeutic candidates and technologies;
- the costs of securing manufacturing arrangements for commercial production; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our current or future therapeutic candidates.

Identifying potential current or future therapeutic candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, our current or future therapeutic candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to continue to rely on additional funding to achieve our business objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our current or future therapeutic candidates. Disruptions in the financial markets in general, and those due to the COVID-19 pandemic in particular, have made equity and debt financing more difficult to obtain and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms favorable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness could result in fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or current or future therapeutic candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly delay, scale back or discontinue one or more of our research or development programs or the commercialization of any therapeutic candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

***The amount of our future losses is uncertain, and our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.***

Our quarterly and annual operating results may fluctuate significantly in the future due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and success or failure of clinical trials for our therapeutic candidates or competing therapeutic candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- our ability to successfully recruit and retain subjects for clinical trials, and any delays caused by difficulties in such efforts;
- our ability to obtain marketing approval for our therapeutic candidates, and the timing and scope of any such approvals we may receive;
- the timing and cost of, and level of investment in, research and development activities relating to our therapeutic candidates, which may change from time to time;
- the cost of manufacturing our therapeutic candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- our ability to attract, hire and retain qualified personnel;
- expenditures that we will or may incur to develop additional therapeutic candidates;
- the level of demand for our therapeutic candidates should they receive approval, which may vary significantly;
- the risk/benefit profile, cost and reimbursement policies with respect to our therapeutic candidates, if approved, and existing and potential future therapeutics that compete with our therapeutic candidates;
- general market conditions or extraordinary external events, such as a recession or the COVID-19 pandemic;
- the changing and volatile U.S. and global economic environments; and
- future accounting pronouncements or changes in our accounting policies.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even if we meet any guidance we may have provided publicly previously.



## Risks related to research and development and the biopharmaceutical industry

***Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.***

We are an early, clinical-stage oncology company with a limited operating history. We commenced operations in 2016, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting limited discovery and research activities, filing patent applications, identifying potential therapeutic candidates, undertaking preclinical studies and preparing for clinical trials, and establishing arrangements with third-parties for the manufacture of initial quantities of our therapeutic candidates and component materials. Our lead therapeutic candidate, TTX-MC138, is currently in the early stages of development. We have not yet demonstrated our ability to successfully conduct or complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third-party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Investment in oncology product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risk that any potential therapeutic candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable.

We are unable to predict the full range of risks that may emerge, and we cannot guarantee that we will meet or achieve the clinical or commercial results we expect. The future of our business depends on us successfully developing, obtaining marketing approval for, and marketing profitably our therapeutic candidates. This requires many complex scientific activities, successful pursuit of regulatory approvals, appropriate market assessments, the strategic management of intellectual property and financial resources and effective management of many other aspects of our business. Products for which we receive regulatory approval must demonstrate safety and efficacy. Competitively, the products must improve patient outcomes, deliver benefits to intended customers, maintain an affordable price, and be superior to competitive products. To be successful, we must also be effective in driving awareness of our therapeutics to achieve market adoption for our approved products and to be profitable. The risks of missteps, setbacks, errors and failings with respect to any aspect of managing our business are an inherent part of attempted innovation in the life sciences industry. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may materially and adversely affect our business.

In addition, as an early-stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

***Because our therapeutic candidates are in an early stage of development, there is a high risk of failure, and we may never succeed in developing marketable products or generating therapeutic revenues.***

Our therapeutic candidates are development-stage technologies which require more, complex future development as well as regulatory approval prior to commercialization. It is impossible to fully mitigate the risks associated with bringing forward new technology and developing therapeutic candidates. These therapeutic candidates may fail at any point in development or in clinical trials. Therefore, there is no assurance that any of our therapeutic candidates will be successfully developed, be approved or cleared for sale by regulators, be accepted in the market or be profitable. Any delay or setback in the development of a product-candidate could materially adversely affect us.

We may not be successful in our efforts to identify or discover additional therapeutic candidates or we may expend our limited resources to pursue a particular therapeutic candidate or indication and fail to capitalize on therapeutic candidates or indications that may be more profitable or for which there is a greater likelihood of success.

In addition to development risks, we also face the risk that existing or evolving drug regulations may create barriers to licensure that we are unable to overcome, making it impossible for us to license any product we develop. Our therapeutic candidates may fail in clinical trials. We may never achieve the product claims necessary to successfully launch any products commercially.

We may not succeed in changing the practice of medicine such that our products are adopted as we anticipate. The data we generate in our clinical programs may not be viewed by physicians as strong enough for them to use and by third-party payers as effective enough for them to reimburse the cost of our products. Further, changes in the practice of medicine may render our approved products obsolete.

We also face the risk of:

- competitors introducing technologies which render our development efforts or approved products obsolete;
- data from our clinical trials not being strong enough to support therapeutic approval or the marketing claims needed for market success and to achieve our financial projections; and
- being unable to manufacture or supply, or have manufactured or supplied on our behalf, approved products cost-effectively.

***Our business is highly dependent on the success of TTX-MC138, our lead candidate which is at the early stages of development. All of our therapeutic candidates may require significant additional preclinical and clinical development before we may be able to seek regulatory approval for and launch a product commercially.***

We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We are very early in our development efforts, and only one of our therapeutic candidates, TTX-MC138, is in preclinical development and has yet to be tested in humans. If we are unable to successfully develop, obtain regulatory approval for and commercialize TTX-MC138, or experience significant delays in doing so, our business will be materially harmed. Advancing TTX-MC138 will require substantial investment before we can seek regulatory approval and potentially launch commercial sales. Further development of TTX-MC138 will require production scaleup, clinical studies, regulatory review and approval in the U.S. and other jurisdictions, development of sufficient commercial manufacturing capacity, and significant marketing efforts before we can generate any revenue from product sales, if approved.

In developing TTX-MC138, among other risks, we may not be successful in synthesizing or producing the components of our proprietary formulation, or there may be toxicology issues from key components of our formulation that we have not anticipated. We have not tested TTX-MC138 using the current synthesis protocol, production processes, equipment and materials in the larger quantities that would be necessary to meet clinical trial treatment demands for all anticipated patients.

We may experience setbacks that could delay or prevent regulatory approval of, or our ability to commercialize, our therapeutic candidates, including:

- negative or inconclusive results from our preclinical studies or clinical trials or positive results from the clinical trials of others for competing therapeutic candidates similar to ours, leading to their approval and a possible decision by us to conduct additional preclinical testing or clinical trials or abandon a program;
- side effects related to our therapeutic candidates experienced by patients or subjects in our clinical trials or by individuals using drugs or therapeutics that we, the FDA, other regulators or others view as relevant to the development of our therapeutic candidates;
- delays in submitting IND applications or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials, including our clinical endpoints;

- delays in enrolling subjects in clinical trials, including due to the COVID-19 pandemic;
- high drop-out rates of subjects from clinical trials;
- inadequate supply or quality of therapeutic candidates or other materials necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial costs;
- inability to compete with other therapies;
- poor efficacy of our therapeutic candidates during clinical trials;
- trial results taking longer than anticipated;
- trials being subjected to fraud or data capture failure or other technical mishaps leading to the invalidation of our trials in whole or in part;
- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays related to the impact of the spread of the COVID-19 pandemic, including the impact of COVID-19 on the FDA's ability to continue its normal operations;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical development generally or with respect to our technology in particular; or
- varying interpretations of data by the FDA and similar foreign regulatory agencies.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and our manufacturing, marketing, distribution and sales efforts or that of any future collaborator.

***Our therapeutic candidates may cause undesirable side effects or death or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.***

Undesirable side effects or death caused by any of our therapeutic candidates could cause IRBs, our contract research organizations, or CROs, the FDA or other regulatory authorities to interrupt, delay or discontinue clinical trials and could result in the denial of regulatory approval for our therapeutic candidates. This, in turn, could prevent us from commercializing our therapeutic candidates and generating revenues from their sale.

Also, any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing the product, which in turn could delay or prevent us from becoming profitable.

***Clinical development involves a lengthy, complex and expensive process, with an uncertain outcome, and the results of preclinical studies and early-stage clinical trials of our therapeutic candidates may not be predictive of the results of later-stage clinical trials.***

To obtain the requisite regulatory approvals to commercialize any therapeutic candidates, we must demonstrate through extensive preclinical studies and clinical trials that our therapeutic candidates are safe and effective in humans. Clinical trials are expensive and can take many years to complete, and its outcome is inherently uncertain. In particular, the general approach for FDA approval of a new drug is dispositive data from two well-controlled, Phase 3 clinical trials of the relevant drug in the relevant patient population. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete. A therapeutic candidate can fail at any stage of testing, even after observing promising signals of activity in earlier preclinical studies or clinical trials. The results of preclinical studies and early clinical trials of our therapeutic candidates may not be predictive of the results of later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of therapeutic candidates proceeding through clinical trials. Therapeutic candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biotechnology and biopharmaceutical industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most therapeutic candidates that commence clinical trials are never approved as therapeutic products, and there can be no assurance that any of our future clinical trials will ultimately be successful or support further clinical development of TTX-MC138 or any of our other therapeutic candidates. Therapeutic candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including:

- preclinical studies or clinical trials may show the therapeutic candidates to be less effective than expected (e.g., a clinical trial could fail to meet its primary endpoint(s)) or to have unacceptable side effects or toxicities;
- failure to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful;
- failure to receive the necessary regulatory approvals;
- manufacturing costs, formulation issues, pricing or reimbursement issues, or other factors that make a therapeutic candidate uneconomical; and
- the proprietary rights of others and their competing products and technologies that may prevent one of our therapeutic candidates from being commercialized.

In addition, differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Our FIH clinical trial is designed as a single dose trial, the purpose of which is to demonstrate safety and proof of delivery of TTX-MC138 to metastatic lesions. This design is not meant or expected to produce efficacy signals or that TTX-MC138 reaches into metastatic tumor cells although these may occur. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their therapeutic candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products.

Additionally, we expect that some of our trials will be open-label studies, where both the patient and investigator know whether the patient is receiving the investigational therapeutic candidate as a monotherapy or in combination with an existing approved drug. Most typically, open-label clinical trials test only the investigational therapeutic candidate and sometimes do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Therefore, it is possible that positive results observed in open-label trials will not be replicated in later placebo-controlled trials.

In addition, the standards that the FDA and comparable foreign regulatory authorities use when regulating our therapeutic candidates require judgment and can change, which makes it difficult to predict with certainty how they will be applied. Although we are initially focusing our efforts on development of small- molecule drug products, we may in the future pursue development of biological products, which could make us subject to additional regulatory requirements. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations. Examples of such regulations include future legislation or administrative action, or changes in FDA policy during the period of product development and FDA regulatory review. We cannot predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any therapeutic candidates that we develop.

We may seek to conduct clinical trials in foreign countries, as well as in the United States. If we continue to seek to conduct clinical trials in foreign countries or pursue marketing approvals in foreign jurisdictions, we must comply with numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval from foreign regulatory agencies may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the United States and vice versa.

Successful completion of clinical trials is a prerequisite to submitting a marketing application to the FDA and similar marketing applications to comparable foreign regulatory authorities, for each therapeutic candidate and, consequently, the ultimate approval and commercial marketing of any therapeutic candidates. We may experience negative or inconclusive results, which may result in our deciding, or our being required by regulators, to conduct additional clinical studies or trials or abandon some or all of our product development programs, which could have a material adverse effect on our business.

***If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The number of qualified clinical trial investigators and sites is limited. We expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use. This could reduce the number of patients available for our clinical trials at such clinical trial site. Clinical trials of other companies may be in similar therapeutic areas as ours. This competition will reduce the number and types of patients and qualified clinical investigators available to us because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by a competitor or clinical trial sites may not allow us to conduct our clinical trial at such site if competing trials are already being conducted there.

We may also encounter difficulties finding a clinical trial site at which to conduct our trials. Because our therapeutics represent a departure from more commonly used methods for cancer treatment, potential patients and their doctors may be inclined to use conventional therapies, such as checkpoint inhibitors, chemotherapy, radiation and monoclonal antibodies, rather than enroll patients in any of our clinical trials.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our planned clinical trials, which could prevent completion of these clinical trials and adversely affect our ability to advance the development of our therapeutic or any other future versions of it.

Our preclinical studies and clinical trials may fail to demonstrate adequately the safety, potency, purity and efficacy of any of our therapeutic candidates, which would prevent or delay development, regulatory approval and commercialization.

Since the number of subjects that we plan to dose in our planned Phase 0 and Phase 1 clinical trials of TTX-MC138 is relatively small, the results from such clinical trials, once completed, may be less reliable than results achieved in larger clinical trials, which may hinder our efforts to obtain regulatory approval for our therapeutic candidates.

***Due to our limited resources and access to capital, we must make decisions on the allocation of resources to certain programs and therapeutic candidates; these decisions may prove to be wrong and may adversely affect our business.***

We have limited financial and human resources and intend to initially focus on research programs and therapeutic candidates for a limited set of indications. As a result, we may forgo or delay pursuit of opportunities with other therapeutic candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. In addition, we may seek to accelerate our development timelines, including by initiating certain clinical trials of our therapeutic candidates before earlier-stage studies have been completed. This approach may cause us to commit significant resources to prepare for and conduct later-stage trials for one or more therapeutic candidates that subsequently fail earlier-stage clinical testing. Therefore, our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities or expend resources on therapeutic candidates that are not viable.

There can be no assurance that we will ever be able to identify additional therapeutic opportunities for our therapeutic candidates or to develop suitable potential therapeutic candidates through internal research programs, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential therapeutic candidates or other potential programs that ultimately prove to be unsuccessful.

***We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of TTX-MC138 or any of our other therapeutic candidates in development.***

Clinical trials are required to apply for regulatory approval to market TTX-MC138 or any of our other therapeutic candidates. Clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. We do not know whether any clinical trials we begin will continue as planned, will need to be restructured or will be completed on schedule or at all. Significant clinical trial delays also could allow competitors to bring products to market before we do and could impair our ability to successfully commercialize our therapeutic candidates, any of which could materially harm our business. CROs have recently indicated that conduct of certain preclinical animal studies to support IND filings may not begin for approximately six to eight months from the signing of contracts due in large part to COVID-19 scheduling and demand and supply chain issues. There is no assurance that we will not experience additional or other delays.

We also may experience numerous unforeseen events during, or as a result of, any future clinical trials that could delay or prevent our ability to receive marketing approval for, or to commercialize, TTX-MC138 or any of our other therapeutic candidates in development, including:

- regulators, IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- the FDA or other comparable regulatory authorities may disagree with our clinical trial design, including with respect to dosing levels administered in our planned clinical trials, which may delay or prevent us from initiating our clinical trials with our originally intended trial design;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs, which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- the number of subjects required for clinical trials of any therapeutic candidates may be larger than we anticipate, or subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;

- due to the impact of the COVID-19 pandemic, we have experienced delays in our preclinical development, including access to our lab and access to our animal facility, and may continue to experience delays and interruptions to our preclinical studies and clinical trials, we may experience delays or interruptions to our manufacturing supply chain, or we could suffer delays in reaching, or we may fail to reach, agreement on acceptable terms with third-party service providers on whom we rely;
- delays and interruptions to our clinical trials could extend the duration of the trials and increase the overall costs to finish the trials as our fixed costs are not substantially reduced during delays;
- we may elect to, or regulators, IRBs, Data Safety Monitoring Boards, or DSMBs, or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- we may not have the financial resources available to begin and complete the planned trials, or the cost of clinical trials of any therapeutic candidates may be greater than we anticipate;
- the supply or quality of our therapeutic candidates or other materials necessary to conduct clinical trials of our therapeutic candidates may be insufficient or inadequate to initiate or complete a given clinical trial; and
- the FDA or other comparable foreign regulatory authorities may require us to submit additional data such as long-term toxicology studies or may impose other requirements before permitting us to initiate a clinical trial.

Our product development costs will increase if we experience delays in clinical trials or in obtaining marketing approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. If we do not achieve our product development goals in the time frames we announce and expect, the approval and commercialization of our therapeutic candidates may be delayed or prevented entirely. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our therapeutic candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our therapeutic candidates and harming our business and results of operations. Any delays in our clinical development programs may harm our business, financial condition and results of operations significantly.

***Changes in methods of therapeutic candidate manufacturing or formulation may result in additional costs or delay.***

As therapeutic candidates progress through preclinical to late-stage clinical trials to marketing approval and commercialization, various aspects of the development program, such as manufacturing methods and the product's formulation, may be altered along the way in an effort to optimize yield, manufacturing batch size, minimize costs and achieve consistent quality and results. These changes carry the risk that they will not achieve their intended objectives. Any of these changes could cause our therapeutic candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our therapeutic candidates and jeopardize our ability to commercialize our therapeutic candidates and generate revenue.

In addition, there are risks associated with process development and large-scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with current good manufacturing practice, or cGMP, requirements, lot consistency and timely availability of raw materials. Even if we obtain marketing approval for any of our therapeutic candidates, there is no assurance that our third-party manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential commercial launch of the product or to meet potential future demand. If our contract manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

***Quality problems could delay or prevent delivery of our products to clinical trials or the market.***

Quality is important due to (i) the serious and costly consequences of process or product failure and (ii) it being one required element of the regulatory approval process. Receiving quality certifications is critical to the development and marketing success of our technologies. If we fail to meet existing or future quality standards, development or commercialization of our technologies could be materially and adversely affected.

We are required to comply with FDA's good clinical practice, or GCP, regulations for our clinical programs. As it relates to the manufacturing of both our drug substance and drug product, we are required to adhere to FDA's cGMP regulations. Additionally, we must follow guidelines promulgated by the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use, or ICH Guidelines. The ICH Guidelines to which we are subject are ICH E6 (R2) and ICH E8 (R1), "Designing quality into clinical studies," for all tasks related to clinical programs, and ICH Q7 for the manufacture of our drug substance and drug product.

We need to implement a quality system designed to meet applicable requirements to conduct clinical trials and sell any therapeutic and diagnostic candidates for which we obtain approval in the U.S., Europe and in other countries. We cannot guarantee that our development standards, processes and procedures will meet applicable requirements for regulatory approval in any jurisdiction or that they will mitigate all of the risks associated with the development and commercialization of our therapeutic candidates. Even if we receive quality certifications, we could subsequently lose them or be required to take corrective actions if we do not continue to meet the requirements under applicable standards. If we fail to meet applicable quality requirements, it could have a material adverse effect on us.

***We may not be successful in our efforts to identify or discover additional therapeutic candidates in the future.***

Our research programs may initially show promise in identifying potential therapeutic candidates, yet fail to yield therapeutic candidates for clinical development for a number of reasons, including:

- our inability to design such therapeutic candidates with the pharmacological properties that we desire or attractive pharmacokinetics;
- our inability to design and develop a suitable manufacturing process; or
- potential therapeutic candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be medicines that will receive marketing approval and achieve market acceptance.

Research programs to identify new therapeutic candidates require substantial technical, financial and human resources. If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

***If product liability lawsuits are brought against us, we may incur substantial financial or other liabilities and may be required to limit commercialization of our therapeutic candidates.***

We face an inherent risk of product liability once we begin testing TTX-MC138 and any of our other therapeutic candidates in clinical trials and will face an even greater risk if we commercialize any products. For example, we may be sued if our therapeutic candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our therapeutic candidates. Even a successful defense of these claims would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- inability to bring a therapeutic candidate to the market;



- decreased demand for our products;
- injury to our reputation;
- withdrawal of clinical trial subjects and inability to continue clinical trials;
- initiation of investigations by regulators;
- fines, injunctions or criminal penalties;
- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any therapeutic candidate, if approved; and
- decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We will need to obtain insurance for clinical trials as TTX-MC138, and any of our other therapeutic candidates begin clinical development. However, we may be unable to obtain, or may obtain on unfavorable terms, clinical trial insurance in amounts adequate to cover any liabilities from any of our clinical trials. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

#### **Risks related to regulatory approval, healthcare regulations and ongoing regulatory compliance**

***We are very early in our development efforts. All of our therapeutic candidates are still in preclinical development. If we are unable to advance our therapeutic candidates to clinical development, obtain regulatory approval and ultimately commercialize our therapeutic candidates or experience significant delays in doing so, our business will be materially harmed.***

We have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA, and, as a company, we have no experience in obtaining approval of any product-candidate. The time required to obtain FDA and other approvals is unpredictable but typically takes one or more years following completion of clinical trials, depending upon the type, complexity and novelty of the product-candidate. We may encounter delays or rejections during any stage of the regulatory review and approval process based upon the failure of clinical or laboratory data to demonstrate compliance with, or upon the failure of a product-candidate to meet, FDA requirements for safety, efficacy and quality.

The standards that the FDA and its foreign counterparts use when regulating us are not always applied predictably or uniformly and can change. Because the therapeutic candidates we are developing may represent a new class of drug, the FDA and its foreign counterparts have not yet established any definitive relevant policies, practices or guidelines in relation to these therapeutic candidates. The lack of policies, practices or guidelines may hinder or slow review by the FDA of regulatory filings that we may submit. Moreover, the FDA may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in and added costs for the clinical development of our therapeutic candidates.

Any analysis of data from preclinical and clinical activities that we perform is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

In addition, the FDA may delay, limit, or deny approval of a product-candidate for many reasons, including:

- disagreement with the design or implementation of clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA that a product-candidate is safe and effective for any indication;
- we may be unable to demonstrate that a product-candidate's clinical and other benefits outweigh its safety risks;
- the FDA may disagree with our interpretation of data from preclinical studies or clinical trials;
- the results of our clinical trials may not demonstrate the safety or efficacy required by the FDA for approval; or
- the FDA may find deficiencies in our manufacturing processes or facilities; and the FDA's approval policies or regulations may significantly change in a manner rendering our clinical data insufficient for approval.

After submission of a New Drug Application, or NDA, the FDA may refuse to review the application, deny approval of the application, require additional testing or data or, if the NDA is filed and later approved, require post-marketing testing and surveillance to monitor the safety or efficacy of a product. Under the Prescription Drug User Fee Act, or PDUFA, the FDA has agreed to certain performance goals in the review of NDAs. The FDA's timelines are flexible and subject to change based on workload and other potential review issues which may delay FDA's review of an NDA. For example, during the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. FDA may not be able to continue its current pace and review timelines could be extended. Further, the terms of approval of any NDA, including the product labeling, may be more restrictive than we desire which could affect the marketability of our products.

Even if we comply with all FDA regulatory requirements, we may not obtain regulatory approval for any of our product-candidates. If we fail to obtain regulatory approval for any of our product-candidates, we will have no commercialized products for sale and therefore have no ability to generate significant, if any, revenue.

Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular therapeutic candidate for which we are seeking approval. Furthermore, any regulatory approval to market a product may be subject to limitations on the approved uses for which we may market the product or the labeling or other restrictions. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy, or REMS, plan as part of or after approval, which may impose further requirements or restrictions on the distribution or use of an approved product, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may limit the size of the market for the product and affect reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the United States and vice versa.

If we or any collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our products successfully and could harm our reputation and lead to reduced acceptance of our products by the market. Enforcement actions can include, among others:

- adverse regulatory inspection findings;
- warning letters;
- voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals;
- restrictions on, or prohibitions against, marketing our products;
- restrictions on, or prohibitions against, importation or exportation of our products;
- suspension of review or refusal to approve pending applications or supplements to approved applications;
- exclusion from participation in government-funded healthcare programs;
- exclusion from eligibility for the award of government contracts for our products;
- suspension or withdrawal of product approvals;
- product seizures;
- injunctions; and
- civil and criminal penalties and fines.

In addition, if any of our products cause serious or unexpected side effects or are associated with other safety risks after receiving marketing approval, a number of potential significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- we may be required to recall the product, change the way it is administered, conduct additional clinical trials or change the labeling of the product;
- the product may be rendered less competitive and sales may decrease;
- litigation or class action lawsuits;
- our reputation may suffer generally both among clinicians and patients; or

- regulatory authorities may require certain labeling statements, such as warnings or contraindications or limitations on the indications for use or impose restrictions on distribution in the form of a REMS in connection with approval, if any.

We may voluntarily suspend or terminate our clinical trials if at any time we believe that they present an unacceptable risk to participants or if preliminary data demonstrate that our products are unlikely to receive regulatory approval or unlikely to be successfully commercialized.

***We have received Orphan Drug Designation for TTX-siPDL1 for pancreatic cancer and may in the future seek Orphan Drug Designation for TTX-siPDL1 in other indications and for some of our other current and future therapeutic candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.***

Under the Orphan Drug Act, the FDA may grant orphan designation to a therapeutic candidate or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan Drug Designation must be requested before submitting an NDA. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. After the FDA grants Orphan Drug Designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a therapeutic candidate that has obtained Orphan Drug Designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to Orphan Drug Exclusivity, which means that the FDA may not approve any other applications, including an NDA, to market the same biologic for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with Orphan Drug Exclusivity or if the FDA finds that the holder of the Orphan Drug Exclusivity has not shown it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. As a result, even if one of our therapeutic candidates receives Orphan Drug Exclusivity, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease. Furthermore, the FDA can waive Orphan Drug Exclusivity if we are unable to manufacture sufficient supply of the approved product.

We may seek Orphan Drug Designation for TTX-siPDL1 and some of our current or future therapeutic candidates in additional orphan indications in which there is a medically plausible basis for the use of these products. Even when we obtain Orphan Drug Designation, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, although we intend to seek Orphan Drug Designation for other therapeutic candidates, we may never receive such designations. For example, the FDA has expressed concerns regarding the regulatory considerations for Orphan Drug Designation as applied to tissue agnostic therapies, and the FDA may interpret the Federal Food, Drug and Cosmetic Act, or FD&C Act, and regulations promulgated thereunder in a way that limits or blocks our ability to obtain Orphan Drug Designation or Orphan Drug Exclusivity, if our therapeutic candidates are approved, for our targeted indications.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified FDA's pre-existing regulatory interpretation to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive Orphan Drug Exclusivity. The legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. Moreover, in the Consolidated Appropriations Act of 2021, Congress did not further change this interpretation when it clarified that the interpretation codified in FDARA would apply in cases where FDA issued an orphan designation before the enactment of FDARA, but where product approval came after the enactment of FDARA. FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how FDA may change orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

***A Breakthrough Therapy designation by FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.***

We may seek Breakthrough Therapy designation for some or all of our current and future product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by FDA may also be eligible for other expedited approval programs, including Accelerated Approval.

Designation as a breakthrough therapy is within the discretion of FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to candidate products considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, FDA may later decide that the product no longer meets the conditions for qualification. Thus, even though we intend to seek Breakthrough Therapy designation for some or all of our current and future product candidates, there can be no assurance that we will receive Breakthrough Therapy designation.

***A Fast Track designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.***

If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation for a particular indication. We may seek Fast Track designation for some or all of our current and future product candidates, but there is no assurance that the FDA will grant this status to any of our current or future product candidates. Marketing applications filed by sponsors of products in Fast Track development may qualify for Priority Review under the policies and procedures offered by the FDA, but the Fast Track designation does not assure any such qualification or ultimate marketing approval by the FDA. The FDA has broad discretion whether or not to grant Fast Track designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, the FDA may withdraw any Fast Track designation at any time.

***Accelerated approval by FDA, even if granted for TTX-MC138 or any other future therapeutic candidate, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our therapeutic candidates will receive marketing approval.***

We may seek approval of TTX-MC138 and may seek approval of future therapeutic candidates using the FDA's accelerated approval pathway. A therapeutic candidate may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. As a condition of approval, FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence. In addition, unless it determines otherwise, FDA currently requires pre-approval of promotional materials for products receiving accelerated approval, which could adversely affect the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval and, even if we do, we may not experience a faster development, regulatory review or approval process for that therapeutic candidate. In addition, receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval.

***A variety of factors, including inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.***

The ability of FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel, accept payments of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result of these and other factors. In particular, it has been reported that FDA's planned expansion of its oncology division is delayed. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at FDA and other agencies may also slow the time necessary for new therapeutic candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times, and certain regulatory agencies, such as FDA and the SEC, have had to furlough critical employees and stop critical activities. Separately, since March 2020 when foreign and domestic inspections of facilities were largely placed on hold in connection with the COVID-19 pandemic, FDA has been working to resume pre-pandemic levels of inspections, including routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel or for other reasons, and FDA does not determine that a remote interactive evaluation will be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the ongoing COVID-19 pandemic and may experience delays in their regulatory activities.

If a prolonged government shutdown occurs, or if global health concerns continue to prevent FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

***Even if we receive regulatory approval of TTX-MC138 or any of our other therapeutic candidates, we will be subject to ongoing regulatory requirements and continued regulatory review, which may result in significant additional expense. We may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our therapeutic candidates.***

Any regulatory approvals that we receive for TTX-MC138 or another product-candidate may require post-marketing surveillance to monitor the safety and efficacy of the product and may require us to conduct post-approval clinical studies. The FDA may also require a REMS in order to approve our therapeutic candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our therapeutic candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our therapeutic candidates will be subject to extensive and ongoing regulatory requirements. These requirements can include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and GCP, for any clinical trials that we conduct post-approval and applicable product tracking and tracing requirements. Compliance with ongoing and changing requirements takes substantial resources and, should we be unable to remain in compliance, our business could be materially and adversely affected.

In addition, if we pursue, and ultimately obtain, accelerated approval of TTX-MC138 based on a surrogate endpoint, the FDA would require us to conduct a confirmatory trial to verify the predicted clinical benefit as well as additional safety studies. The results from the confirmatory trial may not support the clinical benefit, which would result in the approval being withdrawn.

Manufacturers and their facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and

our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our therapeutic candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the therapeutic candidate. The FDA may also require a REMS as a condition of approval of our therapeutic candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our therapeutic candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

Later discovery of previously unknown problems with our therapeutic candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, or the making of unsupported claims, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or withdrawal of approvals;
- product seizure or detention or refusal to permit the import or export of our therapeutic candidates; and
- consent decrees or injunctions or the imposition of civil or criminal penalties.

Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is not inconsistent with the labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. The policies of the FDA and of other regulatory authorities may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our therapeutic candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

***We expect to develop, or enter into a collaboration or partnership to develop, in vitro diagnostics, including potentially complementary diagnostics and/or companion diagnostics, for our current or future therapeutic candidates. If we, or our future collaborators, are unable to successfully develop such diagnostics, or experience significant delays in doing so, we may not realize the full commercial potential of our future therapeutic candidates.***

We have little experience in the development of *in vitro* diagnostics and, as such, we may rely on future collaborators in developing appropriate *in vitro* diagnostics to pair with our current or future therapeutic candidates. We have not yet begun discussions with any potential partners with respect to the development of complementary diagnostics and/or companion diagnostics and may be unsuccessful in entering into collaborations for the development of any complementary and/or companion diagnostics for our programs and our current or future therapeutic candidates.

*In vitro* diagnostics are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices and require separate regulatory approval or clearance prior to commercialization. If we, our collaborators, or any third-parties that we engage to assist us, are unable to successfully develop complementary diagnostics and/or companion diagnostics for our therapeutic candidates and any future therapeutic candidates, or experience delays in doing so:

- the development of our therapeutic candidates and any other future therapeutic candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials; and
- we may not realize the full commercial potential of our therapeutic candidates and any other future therapeutic candidates that receive marketing approval if, among other reasons, we are unable to appropriately identify, or it takes us longer to identify, patients who are likely to benefit from therapy with our products, if approved.

If any of these events were to occur, our business would be harmed, possibly materially.

***Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.***

Although we do not currently have any drugs on the market, if we begin commercializing our current or future therapeutic candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any current or future therapeutic candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our current or future therapeutic candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and wilfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other hand. The term remuneration has been interpreted broadly to include anything of value. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistle-blower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. False Claims Act liability is potentially significant in the healthcare industry because the statute provides for treble damages and mandatory penalties. Government enforcement agencies and private whistle-blowers have investigated pharmaceutical companies for or asserted liability under the False Claims Act for a variety of alleged promotional and marketing activities, such as providing free products to customers with the expectation that the customers would bill federal programs for the products; providing consulting fees and other benefits to physicians to induce them to prescribe products; engaging in promotion for “off-label” uses; and submitting inflated best price information to the Medicaid Rebate Program. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and wilfully falsifying, concealing or covering



up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the federal physician payment transparency requirements, sometimes referred to as the “Sunshine Act” under the ACA require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program to report to the Department of Health and Human Services information related to physician payments and other transfers of value and the ownership and investment interests of such physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Ensuring that our future business arrangements with third-parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, were to be found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

***Obtaining and maintaining regulatory approval for our therapeutic candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval for that or of any of our other therapeutic candidates in other jurisdictions.***

Obtaining and maintaining regulatory approval for our therapeutic candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval for TTX-MC138, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product-candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials, as preclinical studies and clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product-candidate must be approved for

reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we charge for our product is also subject to regulatory approval.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of therapeutic candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our therapeutic candidates will be harmed.

***Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.***

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example, changes to our manufacturing arrangements; additions or modifications to product labeling; the recall or discontinuation of our products; or additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and likely will continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA was passed, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. biotechnology and biopharmaceutical industries. The ACA, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts from the negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. On December 14, 2018, a U.S. District Court Judge in Texas ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review this case. On June 17, 2021, the Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. It is unclear how such litigation and other efforts to repeal and replace the ACA will impact the ACA and our business. In addition, the former Trump administration issued various Executive Orders which eliminated cost sharing subsidies and included provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Additionally, Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. On December 20, 2019, former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repealed the so called "Cadillac" tax, the health insurance provider tax, and the medical device excise tax. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended. We cannot predict what affect further changes to the ACA would have on our business.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. The Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs, including aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013, and subsequent legislative amendments to the statute, including the Bipartisan Budget Act of 2018, or BBA, will remain in effect through 2030, unless additional congressional action is taken. However, these Medicare sequester reductions will be suspended from May 1, 2020, through December 31, 2020, due to the COVID-19 pandemic. The BBA also amended the ACA, effective January 1, 2019, by

increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole.” On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our therapeutic candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

At the federal level, the former Trump administration’s budget for fiscal year 2021 included a \$135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the former Trump administration sent “principles” for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. The former Trump administration previously released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contained proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out-of-pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services, or HHS, has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule that would allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. This final rule codified CMS’s policy change that was effective January 1, 2019. On July 24, 2020, former President Trump signed four Executive Orders aimed at lowering drug prices. The Executive Orders direct the Secretary of HHS to: (1) eliminate protection under an AKS safe harbor for certain retrospective price reductions provided by drug manufacturers to sponsors of Medicare Part D plans or pharmacy benefit managers that are not applied at the point-of-sale; (2) allow the importation of certain drugs from other countries through individual waivers, permit the re-importation of insulin products, and prioritize finalization of the proposed rule to permit the importation of drugs from Canada; (3) ensure that payment by the Medicare program for certain Medicare Part B drugs is not higher than the payment by other comparable countries (depending on whether pharmaceutical manufacturers agree to other measures); and (4) require Federally Qualified Health Centers, or FQHCs, participating in the 340B drug program to provide insulin and injectable epinephrine to certain low-income individuals at the discounted price paid by the FQHC, plus a minimal administrative fee. On October 1, 2020, the FDA issued the final rule allowing importation of certain prescription drugs from Canada. On August 6, 2020, former President Trump signed an additional Executive Order directing U.S. government agencies to encourage the domestic procurement of Essential Medicines, Medical Countermeasures, and Critical Inputs, which include among other things, active pharmaceutical ingredients and drugs intended for use in the diagnosis, cure, mitigation, treatment, or prevention of COVID-19. The FDA has been directed to release a full list of Essential Medicines, Medical Countermeasures, and Critical Inputs affected by this Order by November 5, 2020. On September 13, 2020, former President Trump signed an Executive Order directing HHS to implement a rulemaking plan to test a payment model, pursuant to which Medicare would pay, for certain high-cost prescription drugs and biological products covered by Medicare Part B, no more than the most-favored-nation price (i.e., the lowest price) after adjustments, for a pharmaceutical product that the drug manufacturer sells in a member country of the Organization for Economic Cooperation and Development that has a comparable per-capita gross domestic product. Although a number of these and other measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors.

Additionally, on July 9, 2021, President Biden issued an executive order directing the FDA to, among other things, continue to clarify and improve the approval framework for generic drugs and identify and address any efforts to impede generic drug competition.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biologic product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain

product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our therapeutic candidates for which we may obtain regulatory approval or the frequency with which any such therapeutic candidate is prescribed or used. Additionally, we expect to experience pricing pressures in connection with the sale of any future approved therapeutic candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes.

***We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations.***

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We plan to engage third-parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals, and we could be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

***Healthcare reform in the U.S. and other countries may materially and adversely affect us.***

In the U.S. and in many foreign jurisdictions, the legislative landscape continues to evolve. Our revenue prospects could be affected by changes in healthcare spending and policies in our target markets. We operate in a highly regulated industry and new laws or judicial decisions, or new interpretations of existing laws or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could materially and adversely affect us.

There is significant interest in promoting healthcare reform, as evidenced by the enactment in the U.S. of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act in 2010, or together, the ACA. It is likely that many governments will continue to consider new healthcare legislation or changes to existing legislation. We cannot predict the initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified, or how they may affect us. The continuing efforts of governments, insurance companies, managed care organizations and other third-party payors to contain or reduce healthcare costs may adversely affect:

- the demand for any products for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to generate revenues and achieve or maintain profitability; and
- the level of taxes that we are required to pay.

Under the ACA, there are many programs and requirements for which details or consequences are still not fully understood. We are unable to predict what healthcare programs and regulations will ultimately be implemented at any level of government in or outside the U.S., but any changes that decrease reimbursement for our approved products, reduce volumes of medical procedures or impose new cost-containment measures could adversely affect us.

### **Prescription Drug Pricing Reduction Act**

On August 16, 2022 the Inflation Reduction Act of 2022 was passed, which among other things, allows for CMS to negotiate prices for certain single-source drugs and biologics reimbursed under Medicare Part B and Part D, beginning with ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. The legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The legislation also caps Medicare beneficiaries’ annual out-of-pocket drug expenses at \$2,000. The effect of Inflation Reduction Act of 2022 on our business and the healthcare industry in general is not yet known.

***We are subject to geopolitical risks, economic volatility, anti-corruption laws, export and import restrictions, local regulatory authorities and the laws and medical practices in foreign jurisdictions.***

The costs of healthcare internationally have risen significantly over the past decade. Numerous initiatives and reform by legislators, regulators and third-party payers to curb these costs have reduced reimbursement rates. One outcome of these dynamics is that hospitals and others are consolidating into larger integrated delivery networks and group purchasing organizations in an effort to reduce administrative costs and increase purchasing power. This consolidation has resulted in greater pricing pressure on suppliers, decreased average selling prices and changes in medical practices. If we secure marketing approval for our therapeutic candidates, our commercial success will be determined by, among other things, our ability to obtain acceptable pricing for approved products which will be subject to, among other things, the factors described above.

The expansion of group purchasing organizations, integrated delivery networks and large single accounts among hospitals could also put price pressure on our approved products. We expect that market demand, government regulation, third-party reimbursement policies, government contracting requirements and societal pressures will continue to change the worldwide healthcare industry, resulting in further business consolidations and alliances among our customers and competitors. The result may be further downward pressure on the prices we are able to obtain, thus adversely affecting us.

Even if we obtain regulatory approval of our therapeutic candidates, the products may not gain market acceptance among physicians, patients, hospitals, cancer treatment centers and others in the medical community.

### **Risks related to commercialization**

***We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third-parties to market and sell any products for which we obtain regulatory approval, we may not be able to generate product revenue.***

We have no sales, marketing or distribution capabilities, nor have we commercialized a product. If any of our therapeutic candidates ultimately receives regulatory approval, we expect to establish a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time consuming. We have no prior experience as a company in the marketing, sale and distribution of pharmaceutical products, and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may also choose to collaborate with third-parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of building our own sales force and distribution systems. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third-parties for these functions than if we were to market, sell and distribute any products that we develop and for which we receive regulatory approval ourselves. We likely will have little control over such third-parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing our products, either on our own or through arrangements

with one or more third-parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

***Coverage and reimbursement may be limited or unavailable in certain market segments for our therapeutic candidates, if approved, which could make it difficult for us to sell any therapeutic candidates profitably.***

In the United States and in other countries, patients who are prescribed treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States, sales of any products for which we may receive regulatory marketing approval will depend, in part, on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities such as Medicare, Medicaid, TRICARE, and the Veterans Administration, managed care providers, private health insurers, and other organizations. Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Patients are unlikely to use our therapeutic candidates unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our therapeutic candidates or assure that coverage and reimbursement will be available for any product that we may develop.

Government authorities and other third-party payors decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Our ability to commercialize any products successfully will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government health care programs and private health insurers. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our therapeutic candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for our products can differ significantly from payor to payor. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of therapeutic candidates, once approved. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our therapeutic candidates, if approved.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, also called the Medicare Modernization Act, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug and biologic benefit to Medicare

beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs and biologics. Unlike Medicare Parts A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs and biologics, and each drug plan can develop its own formulary that identifies which drugs and biologics it will cover, and at what tier or level. However, Part D prescription drug formularies must include products within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs and biologics in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs and biologics may increase demand for products for which we obtain marketing approval. Any negotiated prices for any of our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug or biologic product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the average manufacturer price, or AMP, and Medicaid rebate amounts reported by the manufacturer. As of 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, expanded the types of entities eligible to receive discounted 340B pricing, although under the current state of the law these newly eligible entities (with the exception of children's hospitals) will not be eligible to receive discounted 340B pricing on orphan drugs. As the required 340B discount is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase. The Centers for Medicare & Medicaid Services, or CMS, has previously and may in the future implement reductions in Medicare Part B reimbursement for 340B drugs through notice and comment rulemaking. It is unclear how such reimbursement reductions could affect covered hospitals who might purchase our products in the future, and affect the rates we may charge such facilities for our approved products.

Changes to these current laws and state and federal healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any therapeutic candidates for which we may obtain regulatory approval or the frequency with which any such therapeutic candidate is prescribed or used.

***We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.***

The development and commercialization of new oncology drug products is highly competitive. We may face competition with respect to any therapeutic candidates that we seek to develop or commercialize in the future from major biotechnology and biopharmaceutical companies, specialty biotechnology and biopharmaceutical companies, and other biotechnology and biopharmaceutical companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

Not only must we compete with other companies that are focused on therapeutics that treat cancer, but also any therapeutic candidates that we successfully develop and commercialize will compete with existing and new therapies that may become available in the future. Our competitors may develop more successful products similar to ours sooner than we can commercialize ours, which may negatively impact our results. Companies that we are aware of with targeted therapeutics in the treatment of various cancers include Ionis, Moderna, Alnylam, BioNTech, Dicerna, Siranomics, among others which have therapeutic candidates in various stages of preclinical and clinical developments. Arrowhead Pharmaceuticals is a clinical stage company with a pipeline of investigational RNAi therapeutics. However, we know of no other companies currently in clinical development with miRNA therapeutics targeting metastatic disease. For additional information regarding our competition, see "*Business — Competition.*"

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do.

Mergers and acquisitions in the biopharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, more convenient, or less expensive than any products that we may develop. Furthermore, products currently approved for other indications could be discovered to be effective treatments of the biological processes that drive cancers as well, which could give such products significant regulatory and market timing advantages over TTX-MC138 or other therapeutic candidates that we may identify. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential therapeutic candidates uneconomical or obsolete and we may not be successful in marketing any therapeutic candidates we may develop against competitors. The availability of competitive products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

***If, in the future, we are unable to establish sales and marketing and patient support capabilities or enter into agreements with third-parties to sell and market our current or future therapeutic candidates, we may not be successful in commercializing our current or future therapeutic candidates if and when they are approved, and we may not be able to generate any revenue.***

We do not currently have a sales or marketing infrastructure and have no experience in the sales, marketing, patient support or distribution of drugs. We currently intend to partner with a larger commercial organization to market any of our therapeutic candidates, if approved, though our intentions may change in the future. To achieve commercial success for any approved therapeutic candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, patient support, managerial and other non-technical capabilities or make arrangements with third-parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our current or future therapeutic candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing and patient support capabilities and entering into arrangements with third-parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any drug launch. If the commercial launch of a therapeutic candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our current or future therapeutic candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future drugs, if approved;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third-parties to perform sales, marketing, patient support and distribution services, our drug revenues or the profitability of these drug revenues to us are likely to be lower than if we were to market and sell any current or future therapeutic candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third-parties to sell and market our current or future therapeutic candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third-parties, and any of them may fail to devote the necessary resources and attention to sell and market our current or future therapeutic candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third-parties, we will not be successful in commercializing our current or



future therapeutic candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

***Sales of our products may involve a lengthy sales cycle.***

Many factors are expected to influence the sales cycle for our approved products. These factors include the future state of the market, the perceived value of our therapeutic candidates, the evolution of competing technologies, insurance coverage or prior authorization requirements and changes in medical practices. Any of these may adversely affect our sales cycles and the rate of market acceptance of our approved products.

**Risks related to third-parties and suppliers**

***We expect to rely on third-party manufacturing and supply vendors, and our supply of research and development, preclinical and clinical development materials may become limited or interrupted or may not be of satisfactory quantity or quality.***

We have very limited manufacturing facilities and personnel. We currently rely, and expect to continue to rely, primarily on third-parties for the manufacture of TTX-MC138 and any future potential therapeutic candidates that we may develop. There can be no assurance that our preclinical and clinical development product supplies will not be limited or interrupted, or that they will be of satisfactory quality or continue to be available at acceptable prices. For example, the extent to which the COVID-19 pandemic impacts our ability to procure sufficient supplies for the development of our therapeutic candidates will depend on the severity and duration of the spread of the virus and the actions undertaken to contain COVID-19 or treat its effects. Since the beginning of the COVID-19 pandemic, several vaccines for COVID-19 have received Emergency Use Authorization by the FDA, some of which later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. Any replacement of our manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements.

We may be unable to establish additional agreements, or extend existing agreements, with third-party manufacturers or to do so on terms acceptable to us. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third-party for sufficient quantity and quality at acceptable costs which could delay, prevent or impair our development or commercialization efforts;
- the possible breach of the manufacturing agreement by the third-party;
- failure to meet our manufacturing specifications;
- failure to meet our manufacturing schedule;
- misappropriation of our proprietary information, including our trade secrets and know-how;
- the possible termination or nonrenewal of the agreement by the third-party at a time that is costly or inconvenient for us;
- disruptions to the operations of our manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of a manufacturer or supplier; and
- reliance on the third-party for regulatory compliance, quality assurance and safety reporting.

Our reliance on others for our manufacturing will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all applicable regulations regarding manufacturing. Our therapeutic candidates and any

products that we may develop may compete for access to manufacturing facilities with other therapeutic candidates and products. There are a limited number of manufacturers that operate in accordance with cGMP regulations that might be capable of manufacturing for us which could restrict our ability to supply products and, as a result, have a material adverse effect on us.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval or could otherwise adversely affect our ability to commercialize our approved products. Some of these events could be the basis for costly FDA action, including injunction, recall, seizure or total or partial suspension of production.

We will have limited control over the day-to-day manufacturing and quality operations of our contract manufacturers. While we will exercise commercially reasonable efforts to oversee operations and embed our quality system standards and controls in our manufacturing agreements, we will remain subject to the performance of our contract manufacturers. We must depend on our suppliers for proper oversight and control of their operations. Our outside manufacturers may themselves rely on other parties that they do not control. Our suppliers might fail to obtain, or experience delays in obtaining, regulatory approvals applicable to the aspects of their business that pertains to us. As a result, the development and commercialization of our products may be delayed. If this occurs, we may need to identify alternative sources of supply which may not be feasible, or which may adversely affect our timelines and financial results.

Our dependence upon others for the manufacture of our therapeutic candidates or products may adversely affect our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Thus, our current and anticipated future dependence upon others for manufacturing may adversely affect our timelines, our future profit margins or our ability to commercialize any therapeutic candidates that receive marketing approval on a timely and competitive basis.

***We rely on third-parties to conduct certain aspects of our preclinical studies and clinical trials. If these third- parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential therapeutic candidates.***

We depend, or may depend in the future, upon third-parties to conduct certain aspects of our preclinical studies and clinical trials, under agreements with universities, medical institutions, CROs, strategic collaborators and others. We expect to have to negotiate budgets and contracts with such third-parties, which may result in delays to our development timelines and increased costs.

We will rely especially heavily on universities, medical institutions, CROs and other third-parties for the conduct of our clinical trials. While we are obligated to ensure compliance by third-parties with clinical trial protocols and other aspects of our clinical trials, and to have mechanisms in place to monitor our clinical trials, the sites at which they are conducted, and the investigators and other personnel involved in our clinical trials, we have limited control over these entities and individuals and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol. Our reliance on third- parties does not relieve us of our regulatory responsibilities for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. We and these third-parties are required to comply with GCP requirements, for therapeutic candidates in clinical development. Regulatory authorities enforce GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third-parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with GCP requirements.

Our failure or any failure by these third-parties to comply with these regulations or to recruit a sufficient number of patients meeting requirements for enrollment in the trial may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third-parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third-parties conducting aspects of our preclinical studies or clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third-parties, we cannot control whether or not they devote sufficient time and resources to our preclinical studies and clinical programs. These third-parties may also have relationships with other commercial

entities, including our competitors, for whom they may also be conducting clinical trials or other therapeutic development activities, which could affect their performance on our behalf. If these third-parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the preclinical or clinical data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements or for other reasons or if, due to federal or state orders or absenteeism due to the COVID-19 pandemic, they are unable to meet their contractual and regulatory obligations, our development timelines, including clinical development timelines, may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our therapeutic candidates. As a result, our financial results and the commercial prospects for our therapeutic candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third-parties or to do so on commercially reasonable terms.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

***Parties conducting some or all of our product manufacturing may not perform satisfactorily.***

Outside manufacturers may not be able to or may not comply with cGMP regulations or similar regulatory requirements outside the U.S. Our failure, or the failure of our manufacturers, to comply with applicable regulations could delay clinical development or marketing approval or result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of therapeutic candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

We may not have arrangements for redundant supply or a second source for key materials, components or our products and therapeutic candidates. If our contract manufacturers cannot perform as expected, we may be required to replace such manufacturers. There may be only a small number of potential alternative manufacturers who could manufacture our therapeutic candidates. We may incur added costs and delays in identifying, gaining access to and qualifying any such replacement.

***We are highly dependent on others to provide services for certain core aspects of our business.***

To conserve financial resources, we utilize consultants, advisors and other parties for certain functions including regulatory affairs, clinical trials, medical practice issues, product management and human resources. If other parties are not available to provide services through completion of our programs at the time we require their services, or if the expertise we require is not readily available, the development and commercialization of our therapeutic candidates may be delayed.

***If our third-party manufacturers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.***

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical materials, by our third-party manufacturers. Our manufacturers are subject to federal, state and local laws and regulations in the U.S. governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

***We may not be successful in establishing and maintaining strategic partnerships, which could adversely affect our ability to develop and commercialize products.***

A part of our strategy is to seek, evaluate and, when strategically attractive, enter into development and commercial partnerships. Potential partners may include larger medical products companies. These potential partners often have their own internal development programs and priorities which may be a potential source of competition for our therapeutic candidates. We must develop technologies of value and then demonstrate the value of our technologies and therapeutic candidates if we are to be successful in arranging strategic partnerships on terms that will be attractive. There are no assurances that we will succeed in arranging any partnerships.

Identifying appropriate partners for our therapeutic candidates and the negotiation process is lengthy, time-consuming and complex and we have limited resources to do this. In order for us to successfully partner our therapeutic candidates, potential partners must view these therapeutic candidates as economically and technologically valuable with features or benefits that are superior to existing products or therapeutic candidates in development. We may not be able to maintain such strategic partnerships if, for example, development or approval of a product is delayed or sales of an approved product are disappointing. Any delay in entering into strategic partnership agreements related to our therapeutic candidates could delay their development and commercialization and reduce their competitiveness even if they reach the market.

In addition, strategic partners may not perform as we expect or may breach their agreements with us. We may not be able to adequately protect our rights under these agreements and attempting to do so is likely to be time consuming and expensive. Furthermore, our strategic partners will likely seek to control certain decisions regarding the development and commercialization of our therapeutic candidates and may not conduct those activities in the manner or time we would like.

If we fail to establish and maintain strategic partnerships related to our therapeutic candidates, we will bear all of the risk and costs related to the development and commercialization of our therapeutic candidates. This may require us to seek additional financing, hire additional employees and otherwise develop expertise which we do not have. These factors could materially and adversely affect the development or commercial success of any product-candidate for which we do not arrange a strategic partnership.

#### **Risks related to managing our business and operations**

***We face risks related to health epidemics, pandemics and other widespread outbreaks of contagious disease, including the ongoing COVID-19 pandemic, which could significantly disrupt our operations, impact our financial results or otherwise adversely affect our business.***

Significant outbreaks of contagious diseases and other adverse public health developments could have a material adverse effect on our business operations and operating results. For example, the spread of COVID-19 has had, and identification of new variants of COVID-19 could have, an adverse effect on segments of the global economy and our operations. As a result of the ongoing COVID-19 pandemic or similar public health crises that may arise, we may experience disruptions that could adversely affect our operations, research and development, preclinical studies, clinical trials and manufacturing activities we may conduct, some of which may include:

- delays or difficulties in commencing enrollment of patients in our planned clinical trials;
- the impact from potential delays, including potential difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures that are deemed non-essential, which may impact the integrity of subject data and clinical trial endpoints;

- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- interruptions in preclinical studies due to restricted or limited operations at our laboratory facility;
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; and
- interruption or delays to our sourced discovery and clinical activities.

in March 2021, we moved our laboratory operations to facilities leased from the Massachusetts Biomedical Initiatives, Inc., or MBI, in Worcester, Massachusetts. In December 2022, we signed a two-year sublease for office/lab space in Newton, Massachusetts. In late January 2023, we began moving our operations to this new facility. This new space allows both lab personnel and the rest of the team to be housed in one location. While we believe we will have sufficient access to the Newton facility, there is no assurance that this will be the case. Should access to the Newton facility be limited, or should other pandemic-related restrictions be imposed, our development work would be further adversely affected. The extent of such adverse effects will depend on future developments which are highly uncertain and cannot be predicted. In addition, the Newton facilities may not meet all our requirements.

The extent to which the ongoing COVID-19 pandemic or other health problems ultimately affect our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

***We will need to grow the size of our organization, and we may experience difficulties in managing this growth.***

As of January 30, 2023, we had 19 employees including five with Ph.D.'s. We also utilize various outside companies and individuals under consulting or other arrangements to support our operations. As our clinical development and commercialization plans and strategies develop, and as we continue to operate as a public company, we expect to need additional human resources in areas including management, clinical and regulatory, manufacturing, research, medical, sales, marketing, financial, and other. Future growth would impose significant added responsibilities on members of management, including:

- recruiting, integrating, retaining and motivating additional employees;
- managing our development efforts effectively, including the clinical, manufacturing and quality review process for our therapeutic candidates, while complying with our contractual obligations to contractors, collaboration partners and other third-parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our therapeutic candidates, if approved, will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on third- parties, including independent organizations, advisors and consultants, to provide certain services to support and perform our operations. There can be no assurance that the services of these third-parties will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality, accuracy or quantity of the

services provided is compromised for any reason, our clinical trials may be delayed or terminated, and we may not be able to obtain, or may be substantially delayed in obtaining, regulatory approval of our therapeutic candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other suitable outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully execute the tasks necessary to further develop and commercialize our therapeutic candidates and, accordingly, may not achieve our development and commercialization goals.

***Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.***

Our ability to compete in the highly competitive oncology industry depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are dependent on our management, scientific and medical personnel and advisors, including our co-founder and CEO, Robert Michael Dudley, our co-founder and Chief Technology Officer, Dr. Zdravka Medarova, our CFO and director, Thomas A. Fitzgerald, our chief scientist Dr. Peter Liu, our co-founder Dr. Anna Moore, our board of directors and members of our scientific and business advisory boards as well as our many consultants. The loss of the services of any of these individuals, and our inability to find suitable replacements, could result in delays in product development and materially harm our business.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

***The estimates of market opportunity and forecasts of market growth included in this prospectus or that we may otherwise provide may prove to be inaccurate, and even if the markets in which we compete achieve the forecasted growth, our business may not grow at similar rates, or at all.***

Market opportunity estimates and growth forecasts included in this prospectus or that we may otherwise provide are subject to significant uncertainty and are based on assumptions and estimates which may not prove to be accurate. The estimates and forecasts included in this prospectus relating to size and expected growth of our target market may prove to be inaccurate. Even if the markets in which we compete meet the size estimates and growth forecasts included in this prospectus, our business may not grow at similar rates, or at all. Our growth is subject to many factors, including our success in implementing our business strategy, which is subject to many risks and uncertainties.

***We may be exposed to significant foreign exchange risk.***

We incur expenses, and may in the future derive revenues, in a variety of currencies. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. To date, we have not had significant proportions of our spending tied to foreign currencies but this may change in the future. Thus, fluctuations in currency exchange rates could affect our results as expressed in U.S. dollars. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows.

***Compliance with governmental regulations regarding the treatment of animals used in research could increase our operating costs, which would adversely affect the commercialization of our products.***

The Animal Welfare Act, or AWA, is the federal law that covers the treatment of certain animals used in research. Currently, the AWA imposes a wide variety of specific regulations that govern the humane handling, care, treatment and transportation of certain animals by producers and users of research animals, most notably relating to personnel, facilities, sanitation, cage size, and feeding, watering and shipping conditions. Third-parties with whom we contract are subject to registration, inspections and reporting requirements under the AWA and comparable rules, regulations, and or obligations that may exist in many foreign jurisdictions. Furthermore, some states have their own regulations, including general anti-cruelty legislation, which establish certain standards in handling animals. Comparable rules, regulations, and/or obligations exist in many foreign jurisdictions. If we or our contractors fail to comply with regulations concerning the treatment of animals used in research, we may be subject to fines and penalties and adverse publicity, and our operations could be adversely affected.

***Our ability to use our net operating loss carryforwards and certain tax credit carryforwards may be subject to limitation.***

We have net operating loss carryforwards and tax credit carryforwards for U.S. federal and state income tax purposes which begin to expire in future years. Additionally, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, changes in our ownership may limit the amount of our net operating loss carryforwards and tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50 percentage points within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards before they expire. Private placements and other transactions that have occurred since our inception, as well as our initial public offering, may trigger such an ownership change pursuant to Section 382. Any such limitation, whether as the result of this offering, our initial public offering, prior private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us, could have a material adverse effect on our results of operations in future years.

The reduction of the corporate tax rate under the Tax Cuts and Jobs Act of 2017, or the Tax Cuts and Jobs Act, may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to us. Our ability to utilize those net operating loss carryforwards could be limited by an “ownership change” as described above, which could result in increased tax liability to us.

**Risks related to our intellectual property**

***Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.***

Our business will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our therapeutic candidates, their respective components, synthetic intermediates, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third-parties from making, using, selling, offering to sell or importing our therapeutic candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities and whether a court would issue an injunctive remedy. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any therapeutic candidates we may develop may be adversely affected.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. The patenting process is subject to numerous risks and there can be no assurance that we will be successful in obtaining patents for which we have applied. In addition, we may not pursue, obtain, or maintain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third-parties and are reliant on our licensors or licensees.

The strength of patents in the biotechnology and biopharmaceutical fields involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents with claims that cover our therapeutic candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third-parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our technology, including our therapeutic candidates, or prevent others from designing around the claims in our patents. If the breadth or strength of protection provided by the patent applications we hold with respect to our therapeutic candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our therapeutic candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our therapeutic candidates under patent protection would be reduced.

We cannot be certain that we were the first to file any patent application related to our technology, including our therapeutic candidates, and, if we were not, we may be precluded from obtaining patent protection for our technology, including our therapeutic candidates.

Some of the patents that we control were filed prior to March 16, 2013, and are thus based on the “first-inventor-to-invent” criterion. We cannot be certain that we are the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. Furthermore, for United States applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States Patent and Trademark Office, or USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Similarly, for United States applications in which at least one claim is not entitled to a priority date before March 16, 2013, derivation proceedings can be instituted to determine whether the subject matter of a patent claim was derived from a prior inventor’s disclosure.

We may be required to disclaim part or all of the term of certain patents. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent or patent application claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, would adequately protect our therapeutic candidates, or would be found by a court to be infringed by a competitor’s technology or product. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities and consider that we are free to operate in relation to our therapeutic candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our therapeutic candidates or our activities infringing such claims. The possibility exists that others will develop products that have the same effect as our products on an independent basis and that do not infringe our patents or other intellectual property rights or will design around the claims of patents that may issue that cover our products.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Under the enacted Leahy-Smith America Invents Act, or the America Invents Act, after March 2013, the United States moved from a “first-to-invent” to a “first-inventor-to-file” system. Under a “first-inventor-to-file” system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear, as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the “first-inventor-to-file” provisions. In addition, the courts have yet to address many of these provisions and the applicability of the America Invents Act and new regulations on specific patents discussed herein, for which issues have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.



The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to the compositions of our therapeutic candidates but that are not covered by the claims of our patents or those of our licensors;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any licensed patents and patent applications invented or developed using U.S. government funding, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or licensed issued patents or patent applications, if and when issued, may not cover our therapeutic candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third- parties;
- the inventors of our owned or licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- it is possible that our owned or licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that therapeutic candidates or diagnostic tests we develop may be covered by third- parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business.

***The patents covering the therapeutic use of our lead candidate, TTX-MC138, are currently issued only in the U.S. and there are no foreign applications pending for this invention at this time. We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.***

We have limited intellectual property rights outside the United States. Filing, prosecuting and defending patents on therapeutic candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third-parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to oncology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third-parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***Third-party claims of intellectual property infringement may be costly and time consuming to defend, and could prevent or delay our product discovery, development and commercialization efforts.***

Our commercial success depends in part on our ability to develop, manufacture, market and sell our therapeutic candidates and use our proprietary technologies without infringing the proprietary rights of third- parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and biopharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third-parties having patent or other intellectual property rights alleging that our therapeutic candidates and/or proprietary technologies infringe their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third-parties, exist in the fields in which we are developing our therapeutic candidates. As the biotechnology and biopharmaceutical industries expand and more patents are issued, the risk increases that our therapeutic candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third-parties may allege they have patent rights encompassing our therapeutic candidates, technologies or methods.

If a third-party claims that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the therapeutic candidate or technology at issue infringes on or violates the third-party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;

- a court prohibiting us from developing, manufacturing, marketing or selling our therapeutic candidates, or from using our proprietary technologies, unless the third-party licenses its product rights to us, which it is not required to do;
- if a license is available from a third-party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our therapeutic candidates and any license that is available may be non-exclusive, which could result in our competitors gaining access to the same intellectual property; and
- the need to redesign our therapeutic candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure.

***If we are not able to obtain and enforce patent and other intellectual property protection for our technologies, development and commercialization of our therapeutic candidates may be adversely affected and our business materially harmed.***

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licensing intellectual property rights of others, for our therapeutic candidates, methods used to manufacture our therapeutic candidates and methods for treating patients using our therapeutic candidates, as well as our ability to preserve our trade secrets, to prevent third-parties from infringing our proprietary rights and to operate without infringing the proprietary rights of others.

We and our current or future licensors and licensees may not be able to apply for or prosecute patents on certain aspects of our technologies at reasonable cost, in a timely fashion, or at all. The patent position of oncology companies can be highly uncertain because it involves complex legal and factual questions. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable, or that any issued or granted patents will include claims that are sufficiently broad to cover our therapeutic candidates or delivery technologies or provide meaningful protection from our competitors. If third-parties disclose or misappropriate our proprietary rights, it may materially and adversely affect us.

While we will endeavor to try to protect our technologies with intellectual property rights such as patents, the process of obtaining patents is time-consuming, expensive and sometimes unpredictable. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the process of pursuing patent coverage. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than otherwise would have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in oncology patents. Moreover, changes in either the patent laws or in the interpretations of patent laws may diminish the value of our intellectual property. As such, we do not know the degree of future protection that we might have with respect to our proprietary technologies. Further, patents have a limited lifespan.

In the United States and in industrialized countries generally, a patent expires 20 years after the first claim of priority (or first provisional U.S. patent application). Various limited extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our technologies, we may be more susceptible to competition, including from generic versions of our therapeutic candidates. Further, the extensive period of time between patent filing and regulatory approval for a

product- candidate limits the time during which we can market a product-candidate under patent protection, which may particularly and adversely affect our profitability.

***Intellectual property litigation and administrative patent office patent validity challenges in one or more countries could cause us to spend substantial resources and distract our personnel from their normal responsibilities.***

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their regular responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, patient support or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. As noted above, some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace, including compromising our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third-parties, or enter into development collaborations that would help us commercialize our current or future therapeutic candidates, if approved. Any of the foregoing events would harm our business, financial condition, results of operations and prospects.

***Confidentiality agreements with employees and others may not prevent unauthorized disclosure of proprietary information.***

Among the ways we attempt to protect our intellectual property is by entering into confidentiality agreements with our employees, consultants, and outside scientific advisors, contractors and collaborators. These agreements are intended to protect (i) proprietary know-how that may not be patentable or that we may elect not to patent, (ii) processes for which patents are difficult to enforce and (iii) other elements of our technology not covered by patents. Although we use reasonable efforts to protect our intellectual property, our employees, consultants, contractors, or outside scientific advisors might intentionally or inadvertently disclose our intellectual property to competitors or others. In addition, competitors may otherwise gain access to our intellectual property or independently develop substantially equivalent information and techniques. Enforcing a claim that another party illegally obtained and is using any of our intellectual property is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the U.S. sometimes are less willing than U.S. courts to protect intellectual property. Misappropriation or unauthorized disclosure of our intellectual property could materially and adversely affect our competitive position and may have a material adverse effect on us.

***Third-parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.***

As is common in the biotechnology and biopharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, and although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third-parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

***Patent terms may be inadequate to protect our competitive position on our therapeutic candidates for an adequate amount of time.***

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest claimed U.S. provisional filing date. Various extensions such as patent term adjustments and/or extensions, may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our therapeutic candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new therapeutic candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

***Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our current or future therapeutic candidates.***

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the U.S. and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a “first inventor to file” system. The first-inventor-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the U.S. and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

***If we are unable to adequately protect and enforce our trade secrets, our business and competitive position would be harmed.***

In addition to the protection afforded by patents we may own or license, we seek to rely on trade secret protection, confidentiality agreements, and license agreements to protect proprietary know-how that may not be patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes that involve proprietary know-how, information, or technology that may not be covered by patents. Although we require all of our employees, consultants, advisors and any third-parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, trade secrets can be difficult to protect, and we have limited control over the protection of trade secrets used by our collaborators and suppliers. We cannot be certain that we have or will obtain these agreements in all circumstances, and we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary information.

Moreover, any of these parties might breach the agreements and intentionally or inadvertently disclose our trade secret information and we may not be able to obtain adequate remedies for such breaches. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights and trade secrets to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third-parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, financial condition, results of operations and future prospects.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third-parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third-party, we would have no right to prevent them from using that technology or information to compete with us.

Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third-parties except in specific circumstances. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third-parties. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. Although we require all of our employees to assign their inventions to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third-parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***We may initiate, become a defendant in, or otherwise become party to lawsuits to protect or enforce our intellectual property rights, which could be expensive, time-consuming and unsuccessful.***

Competitors may infringe any patents we may own or license. In addition, any patents we may own or license also may become involved in inventorship, priority, validity or unenforceability disputes. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, in an infringement proceeding, a court may decide that one or more of any patents we may own or license is not valid or is unenforceable or that the other party's use of our technology that may be patented falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1). There is also the risk that, even if the validity of these patents is upheld, the court may refuse to stop the other party from using the technology at issue on the grounds that any patents we may own or license do not cover the technology in question or that such third-party's activities do not infringe our patent applications or any patents we may own or license. An adverse result in any litigation or defense proceedings could put one or more of any patents we may own or in-license at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, patient support or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Depending upon the timing, duration and specifics of FDA marketing approval of our current or future therapeutic candidates, one or more of the U.S. patents we own or license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Different laws govern the extension of patents on approved pharmaceutical products in Europe and other jurisdictions. However, we may not be granted a patent extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. For example, we may not be granted an extension in the U.S. if all of our patents covering an approved product expire more than fourteen years from the date of NDA approval for a product covered by those patents. Moreover, the applicable time period or the scope of patent protection afforded could be less than we

request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected.

Post-grant proceedings provoked by third-parties or brought by the USPTO may be necessary to determine the validity or priority of inventions with respect to our patent applications or any patents we may own or license. These proceedings are expensive, and an unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. In addition to potential USPTO post-grant proceedings, we may become a party to patent opposition proceedings in the EPO, or similar proceedings in other foreign patent offices or courts where our patents may be challenged. The costs of these proceedings could be substantial and may result in a loss of scope of some claims or a loss of the entire patent. An unfavorable result in a post-grant challenge proceeding may result in the loss of our right to exclude others from practicing one or more of our inventions in the relevant country or jurisdiction, which could have a material adverse effect on our business. Litigation or post-grant proceedings within patent offices may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the U.S.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

We may not be able to detect infringement against any patents we may own or license. Even if we detect infringement by a third-party of any patents we may own or license, we may choose not to pursue litigation against or settlement with the third-party. If we later sue such third-party for patent infringement, the third-party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us to enforce any patents we may own or license against such third-party.

#### **Risks related to our common stock and this offering**

***The price of our common stock may be volatile or may decline regardless of our operating performance, and shareholders may not be able to resell their shares at or above the price at which they purchase those shares.***

Prior to our initial public offering, there had been no public market for shares of our common stock and since then the trading volume in shares of our common stock on the Nasdaq Capital Market has been limited. You may not be able to sell your shares quickly or at the market price if trading in shares of our common stock is not active. An active or liquid market in our common stock may not develop or, if it does develop, it may not sustain. As a result of these and other factors, shareholders may not be able to resell their shares of our common stock at or above the public offering price at which they purchase those shares in this offering.

Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies or products by using our shares of common stock as consideration.

***The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.***

Our stock price has been volatile since our initial public offering and has declined significantly from our initial public offering price. The stock market in general, and the market for the stocks of biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations often unrelated or disproportionate to the operating performance of particular companies, for numerous reasons including as a result of the COVID-19 pandemic, economic events and expectations, and the war in the Ukraine. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. As a result of the foregoing, shareholders may not be able to sell their common stock at or above the price at which they

purchase those shares in this offering or otherwise. The market price for our common stock may be influenced by many factors, including:

- the success of competitive drugs or technologies;
- results of clinical trials of our current or future therapeutic candidates or those of our competitors;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our current or future therapeutic candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or license additional current or future therapeutic candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “*Risk Factors*” section.

If the market price of our common stock after this offering does not exceed the public offering price in this offering, you may not realize any return on your investment in us and you may lose some or all of your investment. Additionally, in the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company’s securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management’s attention and resources.

***We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.***

Our management will have broad discretion in the application of the net proceeds from the offering, including for any of the purposes described in “*Use of Proceeds*.” You will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used effectively. Because of the number and variability of factors that will determine our use of the net proceeds, their ultimate use may differ substantially from what we currently intend. The failure by our management to apply these funds effectively could adversely affect us. Pending their use, we may invest the net proceeds in short-term, investment- grade, interest-bearing securities or commercial bank accounts. While we intend to invest the net proceeds conservatively, there is no assurance that these investments will not decline in value or yield reasonable returns.

***If you purchase our common stock in this offering, you may incur immediate and substantial dilution in the book value of your shares.***

Depending on the public offering price of our stock and the number of shares of our stock that we sell in this offering, you may suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Further, we may issue options to purchase common stock at exercise prices significantly below the public offering price in this offering. To the



extent these options are ultimately exercised, investors purchasing common stock in this offering will sustain dilution. See the section of this prospectus titled “*Dilution*” for a more detailed description of these factors.

***There is no public market for the pre-funded warrants being sold in this offering.***

There is no established public trading market for the pre-funded warrants being sold in this offering. We will not list the pre-funded warrants on any securities exchange or nationally recognized trading system, including the Nasdaq Capital Market. Therefore, we do not expect a market to ever develop for the pre-funded warrants. Without an active market, the liquidity of the pre-funded warrants will be limited.

***The pre-funded warrants are speculative in nature.***

The pre-funded warrants do not confer any rights of common stock ownership on their holders, such as voting rights or the right to receive dividends, but merely represent the right to acquire shares of common stock at a fixed price. Commencing on the date of issuance, holders of pre-funded warrants may exercise their right to acquire the underlying common stock and pay the stated warrant exercise price per share.

Until holders of pre-funded warrants acquire shares of our common stock upon exercise thereof, holders of such pre-funded warrants will have no rights with respect to shares of our common stock. Upon exercise of the pre-funded warrants, such holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

***Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, restrict our operations or require us to relinquish rights to our technologies or current or future therapeutic candidates.***

Until such time, if ever, as we can generate the cash we need from operations, we expect to finance our cash needs through a combination of private and public equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of common stock or securities convertible into or exchangeable for common stock, the ownership interest of our shareholders will be diluted, and the terms of these new securities may include liquidation or other preferences that materially adversely affect the rights of our shareholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third-parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or current or future therapeutic candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, scale back or discontinue the development and commercialization of one or more of our therapeutic candidates, delay our pursuit of potential licenses or acquisitions, or grant rights to develop and market current or future therapeutic candidates that we would otherwise prefer to develop and market ourselves.

***Our executive officers, directors, principal stockholders and their affiliates will continue to exercise significant influence over our company after this offering, which will limit the ability of our other shareholders to influence corporate matters and could delay or prevent a change in corporate control.***

The holdings of our executive officers, directors, principal stockholders and their affiliates represent beneficial ownership, in the aggregate, of approximately 32.9% of our outstanding common stock as of January 30, 2023, or approximately 17.1% of our outstanding common stock after giving effect to this offering. The foregoing calculation excludes the possible exercise of options. If the specified individuals exercised all options they hold, and no other options were exercised by any other holder, the holdings of the specified individuals would represent beneficial ownership, in the aggregate, of approximately 39.4% of our outstanding common stock prior to this offering, or approximately 21.5% of our outstanding common stock after giving effect to this offering. As a result of their combined ownership, these stockholders, if they act together, will be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation or sale of all or substantially all of our assets. These stockholders acquired their shares of common stock for substantially less than the price of the shares of common stock sold in our initial public offering and being sold in this offering, and these stockholders may have

interests, with respect to their common stock, that are different from those of investors in our initial public offering or who invest in this offering, and the concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

***Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.***

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, or DGCL, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These antitakeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

***We are an emerging growth company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.***

We are an emerging growth company, or EGC, as defined in the JOBS Act, enacted in April 2012. For as long as we continue to be an EGC, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not EGCs, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-

Oxley Act, or Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an EGC for up to five years following the year in which we completed our initial public offering, although circumstances could cause us to lose that status earlier. We will remain an EGC until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the completion of our initial public offering (i.e., December 31, 2026), (b) in which we have total annual gross revenue of at least \$1.235 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed \$700.0 million as of the prior June 30th, and (ii) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

We may choose to take advantage of some, but not all, of the available exemptions. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, EGCs can also delay adopting new or revised accounting standards until such time as those standards apply to private companies, which may make our financial statements less comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

***If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.***

The trading market for our common stock may be influenced, in part, on the research and reports that industry or financial analysts publish about us or our business. If begun, we may lose research coverage by industry or financial analysts. If no or few analysts maintain coverage of us, the trading price of our stock would likely decrease. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock would likely decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

***We do not intend to pay cash dividends on our common stock, so any returns will be limited to the value of our stock.***

We currently anticipate that we will retain any future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying cash dividends for the foreseeable future. Furthermore, future debt or other financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of the value of their stock, if any, and which could decrease in value resulting in losses to our stockholders.

***We have identified material weaknesses in our internal control over financial reporting. If we are unable to remediate these material weaknesses, or if we identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business.***

As a public company, we are required to maintain internal control over financial reporting and to report any material weaknesses in such internal control. Section 404 of the Sarbanes-Oxley Act requires that we evaluate and determine the effectiveness of our internal control over financial reporting. A material weakness is a deficiency or combination of deficiencies in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis.

To date, we have had limited financial and accounting personnel to fully execute our accounting processes and address our internal control over financial reporting. In connection with the preparation of our financial statements as of and for the years ended December 31, 2021 and 2020, we identified material weaknesses in our control over financial reporting.

We did not design and therefore did not have an effective control environment commensurate with our financial reporting requirements. Specifically, we lacked a sufficient number of professionals with segregated duties with an appropriate level of accounting knowledge, training and experience to appropriately analyze, record and disclose accounting matters timely and accurately.

While these material weaknesses did not result in a misstatement for the years ended December 31, 2021 and 2020, each of the above material weaknesses could have resulted in a misstatement of the aforementioned account balances or disclosures that could have resulted in a material misstatement to the annual or interim financial statements that would not have been prevented or detected.

In order to remediate the material weaknesses in our internal control over financial reporting and address the material weaknesses in our accounting processes, we plan to establish more robust accounting policies and procedures, review the adoption of new accounting positions and the need for financial statement disclosures, and engage consultants to assist us in determining what personnel are needed and in evaluating new accounting policies.

We began implementing and plan to continue to implement steps to address the internal control deficiencies that contributed to the material weaknesses, including the following:

- hiring of additional finance and accounting personnel with requisite experience and technical accounting expertise, supplemented by third-party resources;
- documenting and formally assessing our accounting and financial reporting policies and procedures; and
- assessing significant accounting transactions and other technical accounting and financial reporting issues, preparing accounting memoranda addressing these issues and maintaining these memoranda in our corporate records.

While we believe that these efforts will improve our internal control over financial reporting, implementation of these and other measures will be ongoing and will require validation and testing of the design and operating effectiveness of our internal controls over a sustained period of financial reporting cycles. We cannot reasonably estimate when these remediation measures will be completed nor can we assure you that the measures we have taken to date, and are continuing to take, will be sufficient to remediate the material weaknesses we have identified or avoid potential future material weaknesses. If the steps we take do not correct the material weaknesses in a timely manner, we will be unable to conclude that we maintain effective internal controls over financial reporting. Furthermore, we may not have identified all material weaknesses, and our current controls and any new controls that we develop may become inadequate because of changes in conditions in our business. Accordingly, there continues to be a reasonable possibility that these deficiencies or others could result in a misstatement of our accounts or disclosures that would result in a material misstatement of our financial statements that would not be prevented or detected on a timely basis.

***If we continue to fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.***

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis, and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an EGC, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an EGC for up to five years. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation.

***Our amended and restated bylaws designate a certain court as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.***

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation and our amended and restated bylaws, (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or by-laws or (v) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein, or the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Unless we consent in writing to the selection of an alternate forum, the United States District Court for the District of Massachusetts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision, as our principal office is located in Boston, Massachusetts. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in our shares of common stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision may impose additional litigation costs on stockholders who assert the provision is not enforceable and may impose more general additional litigation costs in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts. In addition, these forum selection clauses in our bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. Moreover, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court were "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

***We could lose our listing on the Nasdaq Capital Market if the closing bid price of our common stock does not return to above \$1.00 for ten consecutive days during the 180 days ending July 7, 2023. The loss of the Nasdaq listing would make our common stock significantly less liquid and would adversely affect its value.***

As initially disclosed on the Current Report on Form 8-K filed on December 9, 2022, with the SEC, we received written notification from Nasdaq notifying us that our stock had failed to comply with Nasdaq Listing Rule 5550(a)(2), or the Minimum Bid Price Requirement, because the bid price for our common stock for 30 consecutive business days prior to such date had closed below the minimum \$1.00 per share requirement for continued listing. In accordance with Nasdaq Listing Rule 5810(c)(3)(A), or the Compliance Period Rule, we have been provided an initial period of 180 calendar days, or until June 7, 2023, or the Compliance Date, to regain compliance with the Minimum Bid Price Requirement. If, at any time during this 180-day period, the closing bid price for our common stock closes at \$1.00 or more per share for a minimum of 10 consecutive business days, as required under the Compliance Period Rule, Nasdaq will provide written notification to us that our stock complies with the Minimum Bid Price Requirement and the common stock will continue to be eligible for listing on the Nasdaq Capital Market.

If we do not regain compliance with the Minimum Bid Price Requirement by the Compliance Date, we may be eligible for an additional 180 calendar day compliance period. To qualify, we would be required meet the continued listing requirement for the market value of publicly held shares and all other initial listing standards for the Nasdaq Capital Market, with the exception of the

Minimum Bid Price Requirement, and would need to provide written notice to Nasdaq of our intention to cure the deficiency during the additional compliance period.

If it appears to the Nasdaq staff that we will not be able to cure the deficiency, the Nasdaq staff will provide written notice to us that our common stock will be subject to delisting. At that time, we may appeal the staff's delisting determination to a Nasdaq Hearing Panel, or the Panel. We expect that our stock would remain listed pending the Panel's decision. There can be no assurance that, if we do appeal any such delisting determination to the Panel, such appeal would be successful.

Upon a delisting from the Nasdaq Capital Market, our stock would likely be traded in the over-the-counter inter-dealer quotation system, more commonly known as the OTC. OTC transactions involve risks in addition to those associated with transactions in securities traded on the securities exchanges, such as the Nasdaq Capital Market, or, together, Exchange-listed stocks. Many OTC stocks trade less frequently and in smaller volumes than Exchange-listed stocks. Accordingly, our stock would be less liquid than it would be otherwise. Also, the prices of OTC stocks are often more volatile than Exchange-listed stocks. Additionally, institutional investors are usually prohibited from investing in OTC stocks, and it might be more challenging to raise capital when needed.

We will continue to monitor the closing bid price of our common stock and seek to regain compliance with the Minimum Bid Price Requirement within the allotted compliance period; however, there can be no assurance that we will regain compliance with the Minimum Bid Requirement or that if we do appeal a subsequent delisting determination, that such appeal would be successful.

### **General Risk Factors**

***Our internal computer systems, or those of our third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our current or future therapeutic candidates' development programs.***

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for our current or future therapeutic candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or current or future therapeutic candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our current or future therapeutic candidates could be delayed.

***We may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential or proprietary information, including personal data, damage our reputation, and subject us to significant financial and legal exposure.***

We rely on information technology systems that we or our third-party providers operate to process, transmit and store electronic information in our day-to-day operations. In connection with our product discovery efforts, we may collect and use a variety of personal data, such as name, mailing address, email addresses, phone number and clinical trial information. A successful cyberattack could result in the theft or destruction of intellectual property, data or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under state (e.g., state breach notification laws), federal (e.g., HIPAA, as amended by HITECH), and international law (e.g.,

the European Union, or EU, General Data Protection Regulation, or GDPR) and may cause a material adverse impact to our reputation, affect our ability to use collected data, conduct new studies and potentially disrupt our business.

We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. We also rely on our employees and consultants to safeguard their security credentials and follow our policies and procedures regarding use and access of computers and other devices that may contain our sensitive information. If we or our third-party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third-party providers could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third-parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business.

Like many other companies, we have on occasion experienced, and will continue to experience, threats to our data and systems and attempts to damage or steal our property, information or financial resources, including through malicious codes and viruses, phishing, business email compromise attacks, and attempted ransomware or other cyber-attacks. Whereas none of these instances has had a material impact on us so far, the number and complexity of these threats continue to increase over time. For example, in July 2021, we were subject to what we believe was a phishing attack. We do not believe this incident had a material impact on our business or financial condition. However, the number and complexity of these threats continue to increase. If a material breach of our information technology systems or those of our third-party service providers occurs, the market perception of the effectiveness of our security measures could be harmed and our reputation and credibility could be damaged. Such a material breach could also have a material adverse effect on our business, financial condition or results of operations.

***We or the third-parties upon whom we depend may be adversely affected by earthquakes, other natural disasters, or political and military events, and our business continuity and disaster recovery plans may not adequately protect us from any such serious disaster.***

Any unplanned or unexpected event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or man-made accidents or incidents that result in us being unable to fully utilize our facilities, or our third-party contract manufacturers being unable to operate their manufacturing facilities normally, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of or reduced access to these facilities or interruptions in the flow of supplies may result in increased costs, delays in the development of our therapeutic candidates or interruption of our business operations. Earthquakes or other natural disasters could further disrupt our operations and have a material and adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event were to occur that prevented us from using all or a significant portion of our facilities, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. Also, Russia's military attack on Ukraine could have a material adverse effect on our business, financial condition, results of operations and prospects.

The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third-party contract manufacturers, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed.

***Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.***

We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the U.S. and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing, patient support and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third- parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Efforts to ensure that our business arrangements with third-parties will comply with applicable healthcare laws and regulations will involve substantial costs. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, and exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, reputational harm, and we may be required to curtail or restructure our operations, any of which could adversely affect our ability to operate our business and our results of operations.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States, such as the U.K. Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is



wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities.

***Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.***

As widely reported, global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including periods of severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability, including most recently in connection with the novel coronavirus pandemic and inflation and potential recession concerns. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, or do not improve, it may make any debt or equity financing we seek to obtain more difficult, more costly, and more dilutive.

Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay, scale back or discontinue the development and commercialization of one or more of our therapeutic candidates or delay our pursuit of potential licenses or acquisitions. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

Furthermore, our stock price may further decline due in part to the volatility of the stock market and general economic conditions.

***Current economic circumstances may harm our business, financial condition and results of operations.***

Our overall performance depends, in part, on worldwide economic conditions. In recent months, we have observed increased economic uncertainty in the United States and abroad. Impacts of such economic circumstances include:

- reduced credit availability;
- higher borrowing costs;
- reduced liquidity;
- volatility in credit, equity and foreign exchange markets;
- declines in equity valuations, especially in the biopharmaceutical sector; and
- bankruptcies.

These developments could lead to supply chain disruption, inflation, higher interest rates, and uncertainty about business continuity, which may adversely affect our business, financial condition and our results of operations. They are likely to make obtaining equity capital more difficult and more expensive.

***Rising inflation rates have increased our operating costs and could negatively impact our operations.***

In addition, inflation rates, particularly in the United States, have increased recently to levels not seen in decades. Increased inflation has resulted in increased operating costs (including our labor costs), and may result in reduced liquidity, and limitations on our ability to access capital, including by raising debt and equity capital. In addition, the United States Federal Reserve has raised, and is expected to again raise, interest rates in response to concerns about inflation. Increases in interest rates, especially if coupled with reduced government spending and volatility in financial markets, may further increase economic uncertainty and heighten these risks.

***We may incur substantial costs in our efforts to comply with evolving global data protection laws and regulations, and any failure or perceived failure by us to comply with such laws and regulations may harm our business and operations.***

The global data protection landscape is rapidly evolving, and we may be or become subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, transfer, security and processing of personal data, such as information that we collect about participants and healthcare providers in connection with clinical trials.

Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, which may (i) create uncertainty in our business, (ii) affect our or our service providers' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal data, (iii) result in liability or (iv) impose additional compliance or other costs on us. Any failure or perceived failure by us to comply with federal, state, or foreign laws or self-regulatory standards could result in negative publicity, diversion of management time and effort, or proceedings against us by governmental entities or others. California passed the California Data Privacy Protection Act of 2018, or the CCPA, which went into effect in January 2020. The CCPA provides new data privacy rights for consumers and new operational requirements for companies, which may increase our compliance costs and potential liability. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as for private rights of action for certain data breaches that result in the loss of personal information. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact certain of our business activities. The CCPA may lead to similar laws in other U.S. states or at a national level, which could increase our potential liability and adversely affect our business.

In addition to our operations in the United States, which may be subject to healthcare and other laws relating to the privacy and security of health information and other personal information, if we establish operations or conduct clinical trials in Europe, we will be subject to European data privacy laws, regulations and guidelines. The General Data Protection Regulation, (EU) 2016/679, or GDPR, became effective on May 25, 2018, and deals with the collection, use, storage, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals in the European Economic Area, or EEA. The GDPR imposes a broad range of strict requirements on companies subject to the GDPR, including requirements relating to having legal bases for processing personal information relating to identifiable individuals and transferring such information outside the EEA, including to the United States, providing details to those individuals regarding the processing of their personal health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, keeping personal information secure, having data processing agreements with third-parties who process personal information, responding to individuals' requests to exercise their rights in respect of their personal information, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, and record-keeping. The GDPR increases substantially the penalties to which we could be subject in the event of any non-compliance, including fines of up to €10 million or up to 2% of our total worldwide annual turnover for certain comparatively minor offenses, or up to €20 million or up to 4% of our total worldwide annual turnover (i.e., revenues), whichever is greater, for more serious offenses. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers.

Further, national laws of member states of the EU are in the process of being adapted to the requirements under the GDPR, possibly implementing national laws which may partially deviate from the GDPR and impose different obligations from country to country. As a result, we do not expect to operate in a uniform legal landscape in the EEA. Also, as it relates to processing and transfer of genetic data, the GDPR specifically allows national laws to impose additional and more specific requirements or restrictions. European laws have historically differed quite substantially in this field, leading to additional uncertainty. The U.K.'s decision to leave

the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the U.K. In particular, it is unclear how data transfers to and from the U.K. will be regulated now that the U.K. has left the EU.

We may conduct clinical trials in the EEA where the GDPR would increase our responsibility and liability in relation to personal data that we process when such processing is subject to the GDPR, and when we are required to have in place additional mechanisms and safeguards to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR is a rigorous and time-intensive process that would increase our cost of doing business or require us to change our business practices. Despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. We expect that we will face uncertainty as to whether our efforts to comply with any obligations under European privacy laws will be sufficient. If we are investigated by a European data protection authority, we may face fines and other penalties. Any such investigation or charges by European data protection authorities could have a negative effect on our business and on our ability to attract and retain new clients or biotechnology and biopharmaceutical partners. We may also experience hesitancy, reluctance, or refusal by European or multi-national vendors or biotechnology and biopharmaceutical partners to use our products due to the potential risk exposure as a result of data protection obligations imposed on them by law, including the GDPR. Such vendors or biotechnology and biopharmaceutical partners may also view any alternative approaches to compliance as being too costly, too burdensome, too legally uncertain, or otherwise objectionable and therefore decide not to do business with us. Any of the foregoing could materially harm our business, prospects, financial condition and results of operations.

***We or any future strategic partners may become subject to third-party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights.***

We or any future strategic partners may be subject to third-party claims for infringement or misappropriation of patent or other proprietary rights. If we, our licensors or any future strategic partners are found to infringe a third-party patent or other intellectual property rights, we could be required to pay substantial damages, potentially including treble damages and attorneys' fees, if we are found to have willfully infringed. In addition, we, our licensors or any future strategic partners may choose to seek, or be required to seek, a license to technology owned by a third-party, which license may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be limited which could give our competitors access to the same technology or intellectual property rights as is licensed to us. If we fail to obtain a required license, we may be unable to effectively market certain approved products which could materially harm us. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in litigation or other proceedings relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and would divert our management's attention from operating the business. Most of our competitors would be better able to sustain the costs of complex patent litigation than us because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could materially delay our research and development efforts and significantly limit our ability to continue our operations.

***We incur significant costs as a result of operating as a public company, and our management devotes substantial time to compliance activities and investor relations.***

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act which requires, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas, such as "say on pay" and proxy access. Recent legislation permits emerging growth companies to implement many of these requirements over a longer period and up to five years from the pricing of an initial public offering. We intend to continue to take advantage of this legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which

may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

In addition to substantially increasing our legal and financial compliance costs, we expect the rules and regulations applicable to public companies to continue to make some of our activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, or increase our costs, they could have a material adverse effect on our business, financial condition and results of operations and may require us to reduce costs in other areas of our business or increase the prices of any products or services we may offer in the future. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to comply with these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

***The increasing use of social media platforms presents new risks and challenges.***

Social media is increasingly being used to communicate about our clinical development programs and the diseases our therapeutics are being developed to treat, and we intend to utilize appropriate social media in connection with our commercialization efforts following approval of our therapeutic candidates, if any. Social media practices in the biotechnology and biopharmaceutical industries continue to evolve and regulations and regulatory guidance relating to such use are evolving and not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us, along with the potential for litigation related to off-label marketing or other prohibited activities and heightened scrutiny by the FDA, the SEC and other regulators. For example, patients may use social media channels to comment on their experience in an ongoing blinded clinical trial or to report an alleged adverse event. If such disclosures occur, there is a risk that trial enrollment may be adversely impacted, that we may fail to monitor and comply with applicable adverse event reporting obligations or that we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our therapeutic candidates. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. In addition, we may encounter attacks on social media regarding our company, management, therapeutic candidates or products. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements within the meaning of the federal securities laws, Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Exchange Act. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995 and are included in this prospectus for purposes of complying with those safe harbor provisions. All statements other than statements of historical facts contained in this prospectus and our other public filings are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “could,” “expects,” “plans,” “intends,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about our clinical development and trials, regulatory review and approvals, our results of operations and financial condition, liquidity, prospects, growth, strategies and the industry in which we operate. These forward-looking statements are subject to known and unknown risks and uncertainties, assumptions and other factors that could cause our actual results to differ materially from those expressed in, or implied by, these forward-looking statements. Factors that could cause these differences include, but are not limited to:

- our ability to expand our therapeutic candidate portfolio through internal research and development or the acquisition or in-licensing of intellectual property assets;
- the impact of the global outbreak of the COVID-19 coronavirus, including the spread of new strains of the virus, on our activities as described above and otherwise, including but not limited to our ability to enroll a sufficient number of patients to advance the above-described clinical trial;
- the results and timing of our preclinical and clinical trial activities;
- the therapeutic benefits, effectiveness and safety of our therapeutic candidates;
- our ability to receive regulatory approval for our therapeutic candidates in the United States, Europe and other geographies;
- the expected regulatory approval pathway for our therapeutic candidates, and our ability to obtain, on satisfactory terms or at all, the financing required to support operations, research, development, clinical trials, and commercialization of products;
- our reliance on third-parties for the planning, conduct and monitoring of clinical trials, for the manufacture of clinical drug supplies and drug product, and for other requirements;
- potential changes in regulatory requirements, and delays or negative outcomes from the regulatory approval process;
- our estimates of the size and characteristics of the markets that may be addressed by our therapeutic candidates;
- market acceptance of our therapeutic candidates that are approved for marketing in the United States or other countries;
- our ability to successfully commercialize our therapeutic candidates;
- the safety and efficacy of therapeutics marketed by our competitors that are targeted to indications which our therapeutic candidates have been developed to treat;
- the impact of natural disasters, global pandemics (including further outbreaks of existing strains of COVID-19 or new variants of the virus), labor disputes, lack of raw materials or other supplies, issues with facilities and equipment or other forms of disruption to business operations at our manufacturing or laboratory facilities or those of our vendors;
- our ability to utilize our proprietary technological approach to develop and commercialize our therapeutic candidates;

- potential collaborators to license and commercialize any therapeutic candidates for which we receive regulatory approval in the future in or outside of the United States;
- our heavy dependence on licensed intellectual property, including our ability to source and maintain licenses from third-party owners;
- our ability to protect our intellectual property and operate our business without infringing the intellectual property rights of others;
- our ability to attract, retain and motivate key personnel;
- our ability to generate revenue and become profitable;
- a potential delisting of our common stock from trading on the Nasdaq Capital Market if the closing bid price of our common stock does not return to above \$1.00 for ten consecutive days during the 180 days ending July 7, 2023; and
- other risks and uncertainties, including those listed under the caption “*Risk Factors*” of this prospectus.

The risks set forth above are not exhaustive. Other sections of this prospectus may include additional factors that could adversely affect our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time and it is not possible for management to predict all risk factors, nor can we assess the impact of all risk factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. Forward-looking statements contained in this prospectus reflect our current views with respect to future events and with respect to our business and future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

## INDUSTRY AND OTHER DATA

This prospectus may include industry, market, competitive position and other data. We obtain such information from industry publications and research, surveys and studies conducted by third-parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. This prospectus also may include data based on our own internal estimates and research, including estimates regarding the impact of the COVID-19 pandemic (or related pandemics caused by coronavirus variants) on our business, prospects, results of operations, and financial condition. Our internal estimates have not been verified by any independent source. While we believe any data obtained from industry publications and third-party research, surveys and studies and our own estimates are reliable, we have not independently verified such data. The industry in which we operate, as well as such third-party data and our internal estimates and research, are subject to a high degree of uncertainty and risks due to a variety of factors, including those described in “*Risk Factors*” elsewhere in this prospectus and our other public filings. These and other factors could cause our results to differ materially from those expressed in this prospectus and our other public filings.

## USE OF PROCEEDS

We estimate that the net proceeds we will receive from the sale of our common stock in this offering, after deducting underwriting discounts and commissions and other offering expenses payable by us and assuming no sale of any pre-funded warrants, will be approximately \$9.7 million (or \$11.2 million if the underwriter exercises its option to purchase additional shares in full), based on an assumed public offering price of \$0.91 per share, which was the last reported sale price of our common stock on the Nasdaq Capital Market on January 30, 2023.

We currently expect to use the net proceeds from this offering, together with our existing funds, for product development activities, including one or more clinical trials with TTX-MC138, our lead therapeutic candidate, including related IND enabling studies, for further research and development of our other therapeutic candidates, and for working capital and other general corporate purposes.

From time to time in the ordinary course of our business, we may evaluate the acquisition of, investment in or in-licensing of additional therapeutic candidates that we believe are commercially viable or to develop ourselves. We could use a portion of the net proceeds from this offering for such purposes. We may also use a portion of the net proceeds of this offering for the acquisition or licensing of additional technologies, other assets or businesses, or for other strategic investments or opportunities, although we currently have no understandings, agreements or commitments with respect to any of the foregoing.

Although we currently anticipate that we will use the net proceeds from this offering as described above, there may be circumstances where we determine that a different use of our funds is in the best interest of the company. The amounts and timing of our actual expenditures will depend upon numerous factors, including results and progress of our clinical trial activities, results of and progress of our preclinical development activities, the progress of any partnering efforts we conduct, our operating costs, technological advances, the competitive environment for our therapeutic candidates and other factors described in the section titled “*Risk Factors*” in this prospectus. Our management will have flexibility in applying the net proceeds from this offering and you will be relying on their judgment with regard to the use of these net proceeds. An investor purchasing shares of our common stock will not have the opportunity, as part of the investment decision, to evaluate the economic, financial or other information on which we base our decisions about how to use the proceeds or to make their own assessment of whether the proceeds are being used appropriately. It is possible that the net proceeds will be used in a way that does not yield a favorable, or any, return for us.

A \$0.10 increase (decrease) in the assumed public offering price per share set forth above would increase (decrease) the net proceeds to us from this offering by approximately \$1.1 million (or approximately \$1.3 million if the underwriter exercises its option to purchase additional shares in full), assuming the number of shares and pre-funded warrants offered by us, as set forth on the cover of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated expenses payable by us. An increase (decrease) of one million shares (or pre-funded warrants) sold by us in this offering would increase (decrease) the net proceeds to us from this offering by approximately \$0.8 million (or approximately \$0.8 million if the underwriter exercises its option to purchase additional shares in full), assuming the public offering price per share described above remains the same and after deducting underwriting discounts and commissions and estimated expenses payable by us. The information in this paragraph is illustrative only and will change based on the actual public offering price and other terms of this offering determined at the pricing of this offering.

The net proceeds from this offering, together with our existing cash and expected receipt of SBIR Award funds, are not expected to be sufficient to fund advancement of any of our therapeutic candidates through regulatory approval. Thus, we expect we will need to raise additional capital to complete development and commercialization of our therapeutic candidates for which results are not guaranteed.

Pending our use of the net proceeds from this offering as described above, we intend to invest the net proceeds in investment grade interest bearing instruments or will hold the proceeds in interest bearing or non-interest-bearing accounts in U.S. banks.



We believe that the net proceeds from this offering, together with our existing cash and our anticipated receipt of funds under our SBIR Award, will enable us to fund our operating expenses and capital expenditure requirements into the third quarter of 2023. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. We also believe that the amount of net proceeds from this offering allocated to preclinical development work on certain of our other therapeutic candidates will be sufficient to substantially complete their preclinical development. We will need to raise substantial additional funds to complete additional clinical trials on TTX-MC138, preclinical development work on other therapeutic candidates, and any clinical trials on our other therapeutic candidates before we can expect to commercialize any of our therapeutic candidates, if approved.

## **DIVIDEND POLICY**

We have never declared or paid any cash dividends on our capital stock. We intend to retain all available funds and future earnings, if any, for development and expansion of our business. Any future determination regarding the declaration and payment of dividends, if any, will be at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors deems relevant. Investors should not purchase our common stock with the expectation of receiving cash dividends.

## CAPITALIZATION

The following unaudited table sets forth our cash and our capitalization at September 30, 2022:

- on an actual basis; and
- on an as adjusted basis to give effect to the sale and issuance by us of 12,000,000 shares of our common stock in this offering, assuming no exercise of the over-allotment option and no sale of any pre-funded warrants, at an assumed public offering price of \$0.91 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on January 30, 2023, after deducting estimated underwriting discounts and commissions and other offering expenses payable by us.

You should read the following table together with the sections of this prospectus titled “*Summary Financial Data*,” as well as our financial statements and the related notes, and “*Management’s Discussion and Analysis of Financial Condition and Results of Operations*.”

	As of September 30, 2022 (unaudited)	
	Actual	As Adjusted
Cash	\$ 8,790,540	\$ 18,496,140
Stockholders’ equity		
Preferred stock – \$0.0001 par value; 10,000,000 shares authorized actual and as adjusted; no shares issued or outstanding actual or as adjusted	—	—
Common stock – \$0.0001 par value; 290,000,000 shares authorized; 12,977,234 shares issued and outstanding actual; 24,977,234 shares issued and outstanding as adjusted	\$ 1,298	\$ 2,498
Additional paid-in capital	30,979,092	40,683,492
Accumulated deficit	(22,736,193)	(22,736,193)
Total stockholders’ equity	8,244,197	17,949,797
Total capitalization	\$ 8,244,197	\$ 17,949,797

The as adjusted information discussed above is illustrative only and will be determined based on the actual public offering price and other terms of this offering determined between us and the underwriter at pricing. The number of shares of common stock at September 30, 2022, in the table above excludes the following:

- 3,017,033 shares of common stock issuable upon exercise of outstanding stock options at a weighted average exercise price of \$0.74 per share;
- 312,500 shares of common stock issuable upon the exercise of outstanding common stock purchase warrants at an exercise price of \$5.00 per share;
- 2,450,351 shares of common stock reserved for future issuance under our 2021 Stock Option and Equity Incentive Plan, or 2021 Plan; and
- 330,000 shares of common stock reserved for future issuance under our 2021 Employee Stock Purchase Plan, or ESPP.

## DILUTION

If you invest in our common stock in this offering, your ownership interest may be diluted immediately depending on the difference between the public offering price per share of our common stock (assuming no pre-funded warrants are sold in this offering) and the as adjusted net tangible book value per share of our common stock immediately after this offering (assuming no pre-funded warrants are sold in this offering).

At September 30, 2022, we had a net tangible book value of \$8,244,197 or \$0.635 per share. Net tangible book value per share represents our total tangible assets (total assets less intangible assets) less total liabilities at that date, divided by the total number of our outstanding shares of common stock at that date.

After giving effect to the sale and issuance of 12,000,000 shares of common stock in this offering, assuming no exercise of the over-allotment option, at an assumed public offering price of \$0.91 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on January 30, 2023, after deducting estimated underwriting discounts and commissions and other offering expenses payable by us, our as adjusted net tangible book value at September 30, 2022, would have been \$17,949,797, or \$0.718 per share of our common stock (assuming no pre-funded warrants are sold in this offering). This represents an immediate increase in net tangible book value of approximately \$0.083 per share to our existing stockholders and an immediate dilution of \$0.192 per share to new investors.

The dilutive or accretive effect per share to investors participating in this offering is determined by subtracting the as adjusted net tangible book value per share after this offering from the public offering price per share paid by investors participating in this offering. The following table illustrates this result (without giving effect to any exercise by the underwriter of its option to purchase additional shares) on a per share basis:

Assumed public offering price per share		\$	0.91
Net tangible book value per share at September 30, 2022	\$	0.635	
Increase in book value per share attributable to new investors	\$	0.083	
As adjusted net tangible book value per share after this offering		\$	0.718
Dilution per share to new investors		\$	0.192

A \$0.10 increase in the assumed public offering price would increase the as adjusted net tangible book value by \$0.128 per share and result in dilution to investors participating in this offering of \$0.247 per share, and a \$0.10 decrease in the assumed public offering price would decrease the as adjusted net tangible book value by \$0.039 per share and result in dilution to investors participating in this offering of \$0.136 per share, in each case assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and assuming no pre-funded warrants are sold in this offering, and after deducting estimated underwriting discounts and commissions and estimated expenses payable by us.

An increase of one million shares in the number of shares offered by us in this offering would increase our as adjusted net tangible book value by approximately \$8.9 million and our as adjusted net tangible book value per share would be \$0.724, representing dilution to new investors in this offering of \$0.186 per share. A decrease of one million shares in the number of shares offered by us in this offering would increase our as adjusted net tangible book value by approximately \$8.9 million resulting in an as adjusted net tangible book value per share of \$0.713 and dilution to investors participating in this offering of \$0.197 per share. The foregoing calculations assume that the public offering price remains the same, and are after deducting estimated underwriting discounts and commissions and estimated expenses payable by us.

If the underwriter's over-allotment option is exercised in full, our as adjusted net tangible book value per share after this offering would be approximately \$0.727 representing dilution to new investors purchasing common stock in this offering of \$0.183 per share. These calculations assume a public offering price of \$0.91 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on January 30, 2023, and are after deducting the estimated underwriting discounts and commissions and other offering expenses payable by us.

The table and discussion above are based on 12,977,234 shares of common stock outstanding at September 30, 2022, assume no sale of any pre-funded warrants, and exclude, as of that date, the following:

- 3,017,033 shares of common stock issuable upon exercise of outstanding stock options at a weighted average exercise price of \$0.74 per share;
- 312,500 shares of common stock issuable upon the exercise of outstanding common stock purchase warrants at an exercise price of \$5.00 per share;
- 2,450,351 shares of common stock reserved for future issuance under our 2021 Plan; and
- 330,000 shares of common stock reserved for future issuance under our 2021 ESPP.

To the extent that outstanding options or warrants are exercised, or shares are issued in connection with our equity incentive plans, you may experience dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that, in the future, additional capital is raised through the sale of equity, convertible debt securities, or securities with equity components, those issuances may result in dilution to our stockholders.

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*You should read the following discussion and analysis of our financial condition and plan of operations together with "Summary Financial Data" and the financial statements and related notes thereto, which are included elsewhere in this prospectus. Certain statements in this "Management's Discussion and Analysis of Financial Condition and Results of Operations" are forward-looking statements that are based on current expectations and involve various risks and uncertainties that could cause our actual results to differ materially from those expressed in these forward-looking statements. We encourage you to review the information in the "Cautionary Note Regarding Forward Looking Statements" and "Risk Factors" sections in this prospectus.*

### Company Overview

TransCode Therapeutics is an RNA oncology company created on the belief that cancer can be more effectively treated through the intelligent design and effective delivery of RNA therapeutics. For decades, RNA has been a topic of investigation by the scientific community as a potentially attractive therapeutic modality because it can target any gene and it lends itself to rational and straightforward drug design. RNA-based therapeutics are highly selective to their targets, potentially making available a broad array of previously undruggable targets in the human genome. The therapeutic potential of RNA in oncology remains unrealized due in large part to the difficulty in safely and effectively delivering synthetic RNAs called oligonucleotides to tumors. TransCode believes it has solved this challenge. The company has developed an RNA delivery platform, the TTX platform, which leverages an iron oxide nanoparticle already approved as a clinical cancer imaging agent and treatment for iron deficiency anemia, as the physical carrier of the oligonucleotide.

Our TTX delivery system is built around a core iron oxide nanoparticle designed to minimize kidney and liver clearance. This is expected to translate into a long circulation half-life that allows for efficient accumulation of the therapeutic candidate in tumor cells and metastatic sites. Nanoparticles similar in design to those we use have an excellent clinical safety record of low toxicity and low immunogenicity. Further, the ability to image these particles enables quantification of their delivery to target tissues.

### Advancing new RNA therapies through a modular approach

The TransCode TTX platform is modular by design, both at the level of the core nanoparticle and at the therapeutic loading. The size, charge, and surface chemistry of the core nanoparticles can be tuned to optimize them for the intended target and therapeutic load. Also, the therapeutic load can be adapted to the specific approach being developed, ranging from RNA interference, or RNAi, which includes small interfering RNAs, or siRNAs, antisense oligonucleotides, non-coding RNA mimics to mRNA-based cancer vaccines, and Clustered Regularly Interspaced Palindromic Repeats, or CRISPR, -based gene repair and replacement platforms as well as Pattern Recognition Receptors such as retinoic acid inducible gene, or RIG-I. The company believes that the TTX platform can further be used for developing RNA-targeted radiolabeled therapeutics and diagnostics candidates and other custom products targeting known and novel biomarkers and other genetic elements as they are discovered and validated. The TTX platform is intended to overcome issues of stability, efficiency, and immunogenicity faced by existing lipid and liposomal nanoparticle platforms while optimizing delivery to, and accumulation in, tumor cells and metastatic sites.

The company's lead therapeutic candidate, TTX-MC138, targets microRNA-10b, or miRNA-10b, a master regulator of metastatic cell viability in a range of cancers, including breast, pancreatic, ovarian, colon, glioblastomas, and others. TransCode submitted to FDA an eIND application on November 30, 2022, to conduct a FIH clinical trial with TTX-MC138-NODAGA-Cu<sup>64</sup> and received written authorization from the agency on December 23, 2022, that we are allowed to proceed with the Phase 0 clinical trial. In parallel, the company is conducting IND-enabling studies for a Phase I/II clinical trial with TTX-MC138.

The company's other preclinical programs include two solid tumor programs: TTX-siPDL1, an siRNA-based modulator of programmed death-ligand 1, or PD-L1, and TTX-siLIN28B, an siRNA-based inhibitor of RNA-binding protein LIN28B. TransCode also has three cancer agnostic programs: TTX-RIGA, an RNA-based agonist of the RIG-I-driven immune response in the tumor microenvironment; TTX-CRISPR, a CRISPR/Cas9-based therapy platform for the repair or elimination of cancer-causing genes inside tumor cells; and TTX-mRNA, an mRNA-based platform for the development of cancer vaccines meant to activate cytotoxic immune responses against tumor cells.

All these therapeutic candidates are intended to utilize our proprietary delivery mechanism and are designed with the goal of significantly improving outcomes for cancer patients.

We are also exploring LIN28B as a potential target in pancreatic cancer and other solid tumors under an option to license an siRNA technology from The General Hospital Corporation, d/b/a Massachusetts General Hospital, or MGH. The option has been extended to allow us time to complete our evaluation of this technology. Should the results of the evaluation meet our criteria for including this technology in our portfolio, we intend to negotiate adding it to our existing MGH license.

Additionally, we are interested in pursuing diagnostic approaches for RNA targets that might be relevant and important to informing treatment of patients using RNA therapeutics. Our 2018 license with MGH includes a patented microRNA screening assay with the potential to detect expression of microRNAs in patient blood. We intend to optimize this diagnostic test to detect miR-10b in blood samples from cancer patients with metastasis to compare our test results to standard of care measurements made using PCR, the gold standard of microRNA detection. Should we be able to determine that our test is able to detect microRNAs in blood samples with accuracy comparable to PCR results, we would expect to seek FDA approval of our assay. If approved, this test could be used as a screening assay to detect metastasis in a variety of tumor types. Also, we may be able to use this test to evaluate miR-10b expression before, during and after treatment to best determine timing of therapeutic intervention.

In September 2021, research conducted by MGH was published in *Cancer Nanotechnology*, entitled “Radiolabeling and PET-MRI microdosing of the experimental cancer therapeutic, MN-anti-miR10b, demonstrates delivery to metastatic lesions in a murine model of metastatic breast cancer.” This paper reported on an MGH study using a radiolabeled derivative of TTX-MC138 (referred to in the paper as MN-anti-miR10b). In this study, TTX-MC138 was tagged with copper-64, or Cu-64. As a result, highly sensitive and specific quantitative determination of pharmacokinetics and biodistribution, as well as observation of delivery of the Cu-64 labeled TTX-MC138 to metastases, was made in laboratory tests using noninvasive positron emission tomography-magnetic resonance imaging, or PET-MRI. The key results of the study suggest that TTX-MC138, when injected intravenously, accumulates in metastatic lesions. These results suggest that our TTX platform delivers its therapeutic candidate as intended and supports clinical evaluation of TTX-MC138. In addition, the MGH investigation describes a microdosing PET-MRI approach to measure TTX-MC138 biodistribution in cancer patients and its delivery to clinical metastases. (Microdoses are minute, subpharmacologic doses of a test compound, not greater than 0.1 micrograms.) The capacity to carry out microdosing PET-MRI studies in patients under an exploratory IND, or eIND, application could be important because it has the potential to facilitate FDA authorization of additional human studies. This research, published by Dr. Zdravka Medarova, our Chief Technology Officer and scientific co-founder, and others describes what we believe is an effective approach to assessing delivery of TTX-MC138 in metastatic cancer patients. Since the PET-MRI technique is sensitive enough to determine the concentration of radiolabeled drug candidate in the sub-picomolar range, microgram quantities of the radiolabeled drug candidate are believed to be sufficient to perform such a study in humans. We believe this capability has significant advantages in the initial phases of drug development. Because the low mass of the radiolabeled drug candidate does not induce reactions in humans, we believe the regulatory process will be less complex.

Dr. Medarova’s paper suggests that the radiolabeling does not impact tumor cell uptake or the ability of TTX-MC138 to engage its target. The paper also shows that the biodistribution of Cu-64 labeled TTX-MC138, when injected at a microdose, reflects its biodistribution at the level of a therapeutic dose. These key findings are expected to enable our FIH microdosing trial with TTX-MC138 in cancer patients with advanced solid tumors. We believe that a microdosing trial has numerous advantages:

- (i) allows more precise quantitation of the amount of TTX-MC138 delivered to the metastatic lesions because of the higher sensitivity and quantitative accuracy of positron emission tomography. By contrast, imaging of drug delivery by MRI alone is much less sensitive and less quantitative;
- (ii) permits measurement of the pharmacokinetics and biodistribution of TTX-MC138 not only in the metastatic lesions but in other tissues throughout the body. This knowledge can inform Phase I/II clinical trial designs by allowing us to determine drug candidate uptake and clearance from vital organs. By contrast, measurement of TTX-MC138 delivery by MRI alone would only allow us to assess drug candidate accumulation in the metastatic lesions;
- (iii) enables measurement of pharmacokinetic endpoints potentially informing dosing for Phase II/III clinical trials. Specifically, because of the high sensitivity and quantitative nature of PET-MRI, it may be possible to derive a precise calculation of drug candidate concentration in the metastatic lesions over time and then correlate that information to the effective dose defined in our preclinical studies; and

- (iv) further informs patient enrollment during Phase II/III trials by allowing patient inclusion in the trials based on which patients' metastases demonstrated accumulation of TTX-MC138 in prior trials.

Because of the benefits we believe we can derive from a microdosing Phase 0 trial, and reflecting the studies described in Cancer Nanotechnology, we have filed for and received written authorization from FDA to proceed with our proposed microdosing Phase 0 First-in-Human clinical trial.

Success in the microdosing trial could also validate delivery generally for our TTX pipeline which potentially opens-up additional relevant RNA targets that have been previously undruggable. Concurrent with the Phase 0 trial, we expect to continue studies to support an IND for a Phase I clinical trial with TTX-MC138.

In the microdose Phase 0 trial, we plan to enroll up to 12 patients with advanced metastatic solid tumors, infuse a single microdose of radiolabeled TTX-MC138, and use PET-MRI to measure TTX-MC138 delivery to metastatic lesions and other tissues in the body. We plan to conduct the clinical portion of the trial at a major cancer center.

### ***Orphan Drug Designation***

In June 2022, the U.S. Food and Drug Administration, or FDA, granted our request for orphan drug designation, or ODD, for TTX-siPDL1 for the treatment of pancreatic cancer. ODD status provides several potential benefits including seven years of marketing exclusivity if the designated candidate subsequently receives FDA marketing approval, tax credits for qualified R&D expenses, and an exemption from payment of the Prescription Drug User Fee Amendment, or PDUFA, filing fee, a savings estimated to be more than \$3 million.

### ***SBIR Award***

In April 2021, we received a Fast-Track Small Business Innovation Research award, or SBIR Award, from the National Cancer Institute. The SBIR Award is expected to provide up to approximately \$2.3 million to fund a two-phased research partnership between us and Massachusetts General Hospital. The program commenced on April 15, 2021, and is expected to end in March 2024. We received SBIR Award funds of \$308,861 in May 2021 and were notified in May 2022 that \$1,129,316 of funding for the second year of the Award has been made available to the company. The company expects to receive up to \$870,684 in the third and final year of the SBIR. There is no guarantee that funds awarded for the third year of the SBIR grant will be received or not reduced in the sole discretion of the funding agency.

In the SBIR Award application, we proposed performing key translational experiments including IND-enabling and supporting imaging studies using MRI to assess delivery and target engagement of TTX-MC138 in metastatic lesions of breast cancer patients. The experiments are designed to achieve the following aims:

SBIR Phase I:

*Aim 1.* Optimize a method for measuring miR-10b expression in breast cancer clinical samples.

SBIR Phase II:

*Aim 2.* File an IND application for TTX-MC138.

*Aim 3.* Use imaging to determine the uptake of TTX-MC138 by radiologically-confirmed metastases in breast cancer patients.

We demonstrated that we achieved the first milestone which included development and validation of a method for the use of a test called qRT-PCR to measure miR-10b expression in patient blood and tissue samples. The qRT-PCR test is often considered the gold standard for quantifying circulating miRNAs with high sensitivity and specificity and with a wide analytical measurement range.



## ***Financial Operations Overview***

From inception in January 2016 through approximately mid-2021, we devoted substantially all of our efforts and financial resources to organizing and staffing our company, business planning, raising capital, securing intellectual property rights, conducting limited research and development activities, and preparing for manufacturing clinical-trial quantities of our lead product candidate. Following our IPO, we have expanded our R&D activities and our company operations. We do not have any products approved for sale and have not generated any revenue from product sales. We may never be able to develop or commercialize a marketable product. We have not yet completed any clinical trials, but we have obtained written FDA authorization to proceed with our Phase 0 clinical trial. We have not manufactured a commercial-scale drug, or conducted sales and marketing activities. Through September 30, 2022, we had received gross proceeds of approximately \$31.5 million primarily from our IPO and from borrowings obtained between 2018 and 2020 under convertible promissory notes.

We have incurred significant operating losses since inception. Our net losses were approximately \$12.4 million and approximately \$6.8 million for the nine months ended September 30, 2022, and the year ended December 31, 2021, respectively. At September 30, 2022, we had an accumulated deficit of approximately \$22.7 million. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates for which there is no assurance of occurrence. We expect that our expenses and capital requirements will increase substantially in connection with our ongoing activities, particularly if and as we:

- continue preclinical studies and initiate clinical trials for TTX-MC138 and other product candidates we may develop;
- advance the development of our product candidate pipeline;
- continue to develop and expand our proprietary TTX platform to identify additional product candidates;
- obtain new intellectual property and maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for our product candidates that successfully complete clinical trials, if any;
- hire additional clinical, scientific, commercial and administrative personnel to increase our overall knowledge base, scientific expertise, experience and capabilities;
- acquire or license additional product candidates or technologies;
- expand our infrastructure and facilities to accommodate increased activities and personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our research and development programs, any future commercialization efforts and our further transition to operating as a public company.

Furthermore, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, insurance, investor relations and other expenses that we did not incur as a private company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our business strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through sales of equity, debt financings or other capital sources, which may include collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential licenses or acquisitions.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate

product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

At December 31, 2022, we had cash of approximately \$5.0 million. We believe that our cash as of December 31, 2022 will be sufficient to fund our operating expenses and capital expenditure requirements through the first quarter of 2023. We expect to receive up to \$870,684 for the third year of the SBIR, although there is no guarantee that these funds will be received. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. To finance our operations beyond that point, we will need to raise additional capital which cannot be assured. If we are unable to raise additional capital in sufficient amounts or on terms we find acceptable, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. See “Liquidity and capital resources.”

### ***Impact of the Novel Coronavirus (COVID-19) Pandemic***

We believe that COVID-19 precautions and effects have affected and will continue to directly or indirectly affect the timeline for some of our preclinical studies and possibly our planned clinical trials. As a result of the outbreak, many companies have experienced disruptions in their operations and in markets served. To date, we have initiated some precautionary measures and we may take additional precautionary measures intended to help ensure our employees’ well-being and minimize business disruptions. These measures include devising contingency plans and securing additional resources from third-party service providers. Certain of our third-party service providers have also experienced delays, shutdowns or other business disruptions. We are continuing to assess the impact of the COVID-19 pandemic on our current and future business operations, including our expenses, preclinical studies and planned clinical studies, and other development timelines, as well as on our industry and the healthcare system.

### **Components of our results of operations**

#### *Revenue*

To date, we have not generated any revenue from any sources, including from product sales, and we do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval of any product candidate, or license agreements with third parties, we may generate revenue in the future from product sales or licensing agreements. However, there can be no assurance as to when, if ever, we will generate any such revenue.

#### *Operating expenses*

##### *Research and development expenses*

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts and the development of product candidates. We expense research and development costs as incurred, which include:

- expenses incurred in performing preclinical and clinical development;
- expenses incurred to conduct the necessary preclinical studies and clinical trials related to seeking regulatory approval to market our product candidates that successfully complete clinical trials;
- expenses incurred under agreements with contract research organizations, or CROs, or collaborators conducting drug discovery work, preclinical studies, and clinical trials for us, and with contract manufacturing organizations, or CMOs, engaged to produce preclinical and clinical drug substance and drug product for our research and development activities;
- other costs related to acquiring and manufacturing materials in connection with our drug discovery efforts and our preclinical studies, materials for our clinical trials, including manufacturing validation batches, as well as costs related to investigative sites and consultants that conduct our clinical trials, preclinical studies and other scientific development services;

- payments made under third-party licensing, acquisition and option agreements;
- personnel-related expenses, including salaries, benefits, travel and other related expenses, and share-based compensation expense for research and development personnel;
- costs related to compliance with regulatory requirements; and
- allocated facilities costs, including rent and utilities, and depreciation and other facilities or equipment expenses.

We recognize external development costs based on an evaluation of the progress toward completion of specific tasks using information provided to us by our employees, consultants and service providers. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. Nonrefundable advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such amounts are subsequently expensed as the related goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

We intend to track our research and development expenses on a program-by-program basis. Our direct external research and development expenses comprise primarily payments to outside consultants, collaborators, CROs, CMOs, research laboratories, and suppliers in connection with our preclinical development, process development, manufacturing and clinical development activities. Our direct external research and development expenses also include fees incurred under license and option agreements. We do not intend generally to allocate all costs of senior management personnel, certain costs associated with our discovery efforts, certain supplies used in the laboratory, and certain facilities costs, including depreciation or other indirect costs, to specific programs when these costs are incurred across multiple programs and where it may not be practical to track them by program. We use internal resources along with outside parties primarily to conduct our research and discovery as well as for managing our preclinical development, process development, manufacturing and clinical development activities.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally are expected to have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect that our research and development expenses will increase substantially over the next several years if we commence planned clinical trials for TTX-MC138, as well as conduct other preclinical and clinical development, including submitting regulatory filings. In addition, we expect our discovery research efforts and related personnel costs will increase and, as a result, we expect our research and development expenses, including costs associated with share-based compensation, will increase significantly over prior levels. Also, we may incur additional expenses related to milestone and royalty payments to third parties with whom we have entered or may enter into license, acquisition and option agreements to assess, use or acquire intellectual property rights or rights to future product candidates.

In September 2021, we signed a statement of work with a European CMO to manufacture TTX-MC138 in accordance with good manufacturing practices, or GMP. Separately, we engaged a contract research organization, or CRO, to assist us in designing and conducting IND-enabling studies including pharmacokinetic, or PK, studies. These studies are designed to examine multiple parameters with a range of analytical support in support of regulatory submissions using radiolabeled or non-radiolabeled test substances. Toxicokinetic assessments can be conducted in parallel or concurrent with ongoing toxicology programs and in compliance with good laboratory practice, or GLP, requirements. We also engage analytical testing laboratories to provide testing and other services, as well as documentation and reporting that meet regulatory requirements.

On July 29, 2022, we signed a five-year strategic collaboration agreement with The University of Texas M. D. Anderson Cancer Center (“MD Anderson”). Under this alliance, the Company anticipates making certain expenditures with respect to Phase I and Phase II clinical trials which it expects will be conducted in part by MD Anderson as a primary investigator site. MD Anderson will also provide preclinical work under the alliance. The details of clinical and preclinical work are to be mutually agreed by the parties prior to commencing work. We have committed to fund up to \$10 million over the term of the collaboration, with \$500,000 of such amount payable within the first year. Subsequent payments are \$2 million on the first anniversary of the effective date of the agreement and \$2.5 million on each of the second, third and fourth anniversaries thereof. These are funds we had already budgeted for research and

development, so do not represent additional spending. We will need to raise additional funds to meet the subsequent payment obligations.

MD Anderson's website indicates that "Strategic alliances and commercialization agreements aim to provide space for innovative solutions to accelerate breakthrough discoveries in cancer research while developing deeper relationships with companies that share a similar vision. This can be done through joint development opportunities, collaborations, licensing or a combination of these elements." Through our alliance, scientists from TransCode and MD Anderson will collaborate on preclinical studies seeking to further validate TransCode's therapeutic and diagnostic candidates, and to expand the reach of TransCode's discovery engine. The results of these studies are expected to inform future clinical trials with these agents, including trials to be led at MD Anderson.

At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our product candidates or when, if ever, material net cash inflows may commence from or related to any of our product candidates. The successful development and commercialization of our product candidates is highly uncertain due to the numerous risks and uncertainties associated with product development and commercialization, including:

- the scope, progress, outcome and costs of our preclinical development activities, clinical trials and other research and development;
- the requirement to establish an appropriate safety and efficacy profile in IND-enabling studies;
- the timing and terms of regulatory approvals, if any, to conduct clinical trials;
- the number of sites and patients needed to complete clinical trials, the length of time required to enroll suitable patients and complete clinical trials, and the duration of patient follow-ups;
- the timing, receipt and terms of marketing approvals, if any, from applicable regulatory authorities including the FDA and regulators outside the U.S.;
- the extent of any post-marketing approval commitments that may be required by regulatory authorities;
- establishing clinical and commercial manufacturing capabilities or making arrangements with third-party manufacturers to supply the quantities and quality of product we need;
- development and timely delivery of clinical-grade and commercial-grade drug formulations as required for use in our clinical trials and for commercial launch;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- significant and changing government regulation;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- competitive developments;
- the impact of any business interruptions on our operations, including the timing and enrollment of patients in our planned clinical trials, or on operations of our manufacturers, suppliers, or other vendors resulting from the COVID-19 pandemic or similar public health crisis or for any other reason; and
- maintaining an acceptable safety profile of our product candidates following their approval, if obtained.

Any changes in or adverse outcome of any of these variables or others with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of our product candidates.

*General and administrative expenses*

General and administrative expenses consist primarily of staffing costs comprising mainly salaries, benefits, and share-based compensation expense for personnel serving in executive, finance, and other business functions; insurance costs, especially directors and officers liability insurance; professional fees for legal, patent, consulting, investor and public relations, accounting, tax and audit services; corporate and office expenses, including facilities costs; and information technology costs.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our R&D and business activities, prepare for potential commercial activities including possible partnerships for the development or marketing of approved product candidates, if any, and the increased requirements of a larger and publicly-traded company. We also anticipate that we will incur significantly increased accounting, audit, tax, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with operating as a public company. Additionally, if and when we believe regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and other personnel-related expenses as we prepare for commercial operations, especially as it relates to the sales and marketing of that product candidate. There is a risk that we could incur the foregoing expenses but not receive the anticipated regulatory approval.

In September 2021, we engaged an independent executive compensation advisory firm to support the continued development of our compensation programs and governance model for officers, directors and employees. Our goal is to ensure that our culture, values, and strategic priorities are effectively represented in our compensation philosophy and strategy.

***Other income (expense)***

*Interest expense*

Interest expense previously consisted primarily of accrued interest on convertible promissory notes and other charges related to the notes. Since the notes converted into shares of common stock concurrent with our IPO, we no longer incur interest expense on these notes. Under our payment program for directors and officers liability insurance, we incur certain financing charges.

*Interest income*

Interest income consists primarily of income earned on our cash balances. Our interest income has not been significant due to low cash balances and, since the IPO, low interest rates earned on our cash balances.

*Grant income*

From time to time, we apply for grant funding from government programs and may, in the future, apply for grants from non-government sources as well. There is no assurance that any grants will be awarded to us or, if awarded, that we will receive all the funds expected from such award. Grant payments received in advance of us performing the work for which the grant was awarded are recorded as deferred grant income on our balance sheets. Grant income is recognized in our statements of operations as and when earned for performance of the specific R&D activities for which the grants are awarded. Grant income earned in excess of grant payments received is recorded as grant receivable on our balance sheets.

## Results of operations

The following table summarizes the approximate amounts of our unaudited results of operations for the periods indicated:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2022	2021	Change	2022	2021	Change
	(in thousands)					
<b>Operating expenses</b>						
Research and development	\$ 3,044	\$ 993	\$ 2,051	\$ 7,546	\$ 1,468	\$ 6,077
General and administrative	1,910	1,367	543	5,593	1,696	3,897
Total operating expenses	4,954	2,360	2,594	13,139	3,165	9,974
<b>Operating loss</b>	(4,954)	(2,360)	(2,594)	(13,139)	(3,165)	(9,974)
<b>Other income (expense)</b>						
Change in fair value of derivative liabilities	—	—	—	—	(867)	867
Change in fair value of warrant liability	—	(1)	1	—	(6)	6
Grant income	655	32	623	697	89	608
Interest expense	—	(0)	0	—	(95)	95
Interest income	9	0	9	11	0	11
Total other income (expense)	664	31	633	708	(879)	1,587
<b>Net loss</b>	<u>\$ (4,290)</u>	<u>\$ (2,329)</u>	<u>\$ (1,961)</u>	<u>\$ (12,431)</u>	<u>\$ (4,044)</u>	<u>\$ (8,387)</u>

### Comparison of the three and nine months ended September 30, 2022 and 2021

#### Research and development expenses

Research and development, or R&D, expenses increased \$2,051 thousand and \$6,077 thousand for the three and nine months ended September 30, 2022, respectively, compared to the same periods the prior year. The increases were primarily due to purchases of materials, compensation and related personnel costs which we largely did not have in the 2021 period except for stock compensation expenses until after our IPO in July 2021, and regulatory, purchased services and consulting costs, offset in part by increased grant income and reduced costs related to development of intellectual property.

#### General and administrative expenses

General and administrative expenses increased \$543 thousand and \$3,897 thousand for the three and nine months ended September 30, 2022, respectively, compared to the same periods the prior year. The increases were primarily a result of increased expenses for directors and officers liability insurance, compensation and related personnel costs which we largely did not have in the 2021 period except for stock compensation expenses until after our IPO in July 2021, and corporate and other costs of being a public company, offset in part by reduced accounting and audit expenses.

#### Grant Income

Grant income increased \$623 thousand and \$608 thousand in the three and nine months ended September 30, 2022, respectively, compared to the same periods the prior year. Grant income was recognized under an NIH grant awarded in April 2021 to fund certain costs to advance our lead therapeutic candidate into clinical trials. Charges under the grant in the three and nine months ended September 30, 2022, did not commence until June 1, 2022, because notice of the second year of the Award was not issued until May 31, 2022.

#### Change in fair value of derivative liabilities

The change in fair value of derivative liabilities was \$0 for the three months ended September 30, 2022 and 2021, compared to \$0 in the nine months ended September 30, 2022, and a credit of \$867 thousand in the nine months ended September 30, 2021. The derivative liabilities were extinguished at the IPO, when the related notes converted into common stock.

*Change in fair value of warrant liability*

The fair value of the warrant liability charge was \$0 for the three and nine months ended September 30, 2022. In the 2021 periods, there was a credit of \$1 thousand for the three months ended September 30, 2021, and \$6 thousand for the nine months ended September 30, 2021. The warrants were exercised shortly prior to our IPO and the warrant liability was extinguished at that time.

*Interest expense*

The charge to interest expense was \$0 for the three months ended September 30, 2022 and 2021, and \$0 and \$95 thousand charged in the nine months ended September 30, 2022 and 2021, respectively. The three \$0 amounts reflect conversion of our convertible promissory notes into our common stock in connection with our IPO while the \$95 thousand in the nine months ended September 30, 2021, related to the notes prior to conversion.

*Comparison of the years ended December 31, 2021 and 2020*

	Years Ended December 31,		
	2021	2020 (in thousands)	Change
Operating Expenses			
Research and development	\$ 2,754	\$ 284	\$ 2,470
General and administrative	3,397	442	2,955
Total operating expenses	6,151	727	5,425
Loss from operations	(6,151)	(727)	(5,425)
Other Income (expense)			
Change in fair value of derivative liability	(867)	(1,208)	341
Change in fair value of warrant liability	(6)	(15)	9
Grant income	278	—	278
Loss on sale of assets	(3)	—	(3)
Interest expense	(95)	(395)	300
Interest income	1	—	1
Total other income (expense)	(692)	(1,617)	926
Net loss	\$ (6,843)	\$ (2,344)	\$ (4,499)

*Research and development expenses*

Research and development, or R&D, expenses increased \$2,470 thousand for the year ended December 31, 2021, compared to the year ended December 31, 2020. The increase was primarily due to purchases of materials, compensation and related personnel costs which we did not have in 2020, except for stock compensation expenses, license fees and costs related to development of intellectual property, and lab facility expenses.

*General and administrative expenses*

General and administrative expenses increased \$2,955 thousand for the year ended December 31, 2021, compared to the year ended December 31, 2020. The increase was primarily a result of increased expenses for directors and officers liability insurance, compensation and related personnel costs which we did not have in 2020, except for stock compensation expenses, and investor relations and other costs of being a public company.

*Grant Income*

Grant income of \$278 thousand in the year ended December 31, 2021, was recognized under an NIH grant awarded in April 2021 to fund certain study costs to advance our lead therapeutic candidate into clinical trials. No grant income was recognized in the prior year.

#### *Change in fair value of derivative liabilities*

The fair value of derivative liabilities charge was \$867 thousand for the year ended December 31, 2021. The derivative liabilities represent an embedded derivative in our convertible promissory notes which were issued at various times between 2018 and 2020. At each balance sheet date, we estimated the fair value of the derivative liability and recognized any change in our statements of operations. At the IPO, when these notes converted into common stock, the balance of the derivative liabilities was extinguished.

#### *Change in fair value of warrant liability*

The fair value of the warrant liability charge was \$6 thousand for the year ended December 31, 2021. We issued warrants to purchase shares of our common stock in consideration for finder's services in connection with a sale of one of our convertible promissory notes in 2018. We classified these warrants as a liability on our balance sheets which we remeasured to fair value at each reporting date. Changes in the fair value of the warrant liability were recognized as a component of other income (expense) in our statements of operations. The warrants were exercised shortly prior to our initial public offering. Thereafter, there will be no liability related to these warrants.

#### *Interest expense*

Interest expense decreased \$300 thousand for the year ended December 31, 2021, compared to the year ended December 31, 2020. The decrease reflects conversion of our convertible promissory notes into our common stock in connection with our IPO, and the agreement by noteholders to cease interest accrual at May 31, 2021.

### **Liquidity and capital resources**

#### ***Sources of liquidity***

Since inception, we have not generated any revenue from product sales or any other sources, and we have incurred significant operating losses and negative cash flows from our operations. We have not yet commercialized any of our product candidates and we do not expect to generate revenue from sales of any product candidates for several years, if ever. We have funded our operations to date primarily with proceeds from borrowings under convertible promissory notes and with funds from our IPO and SBIR Award. Through September 30, 2022, we had received gross cash proceeds of approximately \$31.5 million from these sources.

At September 30, 2022, we had cash of approximately \$8.8 million. We expect to receive up to approximately an additional \$1.8 million under our SBIR Award, including the approximately \$928 thousand remaining from the May 2022 National Cancer Institute Notice of Allowance for the second year of the SBIR, and up to \$870,684 in the third year of the SBIR. We expect to draw down the second year balance before the end of March 2023. There is no assurance that funds for the third year of the SBIR Award will be received as the U.S. Government has broad authority with respect to expenditures, including those awarded under the SBIR.

#### ***Future requirements***

We expect our expenses to increase substantially in connection with our ongoing and planned activities, particularly as we advance preclinical activities and pursue clinical trials of TTX-MC138. In addition, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, tax, investor relations and other expenses that we did not incur as a private company.

The timing and amount of our operating expenditures will depend largely on our ability to, among other things:

- advance clinical development of TTX-MC138;
- manufacture, or have manufactured on our behalf, our preclinical and clinical drug materials and develop processes for commercial manufacturing of any product candidates that may receive regulatory approval;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;



- establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any product candidates for which we obtain marketing approval and intend to commercialize on our own;
- establish collaborations to commercialize any product candidates for which we obtain marketing approval but do not intend to commercialize on our own;
- expand our operational, financial and management systems and hire additional personnel, including personnel to support our clinical development, quality control, scientific research, manufacturing and commercialization efforts, our general and administrative activities and our operations as a public company; and
- obtain or develop new intellectual property and maintain, expand and protect our intellectual property portfolio.

At December 31, 2022, we had cash of approximately \$5.0 million. We believe that our cash as of December 31, 2022 will be sufficient to fund our operating expenses and capital expenditure requirements through the first quarter of 2023. We have based this estimate on assumptions that may prove wrong, and we could utilize our available capital resources sooner than we expect. We do not believe that our existing cash will be sufficient to fund our planned operating and capital expenditures for at least the next 12 months from the date of our financial statements, included elsewhere in this prospectus. Changed circumstances may also result in the depletion of our capital resources more rapidly than we currently anticipate. These factors raise substantial doubt about our ability to continue as a going concern. We anticipate that we will require additional capital for additional research, development, and clinical trials, as we seek regulatory approval of our product candidates, for company operations, and for licenses or acquisitions of other product candidates we may choose to pursue. If we receive regulatory approval for TTX-MC138 or other product candidates we may develop, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, all of which will vary depending on where and how we choose to commercialize approved product candidates.

Because of the numerous risks and uncertainties associated with research, development and commercialization of biologic product candidates, we are unable to estimate the exact amount and timing of our working capital requirements. Our future funding requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, outcome and costs of conducting preclinical development activities, clinical trials, and other research and development;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs, timing and requirements to manufacture our product candidates to supply our preclinical development efforts and our clinical trials;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the costs of manufacturing commercial-grade product and building inventory to support commercial launch;
- the ability to receive non-dilutive funding, including grants from governments, organizations and foundations;
- the revenue, if any, received from commercial sales of our products, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining, expanding and enforcing our intellectual property rights and defending intellectual property-related claims;
- the terms of any industry collaborations we may be able to establish;

- the extent to which we acquire or license other product candidates and technologies; and
- the efficiency with which we operate our business.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of public or private equity offerings, debt financings, governmental funding, collaborations, strategic partnerships and alliances or marketing, distribution or licensing arrangements with third parties. There is no assurance that funding from any of the foregoing sources or otherwise will be available on acceptable terms, if at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interests in our common stock may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. In addition, debt financing would result in fixed payment obligations as might preferred equity financing.

If we raise additional funds through governmental funding, collaborations, strategic partnerships and alliances, or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue or earnings streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us.

If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our research, product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

### **Cash flows**

The following table summarizes the approximate amounts of our unaudited cash flows for the periods indicated:

	<b>Nine months ended September 30,</b>	
	<b>2022</b>	<b>2021</b>
	<b>(unaudited)</b> <b>(in thousands)</b>	
Net cash used in operating activities	\$ (11,743)	\$ (3,666)
Net cash used in investing activities	(73)	(169)
Net cash provided by (used in) financing activities	(220)	25,507
Net decrease in cash	<u>\$ (12,036)</u>	<u>\$ 21,672</u>

### **Comparison of the nine months ended September 30, 2022 and 2021**

#### *Operating activities*

During the nine months ended September 30, 2022, we used cash of \$11,743 thousand in operating activities compared to using \$3,666 thousand in the nine months ended September 30, 2021. The cash used in operating activities in the 2022 period primarily reflected our net loss of \$12,431 thousand, an increase in prepaid expenses and other current assets of \$385 thousand and an increase of \$488 thousand in grant receivable, offset in part by an increase in accounts payable and accrued expenses of \$1,234 thousand and share-based compensation expense of \$265 thousand.

Changes in accounts payable and accrued expenses were generally due to the amounts and timing of vendor invoicing and payments.

#### *Investing activities*

During the nine months ended September 30, 2022, we used cash of \$73 thousand in investing activities, primarily for purchases of laboratory and computer equipment, versus \$169 thousand of such purchases in the 2021 period.

### *Financing activities*

During the nine months ended September 30, 2022, we used cash of \$220 thousand in financing activities, primarily related to additions to deferred offering costs, partly offset by proceeds from an exercise of stock options of \$6 thousand.

During the nine months ended September 30, 2021, we obtained \$25,507 thousand in cash from financing activities, primarily reflecting proceeds from our IPO offset in part by payments of deferred offering costs.

### **Contractual obligations and commitments**

At September 30, 2022, we had no future minimum lease payments under non-cancelable operating lease commitments. We enter into contracts in the normal course of business with CROs, collaborators, CMOs and other third parties for the manufacture of our product candidates, to support clinical trials and preclinical research studies and testing, and for other purposes. These contracts are generally cancelable by us. Any payments due upon cancellation of these contracts generally consist only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation although some agreements provide for termination fees or payments for the balance of the term of the agreement.

#### *Collaboration Obligations*

Our obligations under collaboration agreements to date primarily arise from a strategic collaboration agreement we entered with The University of Texas M. D. Anderson Cancer Center (“MD Anderson”) on July 29, 2022. Under this alliance, we anticipate making certain expenditures with respect to Phase I and Phase II clinical trials which we expect will be conducted in part by MD Anderson as a primary investigator site. MD Anderson will also provide preclinical work under the alliance. The details of clinical and preclinical work are to be mutually agreed by the parties prior to commencing work. We have committed to fund up to \$10 million over the term of the alliance, with \$500,000 payable within the first year. Subsequent payments are \$2 million on the first anniversary of the effective date of the agreement and \$2.5 million on each of the second, third and fourth anniversaries thereof. We will need to raise additional funds to meet the subsequent payment obligations. These are funds we had already budgeted for research and development, so do not represent additional spending. The term of the agreement is five years or until the studies are completed, whichever is later, unless earlier terminated by either party for a material breach of the collaboration agreement or by M.D. Anderson as provided in the collaboration agreement. The amounts we pay under the collaboration agreement will be charged as research and development expenses in our statements of operations.

### **Critical accounting policies and significant judgments and estimates**

We have based our management’s discussion and analysis of financial condition and results of operations on our financial statements. Our financial statements are prepared in accordance with United States GAAP. The preparation of our financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses and the disclosure of contingent assets and liabilities at the date of the financial statements. We base our estimates on historical experience, known trends and events, and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for our judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate estimates and assumptions on an ongoing basis. Our actual results may differ from amounts derived from these estimates or from amounts obtained under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our audited financial statements for the year ended December 31, 2021, and our unaudited financial statements appearing elsewhere in this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

#### *Research and development expenses*

In preparing our financial statements, we are required to estimate our accrued research and development expenses.

We rely to a significant extent on third parties to conduct preclinical studies, provide materials, and to provide clinical trial services, including trial conduct, data management, statistical analysis and electronic compilation. At the end of each reporting period,

we compare payments made to each service provider to the estimated progress towards completion of the related project. Factors that we consider in preparing these estimates include materials delivered or services provided, milestones achieved, the number of patients enrolled in studies, and other criteria related to the efforts of these vendors. These estimates are subject to change as additional information becomes available. Depending on the timing of payments to vendors and estimated services provided, we record net prepaid or accrued expenses related to these costs.

The estimating process involves reviewing open contracts and purchase orders, communicating with our relevant personnel to identify services that have been performed on our behalf or deliveries of materials made to us, and estimating the level of service performed and the associated cost incurred for those services when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. As of each balance sheet date, we make estimates of our accrued expenses based on facts and circumstances known to us at that time. We periodically confirm the accuracy of the estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors, including research laboratories, in connection with preclinical development activities;
- CROs and investigative sites in connection with preclinical testing and clinical trials; and
- CMOs in connection with the production of drug substance and drug product formulations for use in preclinical testing and clinical trials.

The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period.

#### *Share-based compensation*

We measure the expense of share-based awards granted to employees, directors and others based on the fair value of the underlying award on the date of the grant. We recognize the corresponding compensation expense of those awards over the requisite service period, generally the vesting period of the respective award. Between 2016 and 2018, we issued restricted stock to directors, management and others which restricted stock vested generally over three years. All restricted stock had vested as of October 31, 2021, and there is no further compensation expense to be recorded in connection with restricted stock. From time to time beginning in June 2020, we have awarded stock options with service-based vesting conditions and recorded share-based compensation expense resulting from those awards as vesting has occurred. We would apply the graded-vesting method to all share-based awards with performance-based vesting conditions or to awards with both service-based and performance-based vesting conditions.

For share-based awards to consultants and non-employees, we recognize compensation expense over the vesting period during which services are rendered by such consultants and non-employees until completed.

#### *Determination of the fair value of common stock*

As prior to our initial public offering there was no public market for our common stock, the estimated fair value of our common stock was determined by our Board as of the date of each share-based award. Based on the fact that most of our activities from inception through mid-2018 related to organizing the company, including identifying management, directors and advisors, business planning, identifying potential product candidates, acquiring or developing intellectual property, conducting a limited amount of research and development, establishing arrangements with third parties to manufacture initial quantities of our product candidates and component materials, and seeking financing, and that our preclinical development had not advanced significantly, the Board determined that the fair value of our common stock had remained relatively constant at its par value during this period. In

September 2018, the Board retained an independent third-party appraisal firm to provide an estimate of the fair value of our common stock. In November 2018, the appraisal firm estimated that, as of June 30, 2018, the fair value of a single share of our common stock was \$0.07. In March 2020, the appraisal firm estimated that as of December 31, 2019, it was \$0.08 per share and in December 2020, it was estimated to be \$3.91 per share as of October 1, 2020.

The valuations were performed in accordance with the Standards of the National Association of Certified Valuators and Analysts and in consideration of guidance from valuation literature, relevant court decisions, Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, 820, Internal Revenue Service Revenue Ruling, or RR, 59-60, RR 68-609, and 26 Code of Federal Regulations, or CFR, Part 2, Section 1.409A. Estimates and processes used by the independent appraiser in performing the valuation are highly complex and include both objective and subjective factors. Assumptions underlying these valuations included certain estimates provided by the company's management to the appraisal firm, which estimates involved inherent uncertainties and application of management's judgment. Had significantly different assumptions or estimates been used, the fair value of our common stock and our share-based compensation expense could have been materially different. Further, those factors may have changed between the date of the then most recent valuation and the date of the grant.

Factors considered by the appraiser in determining the fair value of our common stock as of each grant date, included:

- our stage of development and business strategy;
- the progress of our research and development programs, including the status and results of preclinical studies and plans for clinical trials for TTX-MC138;
- our capital structure, including, if outstanding at the time of a grant, our convertible promissory notes and the superior rights and preferences of the notes relative to our common stock;
- external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry;
- our financial position, including cash on hand, and our historical and forecasted performance and results of operations;
- the absence of an active public market for our common stock;
- the likelihood of achieving a liquidity event, such as an IPO or sale of our company in light of prevailing market conditions; and
- an analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

If there is an active public trading market for our common stock, we do not expect it to be necessary for our board to estimate the fair value of our common stock in connection with our accounting for share-based awards that we may grant, because the fair value of our common stock will be determined based on the quoted market price of our common stock. We may, despite any development of an active trading market for our common stock, and pending a sufficient history of the volatility of the price of our own common stock, calculate the volatility component of the valuation using volatility measures for a group of publicly-traded companies we deem comparable for this purpose.

#### **Factors that May Affect Future Results**

You should refer to "Risk Factors" beginning on page 15, for a discussion of important factors that may affect our future results.

#### **Off-balance sheet arrangements**

During the periods presented, we did not have, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

## **Recently issued accounting pronouncements**

A description of recently issued accounting pronouncements that may affect our financial position and results of operations is disclosed in Note 2 to our financial statements included elsewhere in this prospectus.

## **Internal control over financial reporting**

In preparation of our financial statements to meet the requirements of our IPO, we determined that material weaknesses in our internal control over financial reporting existed prior to our IPO which remain unremediated. See “Risk Factors” on page 65 under the caption, “We have identified material weaknesses in our internal control over financial reporting. If we are unable to remediate these material weaknesses, or if we identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business.” We have engaged a consulting firm to assist us with designing and implementing internal controls appropriate to regulatory and operating requirements. There is no assurance that any controls we implement will prevent fraud or enable accurate or timely financial reporting.

## **Emerging Growth Company and Smaller Reporting Company Status**

We are an “emerging growth company” as defined in the JOBS Act. We will remain an emerging growth company until the earliest to occur of: (i) the last day of the fiscal year in which we have more than \$1.235 billion in annual revenue; (ii) the date we qualify as a “large accelerated filer,” with at least \$700 million of equity securities held by non-affiliates; (iii) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period; and (iv) the last day of the fiscal year ending after the fifth anniversary of our initial public offering.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards by delaying adoption of these standards until they would apply to private companies. We have elected to use the extended transition period to enable us to comply with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date on which we (i) are no longer an emerging growth company and (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of effective dates applicable to public companies.

We are also a “smaller reporting company” meaning that the market value of our stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of our initial public offering is less than \$700 million and our annual revenue was less than \$100 million during the most recently completed fiscal year. We will continue to be a smaller reporting company until either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies.

## **Information Technology Risks**

Our data and computer systems are subject to threats from malicious software codes and viruses, phishing, ransomware, business email compromise attacks, or other cyber-attacks. In July 2021, we were subject to what we believe was a phishing attack. Although we do not believe this incident had a material impact on our business or financial condition, the number and complexity of these threats continue to increase. See “Risk Factors” on page 66 under the caption, “We may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential or proprietary information, including personal data, damage our reputation, and subject us to significant financial and legal exposure.” The Company has taken and continues to take steps to mitigate the risk of cyberattacks including enhancing its email screening, engaging with a computer support firm to provide forensics and training services, among other services, and enhancing security protocols for vendor payments. The Company intends to take additional steps to continue to enhance its cybersecurity defenses. Despite steps the Company has taken or may take in the future, there is no assurance that it will not suffer material and adverse consequences as a result of cyberattacks or other computer-based activities. In addition, there is no assurance that any steps we may take will be effective or prevent material adverse effects on our financial condition or results of operations.

## BUSINESS

### Overview

TransCode is an RNA oncology company created on the belief that cancer can be defeated through the intelligent design and effective delivery of RNA therapeutics. Our lead therapeutic candidate, TTX-MC138, targets microRNA-10b, or miRNA-10b, a master regulator of metastatic cell viability in a range of cancers, including breast, pancreatic, ovarian, colon cancer, glioblastomas, and several others. TransCode submitted to FDA an eIND application on November 30, 2022, to conduct a First-in-Human clinical trial with TTX-MC138-NODAGA-Cu<sup>64</sup> and received written authorization from the agency on December 23, 2022, to proceed with the Phase 0 clinical trial. The trial is intended to demonstrate quantitative delivery of TTX-MC138 to metastatic lesions in subjects with advanced solid tumors. In parallel, we intend to complete investigational new drug enabling studies, or IND enabling studies for TTX-MC138 in support of our planned IND application filing for a Phase I/II clinical trial with TTX-MC138. Our other preclinical programs include two solid tumor programs, TTX-siPDL1, an siRNA-based modulator of programmed death-ligand 1, or PD-L1, and TTX-siLIN28B, an siRNA-based inhibitor of RNA-binding protein LIN28B. TransCode also has three cancer agnostic programs, TTX-RIGA, an RNA-based agonist of the retinoic acid-inducible gene I, or RIG-I, targeting activation of innate immunity in the tumor microenvironment; TTX-CRISPR, a CRISPR/Cas9-based therapy platform for the repair or elimination of cancer-causing genes inside tumor cells; and TTX-mRNA, an mRNA-based platform for the development of cancer vaccines that activate cytotoxic immune responses against tumor cells.

For decades, ribonucleic acid, or RNA, has been a topic of investigation by the scientific community as a potentially attractive therapeutic modality because it can target any gene and it lends itself to rational and straightforward drug design. RNA-based therapeutics are highly selective to their targets, potentially making available a broad array of previously undruggable targets in the human genome.

TransCode has created a design engine to customize the development of RNA therapeutics that is modular, both at the levels of the core nanoparticle and therapeutic loading. The size, charge, and surface chemistry of the core iron oxide nanoparticle can be tuned to optimize the particles for the intended genetic target and therapeutic load. The therapeutic load consisting of synthetic oligonucleotides can also be adapted to the specific approach being developed. The approach can range from RNA interference, RNAi, including small interfering RNAs, antisense oligonucleotides, and non-coding RNA mimics to mRNA-based cancer vaccines and CRISPR-based gene repair and replacement platforms as well as Pattern Recognition Receptors such as RIG-I. The platform can further be used for developing RNA-targeted radiolabeled therapeutics and diagnostics and other custom products targeting known and novel biomarkers and other genetic elements as they are discovered and validated. The TTX platform, which is described below in more detail, is intended to overcome delivery issues of stability, efficiency, and immunogenicity faced by existing lipid and liposomal nanoparticle platforms while optimizing targeting of and accumulation in tumor cells and metastatic sites.

The ability to deliver RNA therapeutics inside tumors and metastases gives us the potential to target genes of importance for cancer treatment that have remained undruggable up until now using an RNA approach.

### *Delivery System*

The therapeutic potential of RNA in oncology remains an unrealized promise due to the difficulty in safely and effectively delivering oligonucleotides to tumors. TransCode believes it is now closer to solving this challenge by means of a proprietary oligonucleotide delivery platform, our TTX platform, which leverages an iron oxide nanoparticle, approved for clinical use as a cancer imaging agent and in treating iron deficiency anemia, as the physical carrier.

Due to its small size, the TTX delivery system is expected to minimize early kidney and liver clearance, translating into a long circulation half-life that allows for efficient accumulation in tumor cells and metastatic sites. Nanoparticles similar in formulation to ours have an excellent clinical safety record of low toxicity and immunogenicity, and their built-in imaging capabilities have the bonus of enabling quantification of the particles' delivery to target organs. The nanoparticles are functionalized with amino groups to provide stable links through disulfide bonds to the therapeutic oligonucleotides of interest. The nanoparticles are coated with dextran, a glucose polymer, to protect the oligonucleotides from degradation and to provide overall stability to the particle.

The small hydrodynamic size and the charge of the resulting nanoparticles should allow them to infiltrate the tumor microvasculature, extravasate into the interstitium of tumors and metastases, and be readily taken up by tumor cells. The

physicochemical properties of the nanoparticles are expected to further facilitate their rapid uptake by tumor cells by exploiting the high metabolic activity of cancer cells, a process analogous to the mechanism behind the systemic loading of metastatic cancer cells with fluorodeoxyglucose for diagnostic Positron Emission Tomography. The combined result of a hydrodynamically-favored distribution and a metabolically triggered uptake should result in the enhanced ability of TransCode's nanoparticles to access genetic targets inside tumor cells.

The Lancet Oncology Commission on Medical Imaging and Nuclear Medicine published an assessment of imaging and nuclear medicine resources, finding that scale-up of imaging, treatment and care would avert 9.5 million deaths in 11 million cancers globally (Lancet Oncol. 2021 April; 22(4), 136-172). It has been estimated by Guggenheim Securities in a 2022 report that targeted radiopharmaceuticals will grow to a \$22 billion global opportunity by 2026.

The intended therapeutic use of TransCode's TTX delivery system is based in part on the repurposing of the clinically validated imaging agents iron-oxide nanoparticles (combidex) and glucose (fluorodeoxyglucose), and now radiation. The concept of nuclear medicine has an 80-year clinical history, starting with Phosphorus-32 for leukemia in 1941. Exemplified by the recent filing of U.S. provisional application 63/356,449, TransCode has initiated research and development efforts designed to introduce radiotherapy into the delivery of TTX-carrying RNA therapeutic payloads. Two of TransCode's programs TTX-MC138 and TTX-RIGA are being investigated for radio integration in either a systemically or locally delivered manner for both the treatment and diagnosis of solid tumors.

#### *Our Lead Therapeutic Candidate*

Our scientific co-founders developed TransCode's initial therapeutic candidate at The General Hospital Corporation, d/b/a Massachusetts General Hospital, or MGH, to target microRNA-10b, a well-validated biomarker linked to metastatic cancer. In contrast, most anti-cancer therapies target primary tumors and do not address metastatic disease specifically. MicroRNA-10b has been shown to be the master regulator of metastatic disease in multiple tumor types. Effective therapeutics have not been developed targeting microRNA-10b because of challenges in delivering therapeutics to tumors despite microRNA-10b's strong association with cancer metastasis, as documented in over 200 peer-reviewed scientific publications over the last ten years.

TTX-MC138 comprises proprietary iron-oxide nanoparticles and oligonucleotides which are synthetic LNA/DNA molecules that specifically target microRNA-10b, a regulatory RNA. The nanoparticles serve as a vehicle to deliver oligonucleotides to metastatic tumor cells. The magnetic properties of these nanoparticles allow for monitoring of their delivery using non-invasive imaging, which we believe adds value for clinical implementation of this therapeutic approach.

Our scientific co-founders conducted a variety of preclinical animal studies involving human metastatic breast cancer models. In these studies, TTX-MC138 was successfully delivered to existing metastatic lesions in the lymph nodes, lungs, and bones as shown by non-invasive imaging performed 24 hours after injection. In five separate studies involving over 125 mice, TTX-MC138 was injected into mice in which human models of metastatic breast cancer tumors had been implanted. These mouse models included the rodent 4T1-luc2 orthotopic allograft, which is a very aggressive model of stage IV metastatic breast cancer, the human MDA-MB-231-luc-D3H2LN xenograft, which is a stage II/III cancer model, and the human MDA-MB-231-BrM2-831 xenograft, which is a model of breast cancer metastatic to the brain. Tumors in mice implanted with MDA-MB-231 cells typically progress from localized disease to lymph node metastases within 21 days of implantation. Tumors in mice implanted with 4T1-luc2 cells typically progress to distant sites in the animals within 10 days of implantation.

To test TTX-MC138 in the model of lymph node metastatic breast cancer, mice had their primary tumors surgically removed four to five weeks after tumor inoculation, following confirmation of lymph node metastases via imaging. This was done to better simulate a clinical scenario, since the current standard of care involves surgical removal of the primary tumor in patients with lymph node metastatic breast cancer. Treatment with TTX-MC138 was then initiated during the week of tumor removal. Because tumors in mice replicate more rapidly than is typical in humans, we combined low-dose doxorubicin with the TTX-MC138 because doxorubicin slows metastatic cell replication specific to these tumor models. Doing so allowed the TTX-MC138 to reach and inhibit the targeted RNA (miR-10b) inside the tumor cells more efficiently.

After four weeks of therapy, metastases in mice treated with TTX-MC138 regressed. By contrast, in the control groups, there was metastatic progression (Within-Subjects ANOVA:  $p < 0.05$ ). Treatment was discontinued once complete metastatic regression was



observed. By the end of the study at 12 weeks, there was no recurrence and 100% survival in treated subjects having this cancer model.

In similar studies involving mice implanted with 4T1-luc2 breast tumors, we observed regression of distant metastases by week six, at which point treatment was stopped (Within-Subjects ANOVA:  $p < 0.05$ ). Despite stopping treatment, the animals remained metastasis-free and by the end of the study, no recurrence of disease had been observed. There was evidence of complete regression without recurrence in 65% of treated subjects while 35% progressed due to insufficient inhibition of miR-10b in this group. We believe this was due to the high rate of tumor cell replication in this model resulting in dilution of the therapeutic. We do not expect this to be the case in humans with metastatic disease, in whom tumor cell replication is dramatically slower than in mice.

TransCode submitted to FDA an eIND application on November 30, 2022, to conduct a FIH clinical trial with TTX-MC138-NODAGA-Cu<sup>64</sup> and received written authorization from the agency on December 23, 2022, to proceed with the Phase 0 clinical trial. The trial involves injecting a single microdose of radiolabeled TTX- MC138, termed TTX-MC138-NODAGA-Cu<sup>64</sup>, into subjects with advanced solid tumors, followed by imaging by integrated positron emission tomography-magnetic resonance imaging, or PET-MRI. The Phase 0 trial is intended to quantify the amount of radiolabeled TTX-MC138 delivered to metastatic lesions and the pharmacokinetics and biodistribution of the therapeutic candidate in cancer patients. The Phase 0 trial could yield critical data regarding therapeutic dose, timing, and potential safety that could inform our later clinical trials. We believe that demonstrating our ability to overcome the challenge of RNA delivery to genetic targets outside the liver, and specifically to tumors and metastases, would represent a major step forward in unlocking therapeutic access to genetic targets involved in a range of cancers. Assuming the completion of this offering and approval by the institution's IRB, we expect to commence enrollment of the Phase 0 trial during the first half of 2023 and we expect to announce preliminary, topline data from this trial as soon as practical thereafter. Concurrent with the Phase 0 trial, we expect to complete additional IND-enabling studies to support filing an IND for a Phase I/II clinical trial with TTX-MC138.

### *Modular Design Toolbox*

We employ a design engine to enable development of therapeutic candidates that we believe can be efficiently delivered to genetic targets inside tumor cells. This approach is based on four complementary elements that together address the challenges of RNA drug development in oncology:

**Genetic Code** — Our approach to drug development takes advantage of our rapidly expanding knowledge about the human genome and the annotation of the genome — the knowledge about what different genes are responsible for especially in cancer. Armed with this knowledge, we can take advantage of the coded nature of the genome to design specific oligos that correspond to genetic targets of interest. Once we determine the code of the cancer target, we can develop therapeutic candidates using specific oligos that are harmonized to that target and potentially rewrite the story on cancer. This is what TransCode means — to change the code. After determining the genetic target of interest, we may be able to choose from a variety of RNA approaches best suited for that target. Those approaches will likely range from RNAi, which include siRNAs, antisense oligonucleotides, and non-coding RNA mimics; messenger RNA-based cancer vaccines; CRISPR-based gene repair and replacement platforms; or Pattern Recognition Receptors like RIG-I.

**Modular Design for Therapeutic Development** — Our discovery platform consists of a modular 'toolbox' for developing therapeutic candidates designed to attack specific disease-causing RNA targets based on the phenomenon of genetic complementarity. These therapeutic candidates incorporate synthetic oligonucleotides, or oligos, that can be designed as antagomirs, mimics, miRNA sponges, siRNA duplexes, ribozymes, and others depending on the desired therapeutic strategy. In addition to the varied oligo design approach, we can also synthesize nanocarriers with tunable chemistry properties. Combined, the modularity and tunability of these oligonucleotides and nanocarrier components may enable the potential to synthesize libraries of therapeutic agents designed for a given indication or a given patient in terms of therapeutic oligonucleotide design, size, surface coating and charge, hydrophilicity and hydrophobicity, and antigen- targeting through incorporation of targeting peptides.

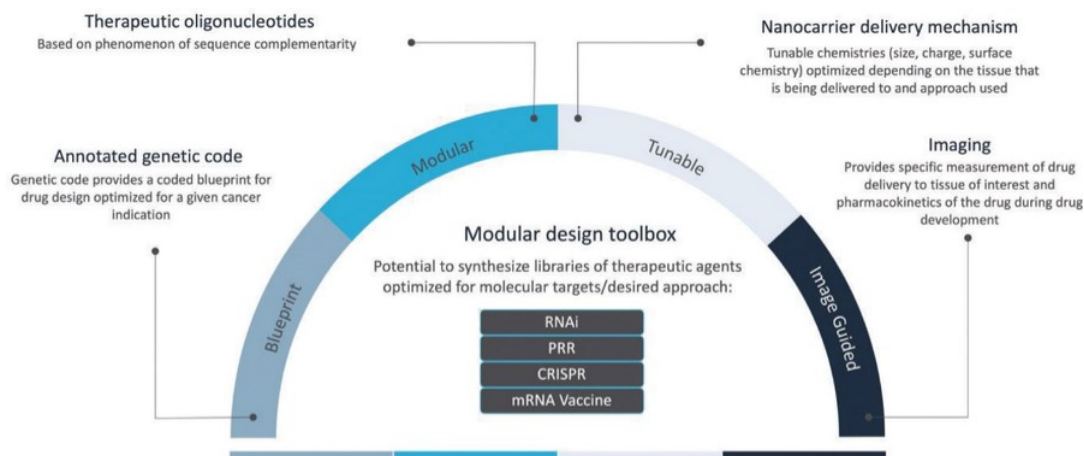
**Nanocarrier Delivery Mechanism** — Our strategy seeks to leverage a nanoparticle that has been extensively used in humans for imaging by repurposing it to deliver oligonucleotides to cancer cells. The nanocarrier is tunable to pre-designed specifications to deliver therapeutic oligonucleotides to an RNA target in tumors and metastases without compromising its integrity. These nanocarriers differentiate us from competitive delivery approaches, many of which rely on lipid particles or chemical structures, such as GalNAc. Competitive delivery approaches effectively target sites in the liver but not sites in tumors and metastases. Our nanocarrier is derived

from, and is chemically similar to, nanoparticles extensively used in imaging (Feridex, from Advanced Magnetics) or for treating iron deficiency anemia (Feraheme, also from Advanced Magnetics).

We believe that our competitive advantages include effectively reaching tumors and metastases, achieving robust target engagement in tumor cells, and an anticipated wide therapeutic window based on prior experience in preclinical models and clinical experience of others with similar iron oxide nanoparticles.

**Image Guided** — Because our therapeutic candidates are innately detectable using non-invasive imaging, we can monitor their delivery to the tissue of interest and measure their bioavailability. The ability to monitor delivery using Magnetic Resonance Imaging, or MRI, can be instrumental in assessing and controlling the amount of oligonucleotide that reaches the targeted tissues. MRI use during the design phase of the therapeutic candidate could guide drug design, delivery schedule, route, and dose and could suggest alternatives should treatment with the therapeutic candidate fail in a given patient. This is critical during drug development because it should allow us to optimize drug design to maximize therapeutic effect.

The following graphic summarizes our modular design approach:



## Our Team

At TransCode, we are driven to change how cancer is treated both as a therapeutic modality and in terms of improving patient outcomes. We believe in the potential of RNA therapeutics to offer patients complete regression of their disease without recurrence rather than the current norm of giving patients additional months of survival. We are led by an experienced team of dedicated scientists and experts with decades of experience in the foundational areas of RNA and drug development, including RNA drug development using antisense oligonucleotide, or ASO, and silencing RNA approaches. Our Co-Founder and CEO, Michael Dudley, has over 40 years of executive leadership experience in the fields of medical device, diagnostics, and therapeutics. Dr. Zdravka Medarova, our Co-Founder and Chief Technology Officer, is a geneticist and cancer biologist by training. She is an internationally recognized leader in the field of non-coding RNAs for cancer therapy and one of the inventors of TransCode's technology. She developed the core TTX delivery platform and validated many of the therapeutic targets. Dr. Anna Moore, our third Co-Founder, is internationally known for her groundbreaking research on targeted imaging and image-guided therapy. Tom Fitzgerald, our CFO, has over 30 years of accomplishments as a CFO and an investment banker for companies from emerging growth to turnarounds to Fortune 500 companies in the life sciences, technology, financial and industrial sectors. Dr. Peter Liu, our VP of R&D and Chief Scientist, has over 20 years of research and development, or R&D, experience and leadership in the biopharma industry. With in-depth knowledge and expertise in chemistry, oligonucleotide biochemistry, and assay development, he has filed nearly 30 US or PCT patents applications of which 25 have issued. In addition, the management team includes Susan Duggan, Senior VP of Operations; Dustan Bonnin, VP of Corporate Strategy; and Alan Freidman, VP of Investor and Client Relations; each of whom has years of experience and expertise in areas of healthcare business development and management, finance, clinical operations, and project management as well as mergers, acquisitions, and other strategic transactions. Our advisory team and industry-leading consultants have many years of experience in chemistry manufacturing controls, or CMC, scaleup and commercialization of oligonucleotide and nanoparticle-based

therapeutics as well as strong expertise in quality systems development, regulatory affairs, business strategy, legal affairs, and clinical trial design.

### Our Pipeline

We plan to continue research on a variety of microRNAs and biomarkers involved in cancer cell proliferation, carcinogenesis and metastasis. Our lead candidate, TTX-MC138, is expected to enter its first phase of clinical assessment in the first quarter of 2023. In addition, we intend to request various FDA designations or approvals including Breakthrough Therapy, Accelerated Approval, Priority Review and Fast Track Designation and Orphan Disease Designation as many cancer indications are classified as orphan diseases. In addition, we amended our worldwide exclusive license with MGH to include a small interfering RNA, or siRNA, therapeutic candidate created at MGH by one of our scientific co-founders against PD-L1 in pancreatic and other cancer types including melanoma, breast and non-small cell lung cancer. We recently evaluated the efficacy of TTX-MC138 applied as monotherapy in a murine model of pancreatic adenocarcinoma. In this study, we treated mice bearing human pancreatic tumors implanted in their pancreata with TTX-MC138 once weekly for eight weeks. The candidate demonstrated a pharmacodynamic response by successfully inhibiting its target, microRNA-10b (miR-10b). Serum miR-10b was down-regulated by TTX-MC138 and was shown to be a potential surrogate biomarker of therapeutic efficacy, opening up the possibility of noninvasive monitoring of therapeutic response in human patients. Forty percent (40%) of animals treated with TTX-MC138 had complete responses, defined as complete regression of disease without recurrence during the length of the study.

In addition, we have secured an exclusive option from MGH to negotiate a license to us of an siRNA technology to inhibit LIN28B in a subset of pancreatic and several other cancer types including hepatocellular, breast, colon, and gastric cancers among others, in which LIN28B expression has been linked to clinical outcome. There is no assurance that these or additional technologies we may license will prove successful or that we will receive any FDA designations or approvals we may seek.

The following table summarizes our development pipeline:

Drug Candidate	Target	RNA Type	Disease Indication	Discovery	Preclinical	Phase 0	Phase 1	Phase 2	Phase 3
TTX-MC138	miR-10b	RNAi	Metastatic Breast Cancer	[Progress bar from Discovery to Phase 0]					
			**Glioblastoma (GBM); Pancreatic Cancer	[Progress bar from Discovery to Phase 0]					
			**SCLC, & Osteosarcoma	[Progress bar from Discovery to Phase 0]					
TTX-siPDL1	PD-L1	RNAi	***Pancreatic Cancer	[Progress bar from Discovery to Phase 0]					
<sup>64</sup> Cu-TTX-MC138*	miR-10b	RNAi	Metastatic Breast Cancer	[Progress bar from Discovery to Phase 0]					
TTX-siLin28b*	Lin28b	RNAi	Pancreatic Cancer	[Progress bar from Discovery to Phase 0]					
TTX-RIGA	Multiple	RIGI	Cancer Agnostic	[Progress bar from Discovery to Phase 0]					
TTX-CRISPR	Multiple	CRISPR	Cancer Agnostic	[Progress bar from Discovery to Phase 0]					
TTX-mRNA	Cancer Vaccine	mRNA	Cancer Agnostic	[Progress bar from Discovery to Phase 0]					

\* TransCode signed Exclusive Option Agreements with The General Hospital Corporation, d/b/a Massachusetts General Hospital, or MGH, for TTX-siLin28b and <sup>64</sup>Cu-TTX-MC138. Under these Options, TransCode has the right to negotiate a license for these candidates with MGH. TransCode's decision will depend on the results of preclinical studies it plans to conduct as shown above. PDAC: Pancreatic ductal adenocarcinoma  
 \*\* Seeking Orphan designation status  
 \*\*\*Received Orphan designation status from FDA

### Our Strategy

Our goal is to become a leading oncology-focused biotechnology company, leveraging our proprietary platform to discover, develop and commercialize transformative treatments that could result in cancer being managed as a chronic disease. Key components of our strategy include the following:

- **Advance the development of our TTX-MC138, TTX-siPDL1 and TCDx programs to deliver potentially transformative therapies and diagnostics to patients.** The modular design toolbox takes advantage of the “coded” nature

of the genome and transcriptome. Because of that, synthetic oligonucleotides provide an ideal platform for rational design of therapeutic and diagnostic agents based on the phenomenon of complementarity. This approach can be used while relying on recent advances in bioinformatics, genomics, and transcriptomics. The therapeutic molecules can be antisense oligonucleotides, siRNA duplexes, ribozymes, miRNA mimics, immunostimulatory RNAs and others. These molecules can be synthesized to target portions of the code that are aberrant in disease and thus the unique genome of the patient would in turn direct us to an equally unique cocktail of therapeutic agents. We are specifically focused on delivering therapeutic solutions that reach previously inaccessible targets, in particular, those in which the biological pathways are clinically and genetically well-validated, to address significant unmet medical needs within broad patient populations. We believe our TTX-MC138 and TTX-siPDL1 programs have the potential to treat multiple cancer indications that fit these criteria. TransCode submitted to FDA an eIND application on November 30, 2022, to conduct a First-in-Human clinical trial with TTX-MC138-NODAGA-Cu<sup>64</sup> and received written authorization from the agency on December 23, 2022, allowing us to proceed with the Phase 0 clinical trial subject to approval by the Institutional Review Board where we intend to conduct the trial. We intend to initiate the Phase 0 trial in patients with advanced solid tumors as soon as practical after IRB approval. We also expect to submit an IND for a Phase I/II trial with TTX- MC138 in adult patients with solid tumors representing a variety of tumor indications.

- **Further expand the capabilities of our TTX delivery platform to additional RNA targets.** We believe our ability to identify and utilize previously undruggable microRNAs, particularly those with selective or restricted expression, may unlock new opportunities across broad therapeutic applications.
- **Continue to build a broad and diverse pipeline of novel oncology therapeutic candidates.** Guided by our drug development principles and the clinical results from our TTX-MC138 program, we intend to continue to identify therapeutic targets that have disruptive therapeutic potential and are predicted to be well-suited for a therapeutic approach. Given the unique genetic profiles in some of the patient populations that we aim to serve, we plan to continue to leverage a precision medicine approach to help identify patients with the highest probability of responding to our therapeutic candidates. The capabilities of our discovery platform, such as our expanded toolbox that includes our image capable delivery system, enable us to pursue targets linked to a wider range of indications.
- **Expand and protect our proprietary know-how and intellectual property.** We are developing a broad patent portfolio meant to protect our intellectual property, which we intend to expand further. Our intellectual property, which includes proprietary know-how as well as various patents, applies not only to our licensed compounds but also to other technologies owned by or licensed to TransCode.
- **Explore synergistic collaboration opportunities.** To further our goal of delivering transformative therapies to the broadest possible patient populations, we expect to leverage strategic partnerships that can contribute initially to complementary capabilities in cancer indications which require clinical studies and/or tumor indications that fall outside our core interests. Secondly we are interested in partners that could potentially assist us in manufacturing, distribution, and commercialization in disease areas within our core area of therapeutic focus.

#### *MDACC Alliance Program*

On July 22, 2022, we were chosen as a strategic research alliance partner by MD Anderson Cancer Center, a world-leading cancer research center, to advance preclinical and clinical development of our RNA therapeutic candidates for oncology applications. Leading the collaboration for MD Anderson are George Calin, MD, PhD, Professor in the Department of Translational Molecular Pathology of Pathology/Lab Medicine, and Co-Director, The RNA Interference and non-coding RNA Center, and a member of our Science Advisory Board, and Vivek Subbiah, MD, Medical Director of the Clinical Center for Targeted Therapy. We believe that being chosen as a strategic research alliance partner by MD Anderson to advance the clinical development of RNA therapeutics is an important step forward for our oncology programs.

Under the five-year strategic collaboration agreement with MD Anderson, we have committed to fund up to \$10 million of research and development over the term of the collaboration, with \$500,000 of such amount payable within the first year. Subsequent

payments are \$2 million on the first anniversary of the effective date of the agreement and \$2.5 million on each of the second, third and fourth anniversaries thereof. This funding is in line with amounts already budgeted for preclinical and clinical development, so does not represent additional spending.

The alliance is expected to result in applied research regarding the role of regulatory RNAs in cancer, and the results then translated into the identification of biomarkers and the development of a clinical pathway to serve as a foundation for Phase I/II clinical trials and beyond.

### **Background of RNA**

RNA has long been viewed as an attractive therapeutic modality because it can be used to target a wide array of diseases; it involves rational and straightforward drug design, the drugs are highly selective for their target, and nominal amounts of drug are required to achieve powerful therapeutic activity. In addition, such drugs have the ability to engage targets that are otherwise ‘undruggable’ by targeted therapeutics, such as small molecules and monoclonal antibodies, thus opening up whole new avenues for treating intractable diseases. Turning this concept into a clinical reality, however, is no small feat. Therapeutic nucleic acids, such as mRNA, ASOs and siRNAs have been in clinical development for decades, and for much of this time, clinical success has been out of reach. This lack of clinical success is due to three delivery-related challenges:

1. protecting the therapeutic oligonucleotide from dismantling by the immune system,
2. maintaining stability long enough to allow for full therapeutic effect on the tumor, and
3. penetrating the target organs and cells.

Because of these challenges, RNA as a cancer treatment modality has been bypassed largely by the interest in other forms of treatment including immunotherapy. One enticing feature of RNA-targeting therapeutics is that once chemistry and delivery are optimized, designing and producing a lead compound for a new target is relatively straightforward, and their *in vivo* pharmacokinetic profiles are highly predictable. This means that the timeline from target identification to preclinical proof of concept in animal models, to having a lead compound ready to be tested in clinical trials, should be measurable in months rather than years, which has been the norm for drug development. This is reflected in a burgeoning clinical pipeline: currently more than a hundred investigational RNA-targeting drugs are under clinical development for disease indications encompassing neurodegeneration, metabolic and cardiovascular disorders and various cancers. Advancements in the field are now accelerating after years of slow progress. In 2016, nusinersen, a splic3 switching ASO, was approved by the FDA and became the first drug to treat spinal muscular atrophy, a rare and often fatal disease of the nervous system, and 2018 witnessed the first ever approval of an RNAi drug — patisiran — to treat polyneuropathy of hereditary transthyretin-mediated amyloidosis, another rare and devastating disease mediated by the liver. These recent successes validated the clinical utility of RNA-targeting therapeutics and brought forward lifesaving drugs for patients who previously had no effective treatment options.

Our scientific approach is based on three complementary elements that address these challenges: the ability to precisely deliver an oligonucleotide to an RNA target without compromising the integrity of the oligonucleotide; a platform to develop oligonucleotides that are designed to attack specific disease-causing RNA targets; and a diagnostic test for optimal targeting which can guide therapeutic intervention.

Our scientific co-founders initially developed the lead therapeutic candidate while at MGH to address the challenge of targeting microRNA-10b, a well validated target linked to metastatic cancer, which has been shown to cause approximately 90% of all cancer deaths. In contrast, most anti-cancer therapies target primary tumors and do not address metastatic disease specifically. So far, no effective therapeutic has been developed to target microRNA-10b because of the delivery challenge despite microRNA-10b’s strong association with cancer metastasis as documented in over 200 scientific publications.

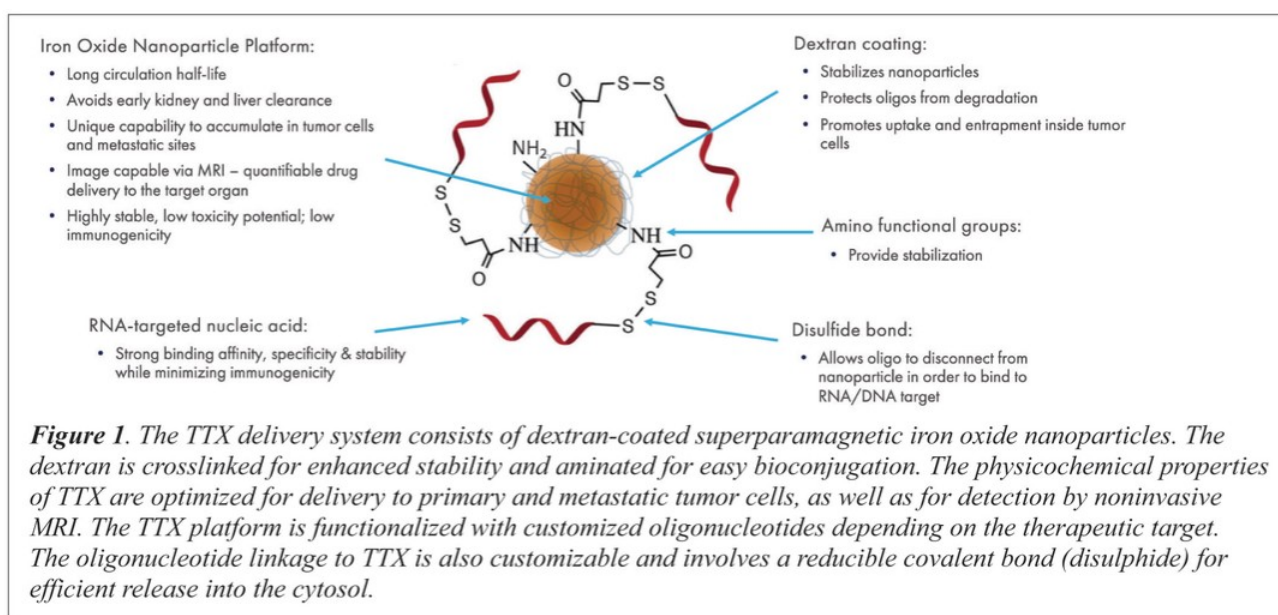
### **TTX Design**

Our delivery solution utilizes a similar construct as products that are already in clinical use for other indications. It leverages a particle that has been extensively used for imaging purposes and has been repurposed to be used as a delivery system for oligonucleotides. The nanocarrier is tunable to pre-designed specifications to shuttle therapeutic oligonucleotides to tumors and

metastases and to precisely deliver oligonucleotides to an RNA target without compromising their integrity. Our platform, which has undergone more than 12 years of research and development optimization at MGH, is designed to deliver the oligonucleotide to the tumor cells with enhanced stability and binding affinity. We believe that the nanocarrier's small size may allow for a long circulation time and efficient accumulation in metastatic tumor cells while minimizing kidney and liver clearance. A dextran coating stabilizes the oligonucleotide by blocking large nuclease proteins from gaining access to it. Our delivery platform allows for the custom development of therapeutic candidates as well as targeting of specific biomarkers in multiple cancer types.

We believe that another advantage of our TTX platform is noninvasive monitoring of delivery of the therapeutic candidate to target tissues using MRI. We believe that this advantage represents an indispensable tool to assess and control delivery to targeted tissues which has the potential to enhance both efficacy and safety. Our most advanced program focuses on metastatic cancers, which have been shown to be responsible for over nine million deaths per year worldwide. In preclinical studies in metastatic breast cancer and pancreatic cancer models in mice, our lead therapeutic candidate demonstrated the ability to be delivered to existing tumors and metastatic lesions and demonstrate complete regression without recurrence of metastasis during the study periods.

In one preclinical study using a stage II/III breast cancer model, our lead therapeutic candidate elicited complete regression without recurrence during the 12-week study period and 100% survival in the treated animals. In another preclinical study using an aggressive stage IV cancer model, our lead therapeutic candidate elicited complete regression without recurrence during the study period in 65% of animals treated. In another preclinical study in an aggressive pancreatic cancer model our lead therapeutic candidate elicited complete regression without recurrence during the study period in 40% of animals treated. TransCode submitted to FDA an eIND application to conduct a First-in-Human clinical trial with a radio-labeled version of TTX-MC138 and received written authorization from the agency on December 23, 2022, allowing us to proceed with the Phase 0 clinical trial which is anticipated to commence in the first half of 2023.

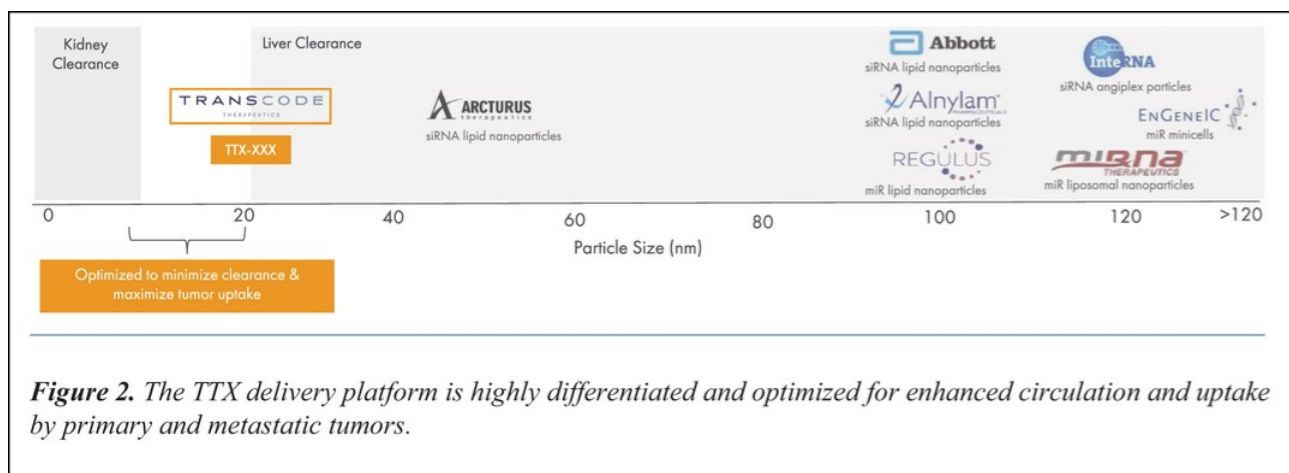


The general design of our therapeutic candidates is described in **Fig. 1**. The modular delivery system that constitutes the core of our therapeutic and diagnostic platform, TTX, comprises iron-oxide nanoparticles that have been designed for optimized delivery to primary and metastatic tumors. Based on the literature and our own studies, we believe that the delivery of TTX-candidates and other similar iron oxide nanoparticles to tumors and metastases relies on a combination of hemodynamic, physicochemical and metabolic factors. An approved iron oxide nanoparticle named Feraheme (ferumoxytol) used to treat iron deficiency anemia has been observed clinically to be long circulating with a blood half-life in humans of 17 – 24 hours. This far exceeds what we believe is the 3 – 6 hours for lipid nanoparticles. Iron oxide nanoparticles distribute to the interstitium (spaces between cells) of tumors and metastases via the enhanced permeability and retention, or EPR, effect, followed by uptake of the nanoparticles into tumor cells. Our nanoparticles are

also coated with crosslinked dextran, a glucose polymer, which stabilizes the nanoparticles and further facilitates uptake. An additional advantage of our design derives from the capability for noninvasive imaging via magnetic resonance imaging, or MRI, resulting from our incorporation of a superparamagnetic iron oxide into the design of TTX.

The clearance pathway for these nanoparticles is also well understood. Like other iron oxide nanoparticles, TTX accumulates in the organs of the reticuloendothelial system. There it is taken up by the cells and rapidly broken down. The iron from the iron oxide core enters the endogenous iron pool, whereas the dextran from the nanoparticle coating is cleared through the kidneys. After over 18 years of R&D optimization, including approximately 12 years at MGH, we have extensively studied our delivery nanoparticle's step-by-step synthesis and characterization, as well as the nanoparticle's hydrodynamic size, surface charge, relaxivity, toxicity, stability and immunogenicity.

The TTX delivery platform is highly differentiated from other oligonucleotide delivery systems that have been developed commercially (**Fig. 2**).



We describe our delivery system as “Oligonucleotide Conjugated Nanoparticle” and believe it offers the following advantages:

- Small size (20nm+/-) gains access to tumors and metastases and avoids early clearance by the liver and kidneys; long circulation half-life;
- Low risk of immunogenicity vs competitor lipid particles which have been shown to induce undesirable immune responses via a number of different mechanisms, including complement activation and inflammatory cytokine overproduction; Quantitative non-invasive imaging via MRI & measurement of drug bioavailability during treatment; Surface coating consisting of a non-metabolizable glucose polymer creates steric hindrance by blocking large nuclease proteins from gaining access to oligonucleotide during the binding process to our target microRNA and at the same time results in improved stability and cell uptake;
- Highly stable, low toxicity potential; and
- Accumulation inside tumors and metastases as well as greater binding affinity and specificity to intended genetic targets inside tumor cells.

#### Recent Publications

In collaboration with scientists from MGH, Harvard Medical School and Michigan State University, we have published the four manuscripts listed below. The publication by Smith et al. reviews recent progress towards translating short non-coding RNAs into the

clinic. The manuscript by Le Fur et al. describes a method for radiolabeling our lead candidate, TTX-MC138, and employing microdosing PET-MRI to assess the tissue distribution of the therapeutic candidate. This manuscript serves as the basis for our FIH Clinical trial. The publication by Chen et al. reviews key microRNA targets, including miR-10b in glioblastoma. The fourth study by Moore et al. presents a case study of a feline patient with metastatic breast cancer treated with TTX-MC138.

*Clinical Applications of Short Non-Coding RNA-Based Therapies in the Era of Precision Medicine. Smith ES, Whitty E, Yoo B, Moore A, Sempere LF, Medarova Z. Cancers (Basel). 2022 Mar 21;14(6):1588.*

*Radiolabeling and PET-MRI microdosing of the experimental cancer therapeutic, MN-anti-miR10b, demonstrates delivery to metastatic lesions in a murine model of metastatic breast cancer.*

*Le Fur M, Ross A, Pantazopoulos P, Rotile N, Zhou I, Caravan P, Medarova Z, Yoo B. Cancer Nanotechnol. 2021;12(1):16.*

*Role of microRNAs in glioblastoma.*

*Chen M, Medarova Z, Moore A. Oncotarget. 2021 Aug 17;12(17):1707-1723.*

*Case Report: microRNA-10b as a Therapeutic Target in Feline Metastatic Mammary Carcinoma and its Implications for Human Clinical Trials. Moore A, Savan NA, Saavedra PV, Halim A, Yuzbasiyan-Gurkan V, Wang P, Yoo B, Kiupel M, Sempere L, Medarova Z. Front. Oncol. Sec. Cancer Molecular Targets and Therapeutics doi: 10.3389/fonc.2022.959630.*

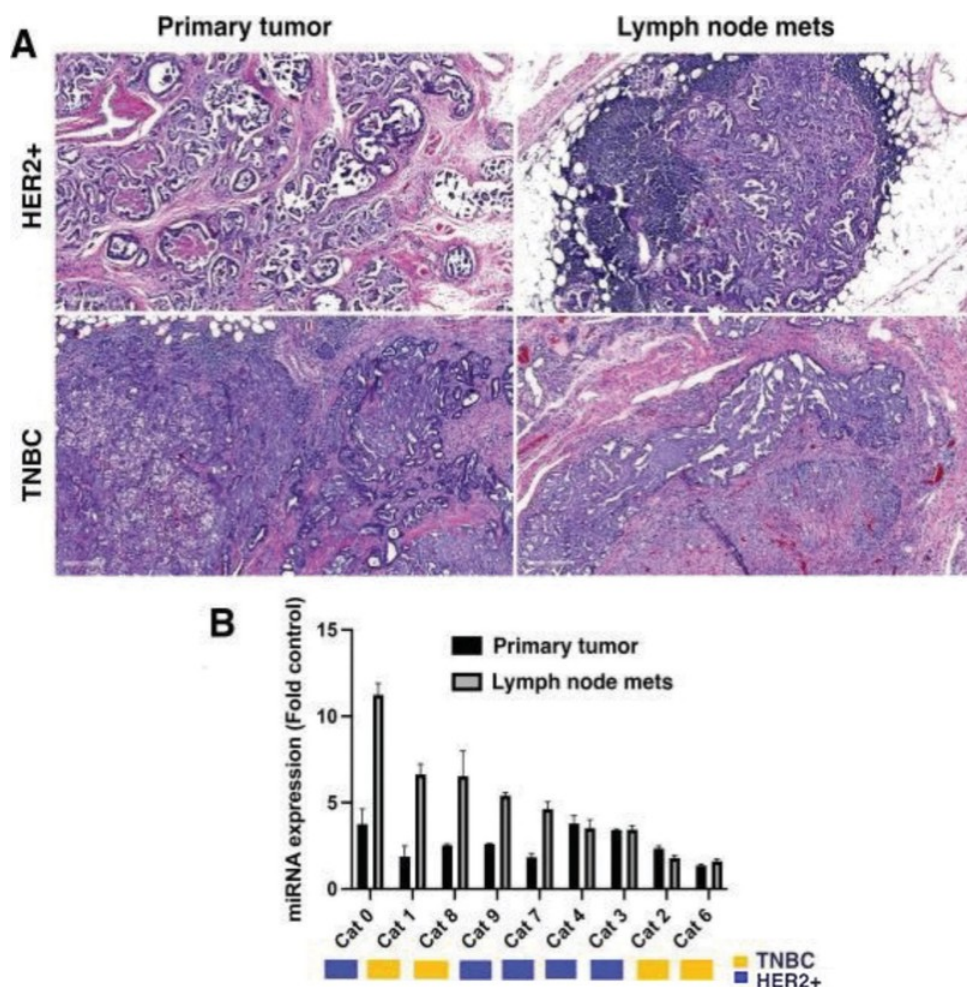
### **Case study in feline patient with metastatic breast adenocarcinoma**

On October 12, 2022, we announced acceptance for publication by *Frontiers in Oncology* of a case study in a feline patient with spontaneous metastatic breast cancer treated with TransCode's lead therapeutic candidate, TTX-MC138. The study was led by Dr. Anna Moore, Professor and Director of the Precision Health Program at Michigan State University and a scientific co-founder of TransCode.

To test the applicability of our therapeutic strategy in a larger animal, our scientific co-founders conducted a case study with a feline that had developed spontaneous mammary carcinoma, or FMC, the third most common cancer in cats and highly metastatic. FMC has high resemblance to human breast cancer compared to mammary carcinomas of other companion animals in terms of relative age at onset, incidence, risk factors, prognostic aspects, histopathology, biological behavior, metastatic pattern and response to therapy.



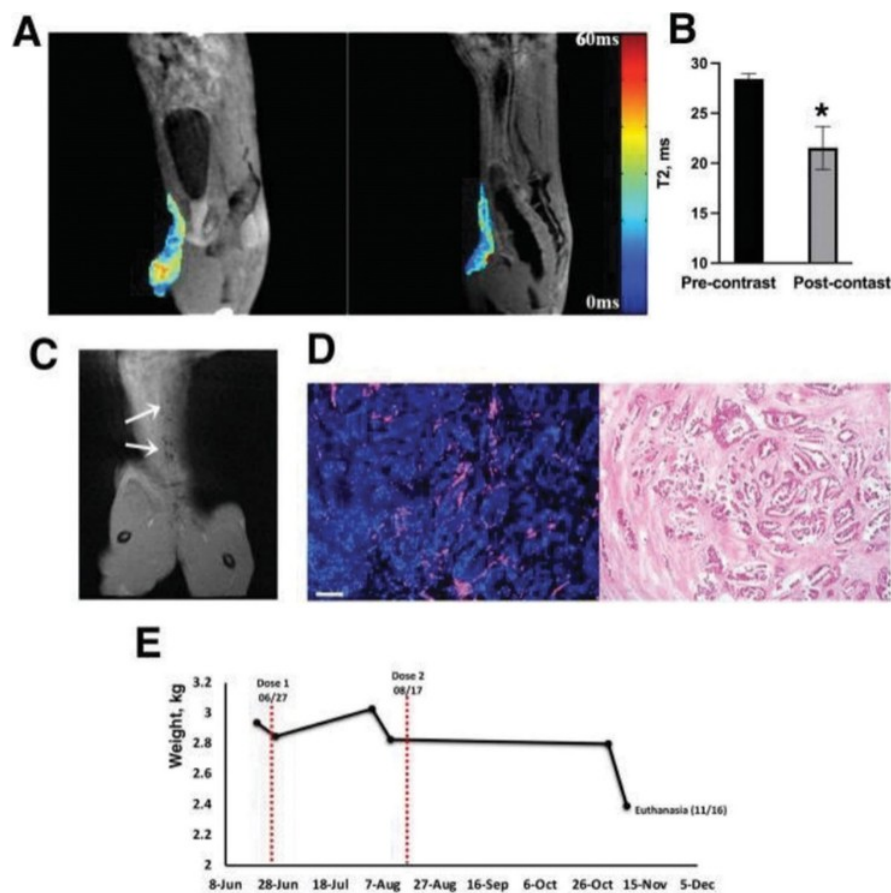
Importantly, felines experience the same environmental risk factors as humans and are immunocompetent, more accurately reflecting the complex interplay between genetics, the immune system, and the tumor microenvironment than in smaller animals. Finally, there is greater homology between cats and humans than between rodents and humans for specific genes.



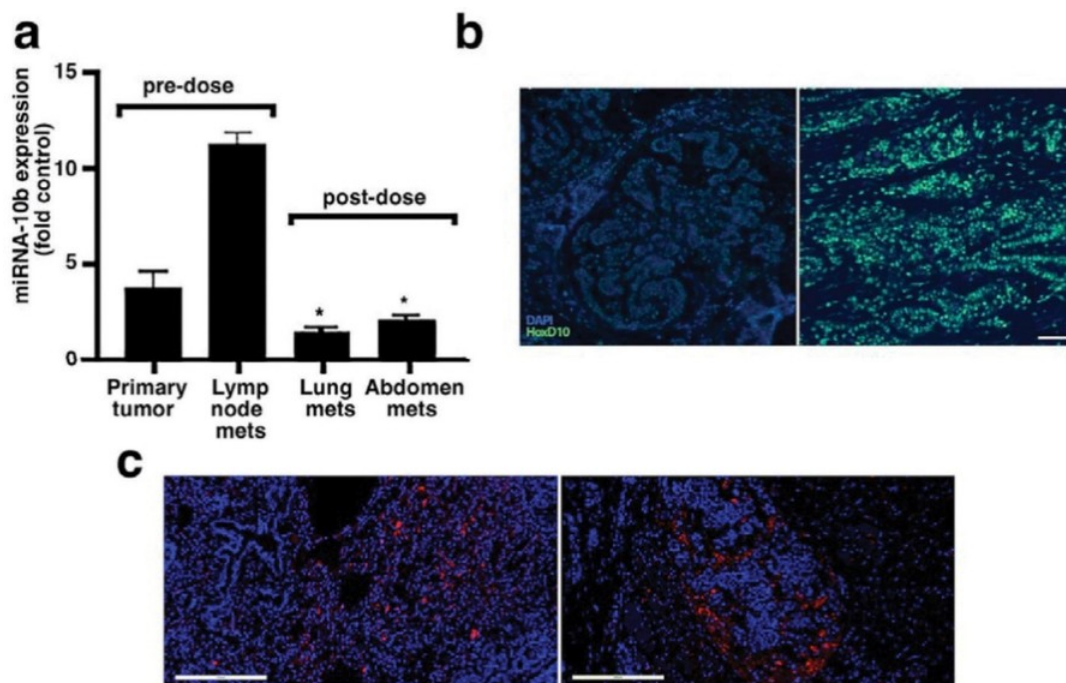
**Figure 3.** miR-10b expression in primary and metastatic tumors from nine feline patients with FMC. 3A): Representative hematoxylin & eosin (H&E) sections of primary tumors and lymph node metastases showing histopathology similar to human breast cancer. Scale bar = 200µm. 3B): miR-10b expression in primary tumors and lymph node metastases in feline patients. Molecular subtypes are indicated by the color legend. In 55.5% of the tumors, miR-10b expression in lymph node metastases was significantly higher than in primary tumors with 60% of the lymph node metastases being HER2+ (n=3 replicates, p < 0.05).

In the study, investigation of miR-10b expression in feline tissues confirmed the diversity and heterogeneity of FMC presentation in terms of miR-10b expression and tumor receptor positivity, which was similar to that in humans (Fig. 3). This points to the necessity of obtaining evidence of miR-10b expression from blood and biopsy samples to stratify patients who can potentially benefit from this therapeutic candidate. In human cancer, miR-10b expression has been shown to be significantly increased in later stage patients and in those with more aggressive types of cancers. We believe that to guide treatment in future clinical trials, patients will be selected based on their levels of miR-10b expression, similar to the current standard diagnostic tests with other cancer markers, such as HER2+. To translate our earlier successful studies in mice to humans, we believe that investigating the effectiveness of the therapeutic candidate in relevant spontaneous diseases in larger animals can be useful.

Previously, we showed that miR-10b plays a pivotal role in supporting metastatic cell viability and proliferation. To inhibit miR-10b, we designed and tested a miR-10b-specific therapeutic candidate, which caused lasting regression of established metastases in immunocompromised and immunocompetent murine models. This case study serves as the logical next step towards the clinical development of TTX-MC138 and may be followed by additional studies aimed at investigating the applicability of feline mammary carcinoma, a spontaneous cancer, as a translational model, bridging human clinical trials centered on noncoding RNAs as therapeutic targets.



**Figure 4.** MRI of TTX-MC138 delivery to metastatic breast cancer in a feline patient. 4A) Pre-contrast and post-contrast T2\* images (sagittal) of a cat injected with one dose of TTX-MC138. There was a notable loss in signal intensity over the secondary mammary lesion after injection of the therapeutic. 4B) Quantitative analysis of relaxation times (T2 pre — T2 post, ms) of the tissues, confirming accumulation of TTX-MC138. Data are represented as mean ± standard deviation, or s.d. 4C) Coronal post-contrast T2-weighted image showing signal voids identified by TTX-MC138 (arrows) corresponding to lesions in the abdominal area. 4D) Left: Fluorescence microscopy showing accumulation of TTX-MC138 in the lesion (red — Cy5.5 on the nanoparticle; blue-DAPI); Right: H&E staining of the consecutive slice. Scale bar =100µm. 4E) Animal weight during the course of the experiment.



**Figure 5.** Target engagement and accumulation of TTX-MC138 in a patient with FMC. 5a) qRT-PCR of miR-10b expression in primary tumor and lymph node metastases before dosing, and lung metastases and abdominal metastases three months after second dose; brain served as control tissue. The expression of miR- 10b was significantly reduced post-dosing relative to pre-dosing, indicating successful target engagement ( $n = 3$ ,  $p < 0.05$ ). Data are represented as mean  $\pm$  sd. 5b) In situ hybridization demonstrating significantly increased HOXD10 expression in metastatic lesions after dosing compared to that in tissues isolated during original tumor excision. Scale bar = 100 $\mu$ m. 5c) Fluorescence microscopy demonstrating accumulation of TTX- MC138 in lung metastases (left) and abdominal area metastases (right) three months after second dose. Scale bar = 200 $\mu$ m.

In the case study, a feline patient that previously had failed multiple rounds of standard-of-care treatment for advanced metastatic FMC and was at the end of its life expectancy, was dosed with TTX- MC138. Delivery of TTX-MC138 to the metastatic lesions was demonstrated using noninvasive magnetic resonance imaging, or MRI, (Fig. 4). Dosing with TTX-MC138 resulted in durable inhibition of the miR- 10b target and induction of the downstream metastasis suppressor, HOXD10, lasting as long as three months after injection (Fig. 5). The patient tolerated the injection well with no adverse effects and vital signs remained within the normal range. The animal resumed normal eating, drinking, and grooming. Complete blood count, or CBC, and blood chemistry profiles did not show significant changes from the normal ranges except for transient elevation of potassium and Na/K ratio possibly due to dehydration. Liver aspartate transaminase, or AST, and creatine kinase, or CK, levels were slightly but transiently elevated after injection. All levels returned to normal two weeks after the injection. Importantly, weight gain of more than 5% was recorded (Fig. 4). Seven weeks after the first dose, the feline patient was dosed a second time and tolerated the injection well.

The case study with our first-in-class miRNA-targeted therapeutic candidate presented here demonstrated its delivery to metastatic lesions. We believe this is an important step in preclinical development and further de-risking of our approach. Initial safety studies demonstrated good tolerability and the general lack of toxicity of the therapeutic candidate, which serves as another important milestone in its translation. Furthermore, we observed target engagement by our lead therapeutic candidate, manifested as a significant decrease in miR-10b expression after two injections seven weeks apart. It is important to note that efficacy studies were not part of this investigation, and the dose of the therapeutic used here was lower than the animal equivalent dose, or AED, calculated based on the effective dose determined in our previous rodent studies. However, even at this reduced dose and suboptimal dosing schedule, we believe we achieved significant inhibition of the miR-10b target with virtually no toxicity. The patient survived for approximately five additional months compared to its life expectancy prior to dosing. Notwithstanding the need for additional therapeutic and toxicology

studies, we believe that in combination with our other preclinical findings, this case study suggests the robustness and tolerability of a novel first-in-class therapeutic approach.

#### *Other Publications*

In addition to the above publications, we recently published our findings in BioRxiv demonstrating the feasibility of our RIG-I targeting approach relevant to our TTX-RIGA candidate.

### **Our Programs**

#### **Target Identification**

##### *microRNAs*

MicroRNAs, or miRNAs, are important post-transcriptional regulators (control of gene expression at the RNA level) of gene expression. The recent literature abounds in examples of the key role played by miRNAs in determining cell fate. These examples are particularly compelling with regard to cancer emergence, progression, and response to therapy. Consequently, miRNAs represent candidates as targets of therapeutic intervention. To specifically inhibit cancer causing miRNAs, we design therapeutics capable of first accumulating in tumor cells which then allow for target engagement of the specific miRNA of interest.

The process for therapeutic target identification is now well established. It involves differential expression analysis in cancer cell lines and animal models of cancer. These targets are then further validated as clinically actionable targets through examination of gene expression in genomic databases, such as The Cancer Genome Atlas, or TCGA, which can give us information about level of expression of each target in large populations of cancer patients and can correlate target expression to parameters such as patient survival and other clinical measures of outcome.

#### **Target Engagement**

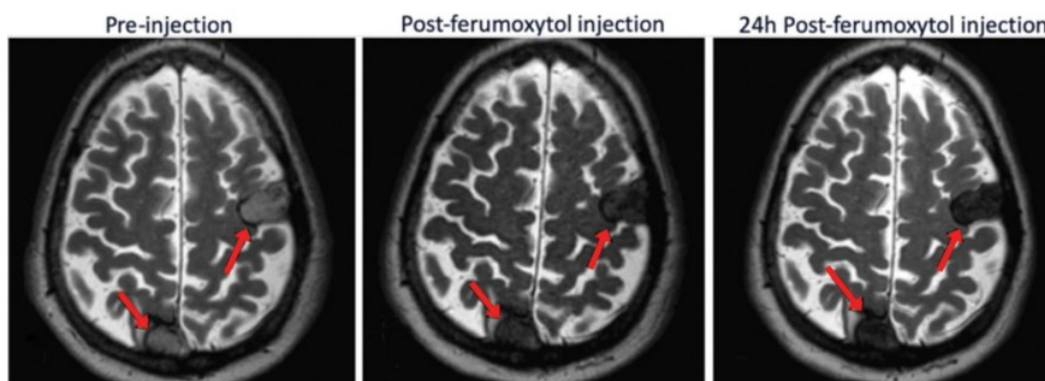
#### **Preclinical Proof of Delivery**

In our preclinical studies, we used our lead therapeutic TTX-MC138, which is designed to specifically target miRNA-10b. The therapeutic candidate which was fluorescently labeled was injected into mice implanted with a murine breast cancer cell line. In this model, orthotopically implanted (breast area) tumors progress from localized disease to lymph node, lung, and bone metastases by 10 days after tumor inoculation. Optical imaging performed 24 hours after intravenous injection of TTX-MC138 revealed uptake by the metastatic lesions in the lymph nodes, lungs, and bone. Fluorescence microscopy confirmed widespread uptake by the metastatic tumor cells in these organs supporting our hypothesis that the therapeutic candidate, as designed can target disseminated cancer to distant organs. In addition to demonstrating delivery, we have also observed efficient target engagement. We analyzed the expression of the miRNA-10b target in a mouse model treated with TTX-MC138 and observed abolition of the target.

#### **Clinical Feasibility of Delivery**

Clinical proof of delivery is based on studies in patients using the clinically approved agent Ferumoxytol, which is marketed as iron replacement therapy for patients with anemia and has also been used off-label in clinical studies as an imaging agent detectable by MRI. Imaging studies in patients with metastatic cancer have shown that clinical metastases accumulate the agent (**Fig. 6**). Results

quantifying the amount of iron oxide delivered to clinical metastases provide preliminary grounds that at clinically acceptable doses of TTX-MC138 (5 mg/kg), we believe we will be able to achieve robust target engagement and therapeutic effects in human patients.



**Figure 6.** Axial MR images in a 59 year-old male with multiple pancreatic carcinoid tumor dural metastases demonstrates two masses (arrows). Axial T2-weighted MR images show a heterogeneous mildly hyperintense appearance of the dural-based masses (arrows) on non-contrast MRI (left). New hypointensity in both masses (arrows) shown immediately after Ferumoxytol injection (middle). Hypointensity progressively darkens at 24 hours (right).

### TTX-MC138

Metastatic cancer is the form of cancer which has spread from an original tumor location to new sites in the body. Treatment of metastatic cancer is more complicated than treating early-stage cancer. Most of the treatments for metastatic cancer are focused on providing palliative care. With increases in the prevalence of disease and in life expectancy, there is also a rise in R&D expenditures in the field of oncology.

According to the November 2020 report by Emergen Research, the global metastatic cancer treatment market size was \$63.03 billion in 2019. This market is expected to reach \$111.16 billion in 2027, representing a compounded annual growth rate of 7.3% over that period. Rising prevalence of cancer and high unmet medical needs of patients suffering from metastatic cancer are the drivers stimulating the growth of the metastatic cancer treatment market. We are developing TTX-MC138 for the treatment of metastatic cancer. TTX-MC138 targets the validated critical driver of metastatic progression, microRNA-10b. We believe that TTX-MC138 has the potential to improve outcomes over current treatment options as well as other drugs currently in development, which are geared towards treating primary cancer but of limited efficacy treating disseminated malignancy. In preclinical studies of animals with metastatic lesions, TTX-MC138 was successfully delivered to those lesions, eliminated metastasis in the animal and elicited complete regression without recurrence, resulting in 100% survival of subjects treated in a stage II/III cancer model and 65% survival of subjects treated in a very aggressive stage IV cancer model.

### MicroRNA-10b (miR-10b)

One of the first miRNAs to be shown as having aberrant expression in cancer was miR-10b. Since the inaugural study on miR-10b in Dr. Robert Weinberg's lab at the Whitehead Institute for Biomedical Research and Department of Biology, Massachusetts Institute of Technology, its role as a metastasis promoting factor has been extensively validated. To date, more than 200 studies have been published on miR-10b and metastasis across 18 different cancer types. This immense set of information holds possibilities for novel methods to improve the lives of many. The therapeutic target, miRNA, is a regulatory RNA. MiRNAs are placed at the apex of the gene regulatory pyramid and play a fundamental role in defining cell fate. Therefore, we believe by targeting microRNAs, it may be possible to achieve a persistent therapeutic response in cancer patients. Our hypothesis is based on the rationale that the tumor cell phenotype is critically dependent on fundamental molecular pathways of oncogenesis and that altering these pathways can result in very specific and robust therapeutic effects. The miRNA genome is a target because it is uniquely altered in tumor cells and represents a "hub" of carcinogenesis, since a single microRNA can coordinately affect the expression of multiple genes resulting in a

comprehensive therapeutic response. In addition, because of the fundamental role played by microRNAs in defining tumor cell phenotypes, evasion of this therapeutic intervention by mutation is less likely.

Metastatic cells are uniquely capable of leaving the primary tumor, surviving in circulation and colonizing a distant organ which has properties distinct from the primary tumor where the cells originated. Cells endowed with this capability evolve in response to an adaptive process driven by a cellular “survival instinct.” Specifically, as tumors proliferate, pockets arise inside them characterized by inadequate resource supply due to failure of the tumor vasculature to keep up with the rapidly increasing tumor cell burden. This generates local inhospitable areas of low pH, high inflammation, and insufficient stromal supportive network necessary to maintain the survival of the tumor cells. As a result, some of the tumor cells within these pockets evolve by activating mechanisms, such as those driven by high miR-10b expression, that allow them to survive in the absence of abundant nutrient supply and to persist without the strong attachment to the extracellular matrix. These newly emergent cells become “refugees” from the primary tumor, invisible to most diagnostic/imaging modalities and resistant to most currently available therapeutic modalities.

In our search for the ideal therapeutic target, our co-founders identified microRNA-10b as critical for the survival of these cells. Our lead candidate is designed to enter these tumor cells and inhibit miR-10b. Without the high level of expression of miR-10b, these cells, stripped out of their natural microenvironment, do not have the adaptive mechanism they need in order to survive, so they simply die.

### **Preclinical and clinical evidence of miR-10b’s role in cancer**

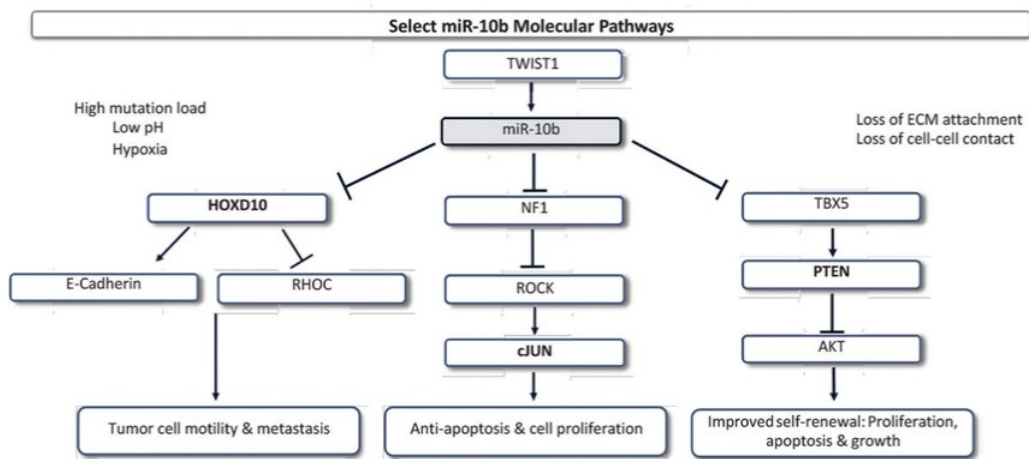
Against this conceptual framework, we have designed our lead therapeutic-candidate, TTX-MC138, which is designed with the potential to efficiently inhibit microRNA-10b in metastatic cancers. Studies in mouse models implanted with human metastatic breast cancer concluded that weekly treatment with TTX- MC138 in combination with low-dose chemotherapy was the likely reason for regression of established metastatic lesions in the lymph nodes, as well as distant organs such as the lungs and bone. Once disappearance of the metastatic lesions was observed in treated subjects with stage II, III and IV cancer models, treatment of the animals was stopped, and they were monitored for recurrence of tumors. The study observed no recurrence of metastatic disease within the observational period, suggesting that metastasis had been eliminated.

The choice of microRNA-10b as a target is supported by its potentially broad relevance to cancer. Recent studies have demonstrated that the influence of microRNA-10b extends beyond breast cancer to 17 other tumor types including pancreatic, lung, colorectal, gastric, bladder, ovarian, and hepatocellular cancer amongst others, suggesting that the described approach may be broadly applicable to metastatic disease. In addition, TTX-MC138 is hormone receptor independent, and its mechanism of action has been observed to treat metastatic breast cancer in rodents regardless of hormone receptor type (ER+/-, PR+/-, HER2+/-, or combinations thereof).

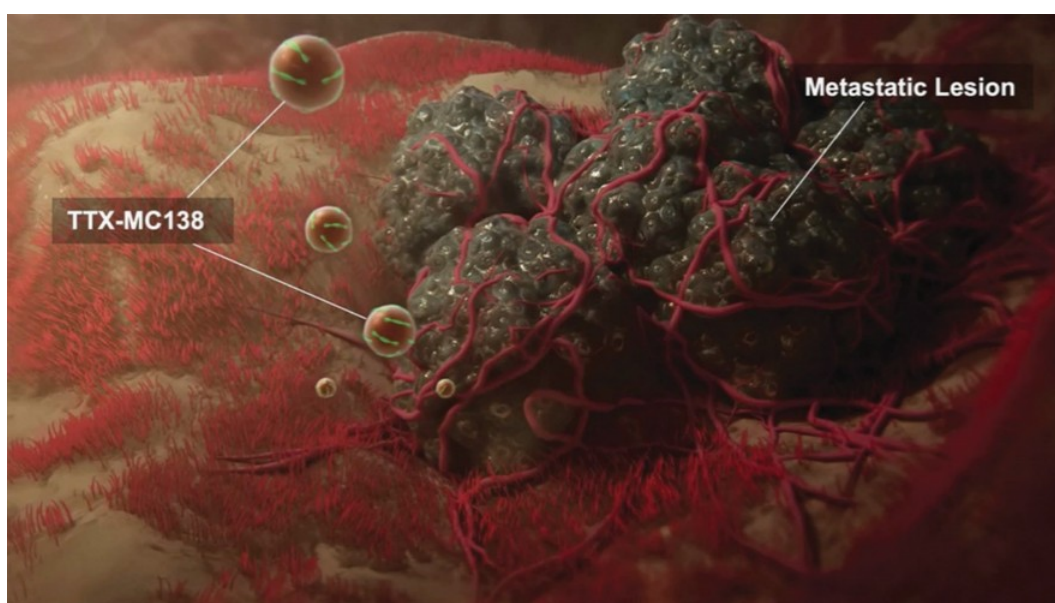
Our understanding of the miR-10b pathway and its effects is constantly evolving. However, the downstream effects of miR-10b as we currently understand them can be divided into six pathways: promotion of migration and invasion, promotion of epithelial-mesenchymal transition (EMT), inhibition of apoptosis, promotion of proliferation, induction of angiogenesis, and self-renewal.

Known microRNA-10b targets include Homeobox D10, or HOXD10, implicated in tumor cell migration and invasion, c-JUN, a critical inducer of cell proliferation and tumor progression, and phosphatase and tensin homolog (PTEN), which results in maintained AKT activation, a Ser/Thr kinase associated with proliferation, apoptosis, and growth. This effect on the AKT pathway allows for the

improved self-renewal found in cancer stem cells highly expressing miR-10b. The key pathways through which miR-10b exerts its pro-metastatic effects are summarized in **Fig. 7**.



**Figure 7.** Key signaling pathways influenced by miR-10b.



**Figure 8.** Depicts TTX-MC138 delivery to metastatic lesions, infiltrating tumor cells to engage and inhibit miR-10b, designed to lead to tumor cell death.

#### Mechanism of Action of TTX-MC138

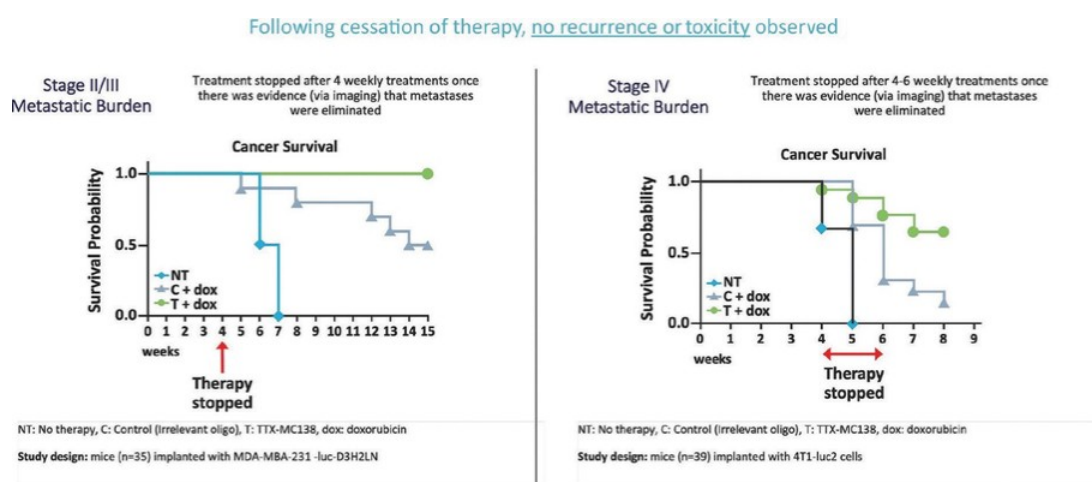
Our therapeutic concept is summarized in **Fig. 8**. TTX-MC138 represents a proprietary therapeutic candidate that inhibits microRNA-10b. In primary tumors, inhibition of microRNA-10b by TTX-MC138 leads to arrest of tumor cell dissemination to local and distant organs. We believe a combination of TTX-MC138 with low-dose doxorubicin may lead to metastatic cell death and complete and persistent regression of already formed metastatic lesions in local and distant organs. Low-dose doxorubicin was used to

slow down cell division in tumor cells. In preclinical studies that utilize aggressive metastatic tumor models, the use of low dose doxorubicin was necessary to allow TTX-MC138 to fully inhibit microRNA-10b. Because metastatic growth is slower in humans, the use of a cytostatic such as doxorubicin will likely be unnecessary. In our mechanistic studies, the studies described an effect of TTX-MC138 on HOXD10. A different study by a group from Tel Aviv University concluded that it likely had a robust effect on c-JUN. Specifically, the study showed that loss of cell contacts or restructuring of the cytoskeleton, manifested as loss of E-cadherin in metastatic cells, led to a significant increase in miR-10b expression. Interestingly, the increase in miR-10b expression was accompanied by an increase in the accumulation of c-Jun. Silencing miR-10b in metastatic breast cancer cells resulted in a reduced c-Jun expression, whereas overexpression of miR-10b elevated the accumulation of c-Jun. Furthermore, detailed mechanistic studies revealed that miR-10b activates the expression of c-Jun through RhoC and NF1, through a novel pathway for promoting migration and invasion of tumor cells.

## Results

In our preclinical studies outlined in **Fig. 9**, when TTX-MC138 was combined with a low-dose cytostatic (doxorubicin), there was complete and persistent regression of pre-existing metastatic cancer with no evidence of recurrence and no systemic toxicity. In preclinical studies that utilized aggressive metastatic tumor models, doxorubicin was used to allow TTX-MC138 to fully inhibit microRNA-10b. Because metastatic cell growth is slower in humans, we do not believe that a cytostatic such as doxorubicin will be necessary.

Specifically, in a model of stage II/III breast cancer in mice with lymph node metastases, just four weekly treatments eliminated metastatic burden. By contrast, in the control groups, there was metastatic progression (Within-Subjects ANOVA:  $p < 0.05$ ). Once metastases were eliminated, therapy was stopped. Thereafter, the animals were observed by bioluminescence optical imaging to detect recurrence. No recurrence of metastatic disease was observed by the end of the study at 12 weeks after tumor implantation. This translated into 100% survival.



**Figure 9.** Preclinical activity of TTX-MC138 in models of metastatic breast cancer.

In a model of stage IV breast cancer in mice, we obtained 65% survival. Specifically, in mice implanted with 4T1-luc2 breast tumors, we observed regression of distant metastases by week six, at which point treatment was stopped (Within-Subjects ANOVA:  $p < 0.05$ ).

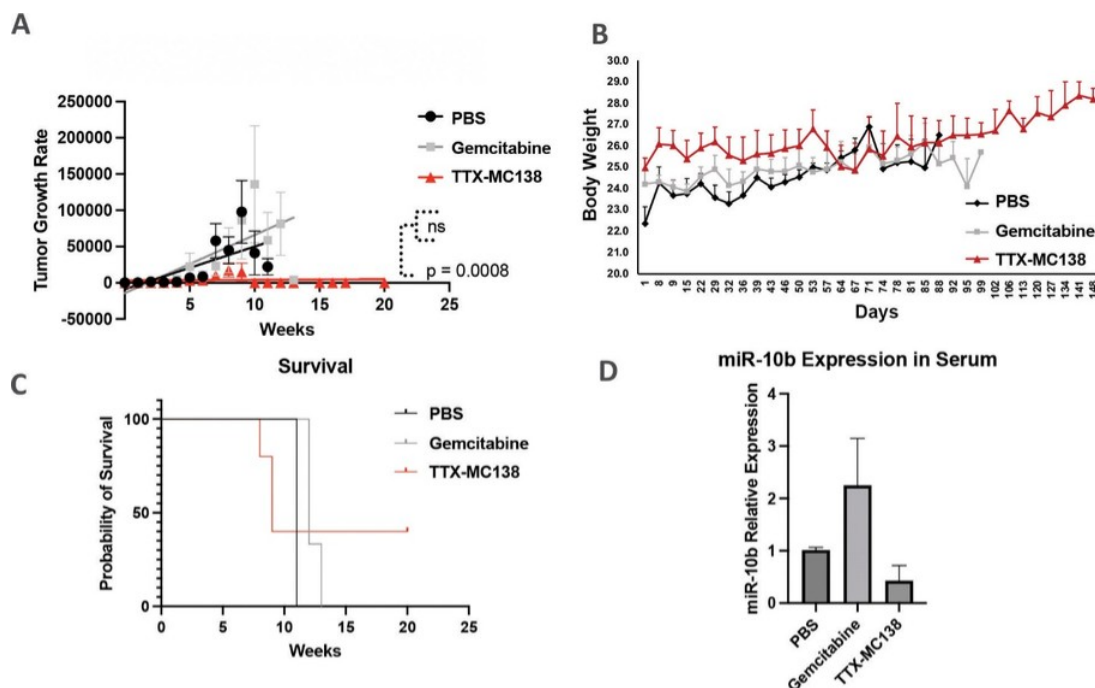
We found no elevation in serum biochemistry markers following treatment suggesting the absence of acute toxicity associated with the therapeutic candidate. In addition, histopathology of major organs resulted in no observed gross tissue abnormalities suggesting that there was no toxicity as a result of treatment.



**Positive Preclinical Results with TTX-MC138 in Pancreatic Adenocarcinoma**

We recently evaluated the efficacy of our lead therapeutic candidate, TTX-MC138, applied as monotherapy in a murine model of pancreatic adenocarcinoma. In this study, we treated mice bearing human pancreatic tumors implanted in their pancreata with TTX-MC138 once weekly for eight weeks. The candidate demonstrated a pharmacodynamic response by successfully inhibiting its target, microRNA-10b (miR-10b). Serum miR-10b was down-regulated by TTX-MC138 and was shown to be a potential surrogate biomarker of therapeutic efficacy, opening up the possibility of noninvasive monitoring of therapeutic response in human patients. Forty percent (40%) of animals treated with TTX-MC138 had complete responses, defined as complete regression of disease and long-term survival without recurrence.

These new findings expand the potential therapeutic relevance of TTX-MC138 beyond breast cancer, in which activity had previously been shown in preclinical studies, to include pancreatic adenocarcinoma. However, there is no assurance that these preclinical results will be duplicated in further preclinical studies or in cancer patients suffering from pancreatic cancer.



**Figure 10.** We recently evaluated the efficacy of our lead therapeutic candidate, TTX-MC138, applied as monotherapy in a murine model of pancreatic adenocarcinoma. In this study, we treated mice bearing orthotopic xenografts derived from human pancreatic adenocarcinoma cells with TTX-MC138 once weekly for eight weeks. The candidate demonstrated a pharmacodynamic response by successfully inhibiting its target, microRNA-10b (miR-10b). Tumor burden was measured by in vivo bioluminescence imaging. Animal survival, body weight, and tumor and metastatic burden at necropsy were also analyzed. Serum miR-10b expression was assessed to provide insight into target engagement and molecular function. Animals treated with phosphate buffered saline or gemcitabine served as controls. Tumor growth rate was found to be significantly lower in animals treated with TTX-MC138 vs. controls ( $p < 0.0001$  for TTX-MC138 vs. PBS and vs. gemcitabine) (Fig. 10A). Importantly, 40% of the animals treated with TTX-MC138 regressed their tumors completely as measured by bioluminescence imaging. Treatment continued for 10 weeks, after which the responding mice were monitored for disease recurrence without treatment for an additional 10 weeks, with no evidence of cancer during the entire observation period (Fig. 10A). The animals showed evidence of continued weight gain (Fig. 10B) and durable survival (Fig. 10C). They were sacrificed 10 weeks after treatment was discontinued, despite no evidence of morbidity, to perform necropsy. No tumors or metastases were found at the time of sacrifice. Importantly, TTX-MC138 demonstrated a pharmacodynamic response by successfully inhibiting its target, microRNA-10b (miR-10b). Serum miR-10b was down-regulated by TTX-MC138 and was shown to be a potential surrogate biomarker of therapeutic efficacy, opening up the possibility of noninvasive monitoring of therapeutic response (Fig. 10D).

## Clinical Development Plan

TransCode submitted to FDA an exploratory IND application to conduct a First-in-Human clinical trial with a radio-labeled version of TTX-MC138 and received written authorization from the agency on December 23, 2022, allowing us to proceed with the Phase 0 clinical trial which is anticipated to commence in the first half of 2023. The primary purpose of conducting this Phase 0 trial is to clinically demonstrate delivery of TTX-MC138 to metastatic tumor lesions. This trial is not designed to demonstrate that TTX-MC138 gets inside tumors although that may be a result. Getting inside tumor cells, as opposed to delivering to metastatic lesions, is expected to be an objective of clinical trials after our Phase 0 trial. In the Phase 0 trial, we also intend to evaluate biodistribution of our therapeutic candidate and measure its pharmacokinetics (bodily absorption, distribution, metabolism, and excretion).

### ***Phase 0 — First-in-Human Clinical Study (Exploratory IND)***

We anticipate commencing our FIH clinical trial conducted at a major cancer center with experience in clinical trials for cancer therapeutic candidates.

This clinical trial has the potential to:

- demonstrate quantifiable evidence of delivery of TTX-MC138 to metastatic lesions in subjects with advanced solid tumors;
- inform Phase I/II clinical trials by measuring pharmacokinetics and biodistribution in vital organs and other tissues;
- inform therapeutic dose levels based on microdose results; and
- validate delivery for the TTX pipeline more broadly, potentially opening-up additional relevant RNA targets that have been previously undruggable due to challenges with RNA delivery.

### ***Anticipated Phase I Clinical Trial***

Concurrent with the Phase 0 clinical trial, we expect to complete additional IND enabling studies to support an IND for a Phase I clinical trial with TTX-MC138.

#### *Description*

The anticipated Phase I dose escalation and expansion clinical trial, which is subject to FDA review and approval, is designed to assess the safety of the therapeutic candidate in humans, including observing potential side effects, and to determine the minimum effective dose, or MED, and maximum tolerated dose, or MTD, of TTX-MC138 in treating subjects with metastatic cancer. It is anticipated that study subjects will have had prior surgical resection of the primary tumors.

#### *Anticipated Design*

- To assess the hypothesis that the therapeutic candidate may demonstrate anti-tumor activity.
- To assess the preliminary efficacy of the therapeutic candidate using key efficacy indicators, such as objective response rate, or ORR, clinical benefit rate defined as complete response, or CR, partial response, or PR, or stable disease, or SD, at 24 weeks, and progression free survival, or PFS.
- Dose Escalation Objectives: dose finding and safety assessment.
- Secondary objectives: Confirm delivery to tumor site using magnetic resonance imaging, or MRI, and pharmacokinetics, measure microRNA-10b inhibition using PCR.

- Dose Expansion Objective: determine clinical response rate according to the common cancer study standard, response evaluation criteria in solid tumors, or RECIST.
- Secondary objectives: ORR according to investigator’s assessment, duration of response, safety and additional pharmacokinetic and pharmacodynamic evaluations.
- Up to 10 investigative sites.
- Course of treatment expected to be over six months per subject.

In a “3 + 3” dose escalation design, three patients are initially enrolled into a given dosage cohort. If no dose limiting toxicity, or DLT, is observed in any of these subjects, the trial proceeds to enroll additional subjects into the next higher dose cohort. If any one subject develops DLT at a specific dose, an additional three subjects are then enrolled into that same dose cohort. Development of DLTs in more than one of six subjects in a specific dosage cohort suggests that the maximum tolerated dose has been exceeded, and no further dose escalation is pursued. In dose expansion, patients are enrolled and treated at the MED.

### **Accelerated Regulatory Programs**

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs addressing unmet medical needs or for treating serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval. The purpose of these programs is to expedite either the development or the review of certain new drugs to get them to patients sooner than under standard FDA development and review procedures. We anticipate seeking one or more of these qualifications, but there is no assurance that we will obtain any of them.

### **Orphan Drug Designation**

The Orphan Drug Act was enacted by the 97<sup>th</sup> Congress in 1983 to facilitate the development of drugs that impact smaller patient populations. Benefits available under the Orphan Drug Act include seven-year marketing exclusivity, 25% tax benefits for research & development activities performed in the U.S., a waiver of Prescription Drug User Fee Act, or PDUFA, Fees, and qualification to compete for research grants.

Based on *in vivo* studies using TTX-PDL1 to treat human pancreatic tumors implanted in animals, we applied for and, in June 2022, received, Orphan Drug Designation for the treatment of pancreatic cancer. We intend to conduct additional *in vivo* studies to support filings of other TTX-based drug candidates in other orphan disease indications including osteosarcoma and small cell lung cancer, or SCLC. In the Michigan State University laboratory of one of our scientific co-founders, animal testing of TTX-MC138 in glioblastoma cells has been completed. Mechanistic studies have produced efficacy signals in combination with temozolomide, or TMZ, in glioblastoma multiforme, or GBM, cell lines. A manuscript summarizing results from this study has been submitted for publication.

There is no assurance that we will obtain any additional Orphan Drug Designations.

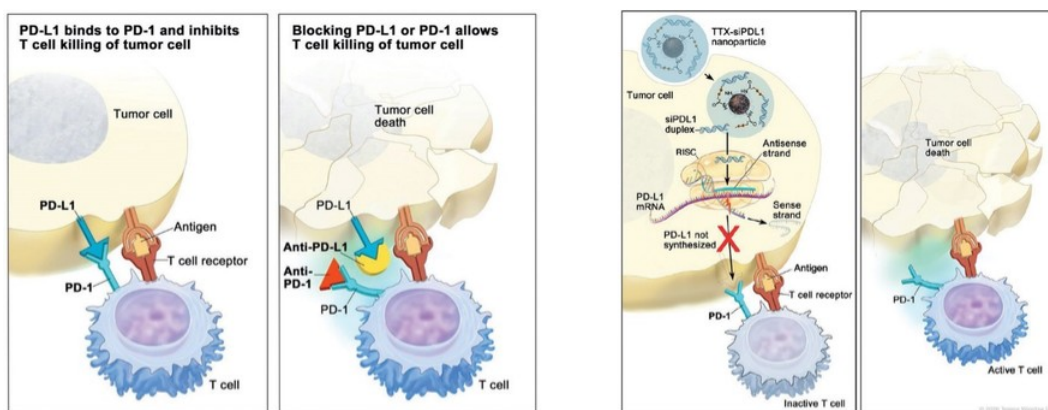
### **TTX-siPDL1**

Pancreatic cancer is the fourth-leading cause of cancer-related death in the United States with an overall 5-year survival rate of only 8%. Surgical resection remains the treatment of choice for patients with resectable disease. However, less than 20% of the diagnosed patients qualify for curative resections, 30% of patients present with regional disease, and 50% present with distal metastases with survival rates of 11% and 2%, respectively. The reasons behind such poor prognosis have been postulated to involve the advanced stage at the time of diagnosis, and resistance to standard chemotherapies. However, these therapies are heavily dependent on the patient’s overall health, and the overall survival benefit for the latest cytotoxic combination therapies is only approximately two to five months.

Considering the tremendous suffering caused by this disease and the modest progress achieved thus far with cytotoxic treatments, we believe there is a need to explore radical, transformative approaches for therapy that attack the disease from multiple angles. The

last decade has seen tremendous progress in the field of cancer immunotherapy. In fact, immunotherapy represents the most promising new cancer treatment approach since the development of the first chemotherapies in the 1940s. Checkpoint inhibitors have worked against lethal cancers such as melanoma and some lung cancers — sometimes with dramatic success — and are being tested in dozens of other cancer types. However, pancreatic cancer has proven difficult to treat with conventional drugs and has been resistant to initial immunotherapy approaches. Partly, the reason for this is the tumor microenvironment that characterizes pancreatic adenocarcinoma, which is both immunosuppressive in nature and a physical barrier for antibody and T lymphocyte infiltration. Consequently, it is important to design alternative approaches that combine innovative checkpoint inhibitors that can be delivered efficiently to tumor cells and tumor resident macrophages, and strategies that enhance the permeation of the tumor by T lymphocytes.

The human immune system has T cells that help fight off diseases. T cells are like soldiers that help the body fight infections and other diseases, including cancer. However, cancer cells can escape T cell attacks by expressing a protein called PD-L1. PD-L1 works like a “stop sign” to inactivate T cells. The far left of **Fig. 11** shows how cancer cells prevent T-cells from recognizing and killing tumor cells by producing PD-L1. To the right of the first graphic in **Fig. 11** is a graphic that shows how current checkpoint inhibitors work to block PD-L1 expression. On the far right in **Fig. 11** is a graphic showing how our therapeutic is designed to work. Using an approach to prevent the synthesis of PD-L1 altogether rather than blocking its function after the cancer cell has produced it. Because TTX-siPDL1 incorporates a siRNA against PD-L1 as its functional component, it inactivates PD-L1 at the post-transcriptional level. Namely, it triggers the degradation and/or translational repression of the PD-L1 messenger RNA (mRNA), preventing the cell from expressing the PD-L1 antigen.



**Figure 11.** Mechanism of action of PD-L1 inhibitors. Cancer cells can escape immune attack by expressing a protein called PD-L1 which works like a “stop sign” to inactivate T cells. On the far left is a graphic showing how tumor cells produce PD-L1 to prevent T-cells from recognizing and killing the tumor cells. Second from the left is a graphic that shows how current checkpoint inhibitors work to block PD-L1 expression. The graphic second from the right shows how our TTX-siPDL1 is designed to work — preventing the synthesis of PD-L1 rather than blocking its function, leading to tumor cell death (far right).

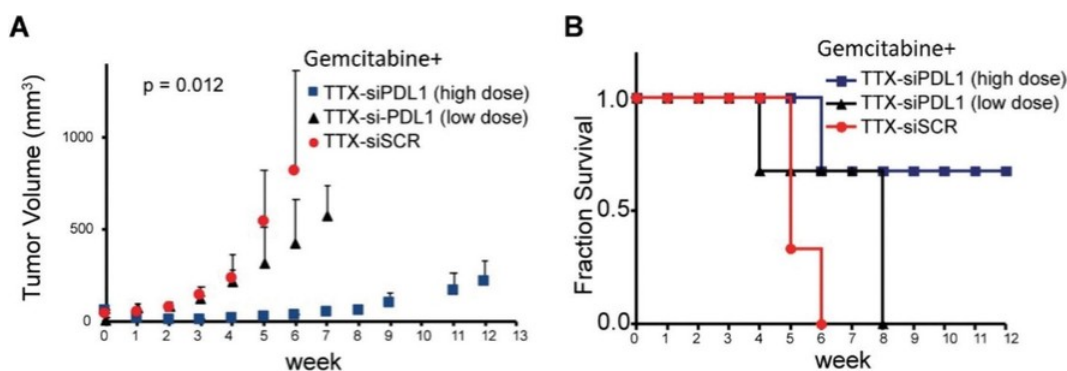
Since we are utilizing an RNAi approach, our therapeutic has the potential to be more efficient, which could allow T cells to recognize and kill tumor cells more robustly than traditional checkpoint inhibitors. At this time, we believe we are the only company targeting PD-L1 using RNAi. As our initial therapeutic candidate, we are developing an alternative strategy that relies on combining gemcitabine (Gem), the standard of care treatment for pancreatic cancer, and our novel PD-L1 inhibitor (termed TTX-siPDL1). TTX-siPDL1 incorporates our proprietary nanoparticle delivery system that is specifically designed to efficiently deliver our therapeutic candidate to tumor cells *in vivo*, inhibiting PD-L1 expression by these cells via the RNA interference mechanism. We believe that this approach is advantageous over small molecules or antibodies because the small interfering RNA component inhibits the target antigen at the post-transcriptional level rather than at the protein level. Also, the RNA mechanism has been shown to be catalytic and has been observed in *in vitro* studies to require delivery of only picomolar amounts of siRNA to the tumor cell for the abolition of the target antigen. By contrast, small molecules or antibodies require the achievement of at least a 1:1 molar ratio of antigen to therapeutic molecule and could be ineffective in the event of a compensatory increase in the tumor cell’s expression of the target antigen.

In our initial preclinical study, we administered combination therapy consisting of gemcitabine and TTX-siPDL1 in a syngeneic murine pancreatic cancer model over a seven-week treatment period. Our study investigators observed significantly lower morbidity and toxicity, tumor regression and a dramatic improvement in survival. In particular, following dose optimization, a 90% reduction in tumor volume was observed after two weeks of treatment. Within the study, 100% of the control animals (i.e., those treated with an inactive version of TTX-siPDL1, named TTX-siSCR, in place of TTX-siPDL1) had succumbed to their tumors within six weeks of after the beginning of treatment, while none of the experimental animals treated with a high dose of the active therapeutic candidate, TTX-siPDL1, had succumbed at week six of treatment, and 67% of these animals survived for 12 weeks.

We believe an additional key advantage of our approach derives from the fact that it offers an opportunity to develop a clinically relevant, image-guided treatment protocol that provides knowledge about therapeutic outcome, expressed both as change in tumor volume and tumor growth rate. Importantly, the combination of hemodynamic and metabolic targeting is expected to achieve highly efficient distribution of the therapeutic in the tumor microenvironment and uptake inside the tumor cells, as opposed to monoclonal antibodies which are not optimally targeted to the tumor microenvironment. As a result, TTX-siPDL1 could potentially have much more potent target engagement than currently-used checkpoint inhibitors, which are based on monoclonal antibodies.

Our pancreatic cancer studies illustrated the potential of a combination treatment with gemcitabine and TTX-siPDL1. Study mice co-treated with TTX-siPDL1 and gemcitabine showed significant inhibition of tumor growth relative to controls ( $p < 0.05$ ). This difference was evident two weeks after beginning treatment (**Fig. 12A**).

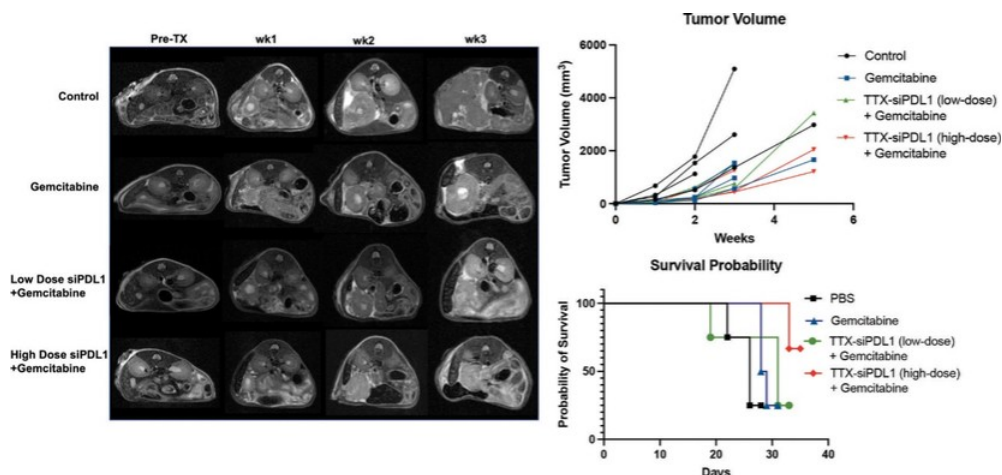
The presumed advantage of the combination treatment was demonstrated in the study when assessing animal survival (**Fig. 12B**). In the study, 67% of the mice treated with gemcitabine and TTX-siPDL1 (high dose) survived for 12 weeks while 67% of the mice treated with gemcitabine and TTX-siPDL1 (low dose) survived until week eight. All of the control mice treated with TTX-siSCR and gemcitabine succumbed by week six. Within the study, all of the mice in the group treated with gemcitabine and TTX-siSCR developed large necrotic tumors, presumably due to the high rate of tumor growth. Tumor necrosis and ulceration were not seen in the animals treated with the combination therapeutic candidate.



**Figure 12.** Outcome of treatment with TTX-siPDL1 and gemcitabine, or Gem. The mice were treated with Gem (333.3 mg/kg) in solution with a low dose of either TTX-siPDL1 or siSCR (10mg/kg Fe; 520 nmoles/kg siRNA in both groups) or a high dose of TTX-siPDL1 or siSCR (10 mg/kg Fe, 937 nmoles/kg siRNA in both groups).

Our preclinical data were used in support of our application for Orphan Drug Designation which we received in June 2022. More recently, we carried out studies in a highly aggressive syngeneic orthotopic animal model of pancreatic ductal adenocarcinoma, or PDAC, that is characterized by intense desmoplasia, similar to human PDAC. Specifically, in this model, in untreated animals, tumor volume grew 788-fold over the course of 5 weeks, with 30-40% of the tumor mass attributed to a fibrous capsule. We implanted Hy15549 cells into the pancreas of C57BL/6 mice. Once tumors measured over 2 mm in diameter, as measured by anatomic MRI, treatment was initiated and involved gemcitabine (6.66 mg/mouse) and TTX-siPDL1 at two doses: low dose (1500 nmoles siRNA/kg) or high dose (2000 nmoles siRNA/kg). Representative MRI images are shown in the left side image of **Fig. 13**. There was a notable reduction in tumor volume in the high-dose TTX-siPDL1 group relative to all control groups (**Fig. 13**, right side, top graph). Quantitative voxel-based analysis of tumor volume from MRI confirmed these observations (**Fig. 13** and the right graph in **Fig. 9**). The improvement in therapeutic outcome was best seen in terms of animal survival (**Fig. 13**, right side, bottom graph), with two thirds

of the animals in the high-dose TTX-siPDL1 group surviving for 35 days after the beginning of treatment, as opposed to just 25% of the control animals. Continued studies to expand the sample size and obtain a more robust indication of the potential of this therapy are ongoing.



**Figure 13.** Combination treatment with gemcitabine and TTX-siPDL1. Image on left: Representative T2- weighted MR images during the course of treatment. Tumors were segmented manually using ImageJ. Graph on right, top: Change in tumor volume during treatment. Graph on right, bottom: Kaplan-Meier survival analysis demonstrating survival improvement in animals treated with high-dose TTX-siPDL1 plus gemcitabine vs. control groups.

### TTX-RIGA

Immunotherapies represent powerful alternatives to traditional clinical treatments for cancer. Recent developments in the use of Pattern Recognition Receptors, or PRRs, specifically retinoic acid-inducible gene I-like receptors, aim to harness the innate power of the immune system for anti-cancer therapy. Retinoic acid-inducible gene I, or RIG-I, is a cytosolic nucleic acid sensing Pattern Recognition Receptor of the innate immune system. It is essential for recognizing certain RNA viruses. RIG-I is ubiquitously expressed in all cell types including tumor cells. RIG-I engagement leads to tumor cell death, and to activation of the innate and adaptive immune systems. These factors suggest it could be an attractive therapeutic approach in oncology.

Understanding how to recruit RIG-I in a tumor-selective manner is critical for its adoption and further development as a clinical treatment modality. We are developing a therapeutic strategy for the tumor- selective template-based activation of RIG-I in cancer cells, directed by the specific overexpression of oncogenic miRNAs in tumors. We are in the early stages of the preclinical development of a novel tumor- selective RIG-I agonist to effectively activate RIG-I and induce type-I Interferon signaling and tumor cell apoptosis. RIG-I is ubiquitously expressed in all cell types including tumor cells. These factors suggest it could be an attractive therapeutic approach in oncology although there is no assurance that our efforts will be successful.

Tumor cell death induced by RIG-I activation has been reported in multiple types of cancer, including pancreatic, prostate, head and neck, gastric, and breast cancer as well as glioblastoma. However, RIG-I- based therapeutic strategies face multiple challenges, such as designing highly specific and stable agonists, and developing efficient agonist delivery modes while avoiding uncontrolled release of pro-inflammatory cytokines.

Our therapeutic candidate, TTX-RIGA, in preclinical development, is designed to utilize our proprietary delivery system to deliver a RIG-I agonist to tumor cells. TTX-RIGA is intended to activate the RIG-I signaling pathway, in turn triggering an immune response that targets cancer. The results of the testing we have completed support continuation of our research with this candidate. A manuscript detailing feasibility studies with RIGA was recently published in BioRxiv.

## **TTX-siLIN28B**

LIN28B is an RNA-binding protein that regulates messenger RNA (mRNA) translation. It may be activated in a variety of human cancers by mechanisms that remain poorly understood. Increasing evidence demonstrates that LIN28B is activated in cancer and serves as a critical oncogene, a mutated gene that contributes to the development of a cancer.

We recently extended our exclusive option from MGH to negotiate a license for a siRNA technology designed to inhibit LIN28B in a subset of pancreatic and several other cancer types including hepatocellular, breast, colon, and gastric cancers among others.

We began preclinical studies on our TTX-siLIN28B targeting LIN28B in 2022. Should test results meet our objectives, we anticipate conducting animal studies with this therapeutic candidate after which we will consider adding this candidate to our MGH license agreement. If we achieve success with any of our other therapeutic candidates in preclinical animal studies and have the resources to do so, we anticipate advancing these candidates into clinical trials.

## **TRANSCODE DIAGNOSTIC PROGRAM (TCDx)**

### **CDx Mechanism of Action**

One key to reducing cancer mortality is early detection. TransCode is considering applications of its technology to diagnostic product candidates designed to identify the right therapy for particular patients.

### **TCD-miRNA Screening and Diagnostic Assays**

Building on a foundation of medical imaging, TransCode's scientific co-founders have developed a specific biomarker test designed to measure microRNA expression in single intact live cells, tissues and serum. In this manner, TransCode's microRNA nanosensor (CDx) is being developed to address a major unmet need in the areas of cancer biology, diagnosis and therapy.

Importantly, the nanosensor could permit measurement of microRNAs in *single cells*, e.g., from circulating tumor cells, allowing the capture of the heterogeneity of microRNA expression in a patient and observation of individual populations of rare cells, such as cancer stem cells.

The fluorescent read-out generated by the nanosensor is highly specific and has nanomolar sensitivity.

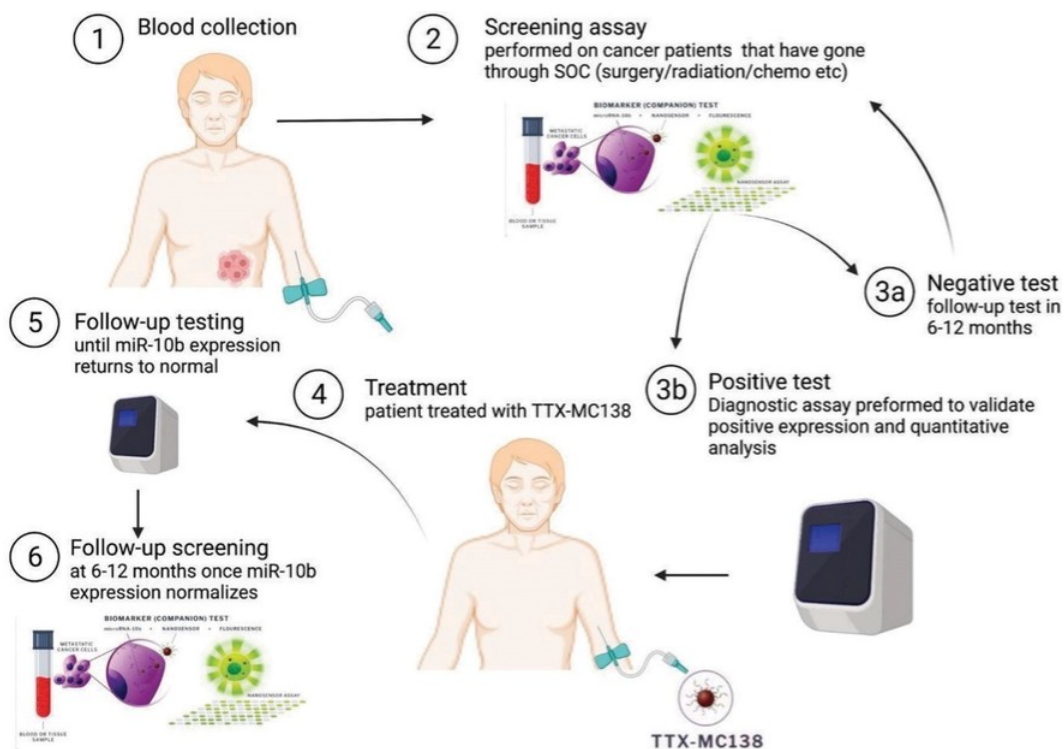
The nanosensor assay is inexpensive and rapid; could be used to determine microRNA expression in biopsies, serum, and circulating tumor cells in multiple clinical settings throughout a patient's treatment.

### **TCD-miR10b**

One of the most promising features of microRNA-10b is the potential to use its expression in diseased tissue and in circulation as a diagnostic biomarker to determine the presence of metastases and potentially as a predictive biomarker of overall/disease free survival in cancer. Our TCD-miR10b assay has been designed to allow for identification of patients at increased risk of disease progression, a capability not currently available. It could help stratify tumors based on aggressiveness, which could better inform the need for more aggressive treatment or the need for increased surveillance. TCD-miR10b could serve as a diagnostic biomarker for the presence of metastases, better informing therapeutic decisions as evidenced in recent studies showing that microRNA-10b expression is negatively correlated to sensitivity to 5-fluorouracil (5-FU)- based therapies and can induce greater tamoxifen resistance.

We have completed preclinical studies to validate TCD-miR10b and a small *in vitro* pilot study using human serum from healthy subjects and patients with metastatic breast cancer. TCD-miR10b is also being investigated for potential use in monitoring response to

treatment with TTX-MC138 in clinical trials. This capability could be instrumental in identifying which patients might better respond to TTX-MC138 therapy in clinical trials and then in measuring therapeutic response during those trials (Fig.14).

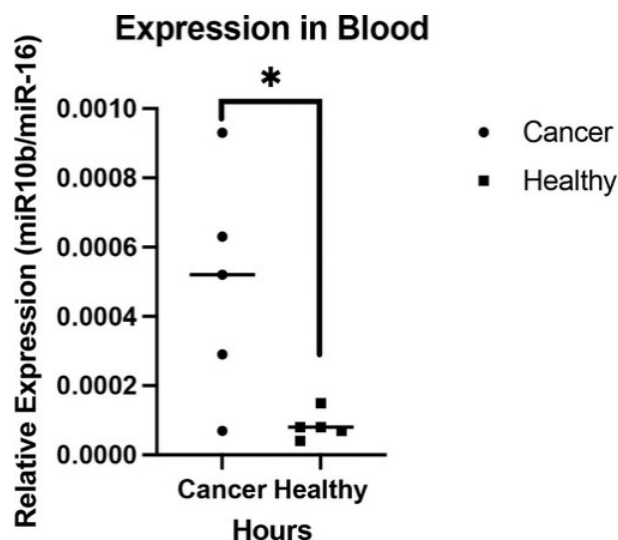


**Figure 14.** Depicts work-flow that incorporates TransCode’s planned screening and diagnostic assays to support therapy with TTX-MC138.

We have evaluated the performance of our assay in detecting miR-10b in human blood and tissue compared to the gold-standard, qRT-PCR. We have characterized the performance of the diagnostic assay in terms of specificity, reproducibility, dynamic range, and detection limit. Our results support continued development of this assay in human blood. We have now tested TCD-miR10b with



blood and tissue samples from both cancer patients and healthy subjects and have demonstrated its ability for patient stratification (Fig. 15).



**Figure. 15.** Relative miR-10b expression in blood from colorectal carcinoma patients and healthy subjects using diagnostic assay.

## INTELLECTUAL PROPERTY

Our intellectual property, or IP, portfolio is directed to our therapeutic and diagnostic candidates and their targeted use and development in specific patient populations and in specific indications. Our portfolio currently consists of seven different patent families comprising issued patents, pending patent applications and new provisional patent applications. Patents for TTX-MC138 have issued in the U.S. while patents for an associated biomarker test have issued in the U.S. and the E.U. We obtained rights to use patents and patent applications under our MGH License. While our MGH-related patents for TTX-MC138 were granted only in the U.S., which we believe represents a significant portion of the total market, we are currently in the process of pursuing new filings with broader coverage in both the U.S. and elsewhere.

### Therapeutic Patent Rights Assigned to TransCode

#### *Template Directed Immunomodulation for Cancer Therapy*

- Provisional (63/132,315) filed 12/30/20 converted into International PCT Application (PCT/US21/ 65580).

#### *Radiolabeled Nanoparticles and Template Directed Immunomodulation for Cancer Therapy*

- Provisional (63/356,449) filed 06/28/22.

### Therapeutic Patent Rights (Covered under MGH License)

#### *Therapeutic Nanoparticles and Methods of Use Thereof*

- US 9,763,891 — Granted (Issued September 2017). Expires 2031.
- US 9,629,812 — Granted (Issued April 2017). Expires 2031.

- US 10,463,627 — Granted (Issued November 2019). Expires 2031.

*Biomarker Patent Rights (Diagnostic test)*

*miRNA Profiling Compositions and Methods of Use*

- US 10,086,093 — Granted (Issued October 2018). Expires 2033.
- EP 2961386 — Granted (Issued July 2019). Expires 2033.

*Compositions and Methods for Tunable Magnetic Nanoparticles*

- PCT/US 2020/63635 — Application filed December 7, 2020. PCT filed. Expires 2039.

*Compositions and Methods for Immune Checkpoint Inhibition*

- PCT/US 2019/050003 — Application filed September 6, 2019. Corresponding national stage filings pending in Australia, Canada, China, Europe, Japan, Korea, and the United States. Estimated expiration 2038.

*Agents and Methods for Treating Pancreatic Ductal Carcinoma*

- US 10,588,920 — Granted (Issued March 2020). Expires 2035.

*Radiolabeled Therapeutic Nanoparticles and Methods of Using the Same*

- Provisional (63/109,298) filed November 3, 2020. PCT application PCT/US2021/057912 filed 11/03/21 published 05/12/22 under WO2022/098768.

*Compositions and Methods for Immune Checkpoint Inhibition*

- PCT/US 2019/050003 — Application filed September 6, 2019. Corresponding national stage filings pending in Australia, Canada, China, Europe, Japan, Korea, and the United States. Estimated expiration 2038.

**EXCLUSIVE LICENSE AGREEMENT**

In November 2018, we entered into a license agreement with MGH, or the MGH License, pursuant to which MGH granted us an exclusive, world-wide, royalty-bearing, sub-licensable license to certain MGH intellectual property which we collectively refer to as the Licensed Patents.

We are required to pay tiered royalties of a low to middle single-digit percentage on annual net sales of products related to the Licensed Patents. Initially, there were minimum royalties of \$25,000 per year prior to the first commercial sale of a product or process covered by the Licensed Patents, and a minimum of \$50,000 per year after the first commercial sale of a product or process covered by the Licensed Patent.

Upon the occurrence of certain milestones, we are also obligated to make payments of up to an additional \$1.55 million in aggregate. As of the date of this prospectus, no milestone events had been achieved.

Unless earlier terminated, the MGH License will expire upon the latest of (i) the date on which all issued patents and filed patent applications subject to the License have expired or been abandoned; (ii) expiration of the last to expire regulatory exclusivity covering a covered product or process; or (iii) 10 years after the first commercial sale of a product or process covered by the Licensed Patents.

In the event of a default in our performance of the MGH License that we fail to cure, MGH may terminate the MGH License with respect to the country or countries in which the default occurs. MGH may terminate the MGH License immediately upon written

notice to us in the event of our bankruptcy, insolvency, dissolution or winding up, or if we fail to maintain the insurance required pursuant to the MGH License. MGH may also terminate the MGH License upon written notice if we fail to make payments due under the MGH License. We may terminate the MGH License at any time by providing ninety (90) days written notice to MGH. Any sublicenses granted by us under the MGH License shall be automatically terminated upon the termination of the MGH License, but MGH is required to make a good faith effort to enter into a direct license agreement with any sublicensee who so requests.

#### *Amendment to License Agreement*

In November 2020, we and MGH amended the MGH License. Under the amendment, the intellectual property licensed in 2018 was categorized as “Patent Family 1” and a provisional patent filing related to MGH’s nanoparticle technology was added to Patent Family 1. A second patent family, “Patent Family 2,” was created which includes MGH intellectual property targeting PD-L1.

The minimum annual license fee prior to the first commercial sale of a product or process covered by the MGH License was increased to \$30,000 per year for Patent Family 1 and a minimum annual license fee of \$10,000 per year was added related to Patent Family 2. All other terms of the MGH License including milestone payments, royalties and payment terms related to sublicense income we may receive remain the same as in the original MGH License.

Upon expiration of the MGH License, the licenses granted to us pursuant thereto will be considered fully paid and royalty-free.

#### **EXCLUSIVE OPTION AGREEMENTS**

On May 5, 2022, we executed an option agreement with MGH giving us the right to negotiate an exclusive, worldwide, royalty-bearing license related to a radiotheranostic technology disclosed in patent application PCT/US2021/057912 entitled THERAPEUTIC, RADIOLABLED NANOPARTICLES AND METHODS OF USE THEREOF. On September 28, 2022, we executed an extension of an option agreement with MGH giving us the right to negotiate an exclusive, worldwide, royalty-bearing license related to LIN28B technology disclosed in U.S. Patent 10,588,920 entitled AGENTS AND METHODS FOR TREATING PANCREATIC DUCTAL ADENOCARCINOMAS.

#### **COMPETITION**

The pharmaceutical industry is intensely competitive and constantly evolving. While we believe that our experience, scientific knowledge and intellectual property provide us with certain competitive advantages, these may not be sufficient to succeed. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies. Most of our potential competitors are larger than we are, and they have substantially greater capital and human resources than we do. Many also have established market positions and expertise and capabilities in sales, marketing, distribution, clinical trials and regulatory matters. Not only must we compete with other companies that are focused on RNA therapeutics and other therapeutics that treat cancer, but also any therapeutic candidates that we successfully develop and commercialize must compete with existing therapies and new therapies that may become available in the future. In addition, we compete with other life sciences companies generally for employees, consultants and advisors, supplies and materials, and laboratory facilities and equipment.

Our competitors may develop more successful products that are similar to ours, but sooner than we can commercialize ours, which may negatively impact our results.

There are several companies operating in the “targeted therapy” space, many of which have existed longer than we have, with the advantages described above. The development of targeted therapies requires the identification of good targets — that is, targets that play a key role in cancer cell growth and survival. (It is for this reason that targeted therapies are sometimes referred to as the product of “rational” drug design.)

One approach to identify potential targets is to compare individual proteins in cancer cells with those in normal cells. Proteins that are present in cancer cells but not normal cells, or that are more abundant in cancer cells, could be potential targets, especially if they are known to be involved in cell growth or survival. An example of such a differentially expressed target is the human epidermal growth factor receptor 2 protein, or HER-2. HER-2 is expressed at high levels on the surface of some cancer cells. Several targeted therapies are directed against HER-2, including trastuzumab (Herceptin), which is approved to treat certain breast and stomach cancers that overexpress HER-2.

Another approach to identify potential targets is to determine whether cancer cells produce mutant (altered) proteins that drive cancer progression. For example, the cell growth signaling protein BRAF is present in an altered form (known as BRAF V600E) in many melanomas. Vemurafenib (Zelboraf) targets this mutant form of the BRAF protein and is approved to treat patients with inoperable or metastatic melanoma that contains this altered BRAF protein.

Researchers also look for abnormalities in chromosomes that are present in cancer cells but not in normal cells. Sometimes these chromosome abnormalities result in the creation of a fusion gene (a gene that incorporates parts of two different genes) whose product, called a fusion protein, may drive cancer development. Such fusion proteins are potential targets for targeted cancer therapies. For example, imatinib mesylate (Gleevec) targets the BCR-ABL fusion protein, which is made from pieces of two genes that join together in some leukemia cells and promotes their growth.

There are a number of oncology companies with targeted therapeutics for various cancers with therapeutic candidates in various stages of preclinical and clinical development. Companies focusing on RNA therapeutics for oncology include Arrowhead Pharmaceuticals, Ionis, Moderna, Alnylam, BioNTech, Dicerna, and Siranomics, among others. We believe these companies lack delivery systems that are able to target genes inside tumors and metastases. We know of no other RNA companies currently in clinical development that have an exclusive focus on cancer and whose pipelines are not limited to a single RNA technology such as siRNA or mRNA vaccines. By contrast, TransCode's pipeline spans a spectrum of RNA technologies and includes ncRNAs, RNA vaccines, CRISPR technology, and immunostimulatory RNAs solely for oncology.

## **Targeted therapy**

Targeted cancer therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific molecules ("molecular targets") that are involved in the growth, progression, and spread of cancer. Targeted cancer therapies are sometimes called "molecularly targeted drugs," "molecularly targeted therapies," "precision medicines," or similar names.

Targeted therapies differ from standard chemotherapy in several ways:

- Targeted therapies act on specific molecular targets that are associated with cancer, whereas most standard chemotherapies act on all rapidly dividing normal and cancerous cells.
- Targeted therapies are deliberately chosen or designed to interact with their target, whereas many standard chemotherapies were identified because they kill cells.
- Targeted therapies are often cytostatic (that is, they block tumor cell proliferation), whereas standard chemotherapy agents are cytotoxic (that is, they kill tumor cells).

Targeted therapies are currently the focus of intense anti-cancer drug development. Spending on targeted therapies continues to grow rapidly in all regions of the world and now represents 48% of total oncology spending, up 36% from 2010. As mentioned above, we are focused on targeted therapies for cancer treatment with its novel therapeutics that have been shown in animals to successfully target the master regulator of metastatic progression, microRNA-10b.

## **Immunotherapy**

Immunotherapy has become an established pillar of cancer treatment improving the prognosis of many patients with a broad variety of hematological and solid malignancies. The two main drivers behind this success are checkpoint inhibitors, or CPIs, and chimeric antigen receptor, or CAR, T cells. For checkpoint blockade, current studies focus on combinational approaches, perioperative use, new tumor entities, response prediction, toxicity management and use in special patient populations. Regarding cellular immunotherapy, recent studies confirmed safety and efficacy of CAR T cells in larger cohorts of patients with acute lymphoblastic leukemia or diffuse large B cell lymphoma. Different strategies to translate the striking success of CAR T cells in B cell malignancies to other hematological and solid cancer types are currently under clinical investigation. Regarding the regional distribution of registered clinical immunotherapy trials, a shift from PD-1 / PD-L1 trials (mainly performed in the U.S. and in the European Union, or EU) to CAR T cell trials (majority of trials performed in the United States and China) can be noted.

The importance of immunotherapy is underscored by the fact that the Nobel prize for physiology and medicine in 2018 was awarded to James P. Allison and Tasuku Honjo for the discovery of cytotoxic T-lymphocyte-associated protein, or CTLA-4, and programmed cell death protein1/ programmed cell death protein ligand 1, or PD-1 / PD-L1. Malignant tumors take advantage of the inhibitory PD-1 / PD-L1 or CTLA-4 pathways to evade the immune system. Disrupting this axis by blocking monoclonal antibodies can induce durable remissions in different cancer types and has led to numerous FDA and European Medicines Agency, or EMA, approvals, among others, for the treatment of melanoma, lung cancer, urothelial cancer, head and neck squamous cell carcinoma, or HNSCC, renal cell carcinoma, or RCC, and Hodgkin's disease.

### **Tyrosine kinase inhibitors**

Tyrosine kinase inhibitors are targeted therapies for cancer. Although some tyrosine kinase inhibitors are used to treat other types of cancer, lapatinib (Tykerb) is the only one that is FDA-approved for the treatment of breast cancer. Lapatinib is only used to treat HER2-positive metastatic breast cancer.

### **PARP inhibitors**

Poly (ADP-ribose) polymerase, or PARP, inhibitors are a class of drugs under study for many types of cancer, including breast cancer. PARP is an enzyme involved in DNA repair. At this time, PARP inhibitors are only offered in clinical trials for people with metastatic breast cancer. Early findings suggest that PARP inhibitors hold the most promise for people with metastatic breast cancer who have a BRCA1 or BRCA2 gene mutation.

### **Cyclin dependent kinase 4 and 6 (CDK4/6) inhibitors**

CDK4 and CDK6 are enzymes important in cell division. CDK4/6 inhibitors are a new class of drugs designed to interrupt the growth of cancer cells. The CDK4/6 inhibitor palbociclib (Ibrance) in combination with hormone therapy is FDA-approved for the treatment of hormone receptor-positive, HER2-negative metastatic breast cancers.

### **PI3 kinase inhibitors**

PI3 kinase is an enzyme important in cell growth. The PIK3CA gene helps control PI3 kinase enzyme activity. Some breast cancers have a mutation in the PIK3CA gene, and this mutation can affect PI3 kinase and cause the tumor to grow. PI3 kinase inhibitors are a new class of drugs designed to interrupt PI3 kinase signals and stop the growth of cancer cells. PI3 kinase inhibitors are under study for the treatment of metastatic breast cancer.

### **Diagnostics**

Existing methods for detecting microRNAs rely on polymerase chain reaction, or PCR, and northern blotting, both of which analyze tissue in bulk, or on high-affinity hybridization probes, such as molecular beacons or SmartFlare probes, which involve cumbersome protocols and cannot be applied to live cells. By contrast, we are designing our diagnostics to:

- a. permit measurement in *single cells*, e.g., from a biopsy sample or circulating tumor cells, potentially allowing accurate capture of the heterogeneity of microRNA expression in a patient and observation of individual populations of rare cells, such as cancer stem cells;
- b. allow measurement in *serum samples*, permitting diagnostics based on circulating cell-free microRNA expression;
- c. be applicable in *intact, live cells* and, therefore, permits longitudinal studies, in which the "evolution" of the tumor cell phenotype is monitored in an intact cellular environment;
- d. be *sensitive*, since each cell can take up over  $1 \times 10^6$  nanoparticles with multiple attached sensor oligonucleotides; and
- e. be *inexpensive and rapid*, involving a simple incubation of the test sample with the sensor and examination using generally available instruments that produce fluorescence readouts.

## **MANUFACTURING**

### **Manufacturing: Chemistry, Manufacturing and Controls (CMC)**

CMC is an extensive aspect of the IND enabling process and is critical to setting appropriate timelines and connecting “deliverables” to human trial start dates. The term “deliverables” refers to more than just the drug product itself. It also includes analytical standards and required documentation on drug purity, dose strength, storage, handling and stability. The materials for the analytical development process are produced as part of the CMC process and must be delivered before CMC development work can begin, as are activities that require analytical support for which time requirements must also be considered.

The design and manufacture of nanodrugs such as TTX-MC138 for miRNA targeting in tumor cells has gone through extensive research and development optimization at MGH prior to our company formation. Optimization work continues in our lab. The basic design of these nanodrugs includes dextran-coated iron oxide nanoparticles conjugated to an LNA-modified antisense oligonucleotide that stably binds and inhibits the complementary mature miRNA inside the metastatic lesion. The oligonucleotide drug substance incorporated in the final therapeutic candidate drug product is currently manufactured by our contract manufacturer, or CMO, in Germany. We believe this CMO will be able to meet our needs for oligonucleotide manufacturing meeting current good manufacturing practices, or cGMP, or good laboratory practices, or GLP, (together sometimes referred to as GxP) at least for the near term. TransCode has been utilizing the manufacturing services of this CMO since 2017.

We engaged a second CMO in the Netherlands to produce the final therapeutic candidate drug product in which our oligonucleotides are attached to aminated dextran-coated iron oxide particles. The dextran-coated iron oxide particles are analogous in structure and size to those used in the FDA-approved, intravenously administered, iron replacement therapy known as Ferraheme®. This second CMO has indicated it has the capacity to handle the clinical manufacture of sterile and complex drug products which meet GxP requirements.

## **COMMERCIALIZATION**

We retain worldwide commercialization rights for our key therapeutic and diagnostic candidates. We currently have no sales, marketing or product distribution capabilities. However, if our therapeutic candidates appear closer to FDA approval, we may explore commercialization partnerships with larger pharmaceutical organizations or out-license sales and marketing of those therapeutic candidates.

We also intend to consider opportunities to license certain of our technologies to other companies with an oncology focus. Our commercial plans and strategy for each particular program may change as programs advance, markets change, we obtain more clinical data, and we assess our capital requirements.

## **GOVERNMENT REGULATION**

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drugs. We, along with our vendors, contract research organizations and contract manufacturers, will be required to navigate the various preclinical, clinical, manufacturing and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our therapeutic candidates. The process of obtaining regulatory approvals of drugs and ensuring subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

In the United States, where we are initially focusing our drug development activities, the FDA regulates drug products under the Federal Food, Drug and Cosmetic Act, or FD&C Act, its implementing regulations and other laws. Our therapeutic candidates are early-stage and none of our therapeutic candidates has been approved by the FDA for marketing in the United States. If we fail to comply with applicable FDA or other requirements at any time with respect to product development, clinical testing, approval or any other legal requirements relating to product manufacture, processing, handling, storage, quality control, safety, marketing, advertising, promotion, packaging, labeling, export, import, distribution, or sale, we may become subject to administrative or judicial sanctions or other legal consequences.

These sanctions or consequences could include, among other things, the FDA's refusal to approve pending applications, issuance of clinical holds for ongoing studies, suspension or revocation of approved applications, warning or untitled letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

The process required by the FDA before our therapeutic candidates are approved as drugs for therapeutic indications and may be marketed in the United States generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with GLP requirements;
- submission to the FDA of an IND application, which must become effective before clinical trials may begin;
- approval by an IRB, or independent ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with applicable IND regulations, good clinical practice, or GCP, requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of a New Drug Application, or NDA;
- a determination by the FDA within 60 days of its receipt of an NDA, to accept the filing for review;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the drug will be produced to assess compliance with current good manufacturing practices, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the clinical trial sites that generated the data in support of the NDA;
- payment of user fees for FDA review of the NDA; and
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our therapeutic candidates will be granted on a timely basis, if at all.

### ***Preclinical and clinical trials for drugs***

Before testing any drug in humans, the therapeutic candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of drug chemistry, formulation and stability, as well as *in vitro* and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulations and requirements, including GLP requirements for safety/toxicology studies. The results of the preclinical studies, together with manufacturing information and analytical data must be submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and must become effective before clinical trials may begin. Some long-term preclinical testing may continue after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the content of the IND or clinical trial design, including concerns that human research subjects will be exposed to unreasonable health risks, and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may result in the FDA not allowing clinical trials to commence or not allowing clinical trials to commence on the terms originally specified in the IND. A separate submission to an existing IND must also be made for each successive clinical trial

conducted during product development of a therapeutic candidate, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin.

The clinical stage of development involves the administration of the therapeutic candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable related to the anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trials to public registries. Information about clinical trials, including clinical trials results, must be submitted within specific timeframes for publication on the [www.clinicaltrials.gov](http://www.clinicaltrials.gov) website.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor must submit data from the clinical trial to the FDA in support of an NDA. The FDA will accept a well-designed and well-conducted foreign clinical trial not conducted under an IND if the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials to evaluate therapeutic indications to support NDAs for marketing approval are typically conducted in three sequential phases, which may overlap.

- *Phase 1* — Phase 1 clinical trials involve initial introduction of the investigational product into healthy human volunteers or patients with the target disease or condition. These studies are typically designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, excretion the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.
- *Phase 2* — Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks.
- *Phase 3* — Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and physician labelling.

FDA additionally allows for the conduct of exploratory IND studies, termed Phase 0 clinical trials. Exploratory IND trials are conducted under an IND early in Phase 1, prior to traditional dose escalation, safety and tolerance studies that ordinarily initiate a clinical drug development program. Exploratory IND studies usually involve very limited human exposure and have no therapeutic or diagnostic intent. The goals of an exploratory IND study may include determining whether a mechanism of action defined in experimental systems can also be observed in humans, providing important information on pharmacokinetics, selecting the most promising lead product from a group of candidates designed to interact with a particular therapeutic target in humans, based on pharmacokinetic or pharmacodynamic properties, or exploring a product's biodistribution characteristics using various imaging technologies.

In March 2022, the FDA released final guidance entitled "Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics," which outlines how drug developers can utilize an adaptive trial design commonly



referred to as a seamless trial design in early stages of oncology drug development (i.e., the First-in-Human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by FDA. Expansion cohort trials can potentially bring efficiency to drug development and reduce developmental costs and time.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators fifteen days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk for human volunteers and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor's initial receipt of the information.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the therapeutic candidate. Companies must also finalize a process for manufacturing the drug product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the therapeutic candidate and manufacturers must develop, among other things, methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the therapeutic candidate does not undergo unacceptable deterioration over its shelf life.

### ***U.S. marketing approval for drugs***

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. An NDA is a request for approval to market a new drug for one or more specified indications and must contain proof of the drug's safety and efficacy. The marketing application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA approval of an NDA must be obtained before a drug may be marketed in the United States.

The FDA reviews all submitted NDAs before it accepts them for filing and may request additional information rather than accepting the NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt, and such decision could include a refusal to file by the FDA. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA targets ten months, from the filing date, in which to complete its initial review of a new molecular entity NDA and respond to the applicant, and six months from the filing date of a new molecular entity NDA for priority review. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Further, under PDUFA, as amended, each NDA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk-minimization tools.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the Sponsor product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP and other requirements and the integrity of the clinical data submitted to the FDA.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, depending on the specific risk(s) to be addressed it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

#### ***Orphan drug designation and exclusivity***

Under the Orphan Drug Act, the FDA may grant Orphan Drug Designation to a therapeutic candidate intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the product available in the United States for the disease or condition will be recovered from sales of the product. Orphan Drug Designation must be requested before submitting an NDA. Orphan Drug Designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan products are eligible for certain incentives, including tax credits for qualified clinical testing and waiver of application fees.

If a product that has Orphan Drug Designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to Orphan Drug Exclusivity, a seven-year period of marketing exclusivity during which the FDA may not approve any other applications to market the same therapeutic agent for the same indication, except in limited circumstances, such as a subsequent product's showing of clinical superiority over the product with orphan exclusivity or where the original applicant cannot produce sufficient quantities of product. Competitors, however, may receive approval of different therapeutic agents for the indication for which the orphan product has exclusivity or obtain approval for the same therapeutic agent for a different indication than that for which the orphan product has exclusivity. Orphan Drug Exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for the same therapeutic agent for the same indication before we do, unless we are able to demonstrate that our product is clinically superior. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to Orphan Drug Exclusivity. Further, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective.

or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

#### ***Rare pediatric disease designation and priority review vouchers***

Under the FD&C Act, the FDA incentivizes the development of drugs that meet the definition of a “rare pediatric disease,” defined to mean a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years and the disease affects fewer than 200,000 individuals in the United States or affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug. The sponsor of a therapeutic candidate for a rare pediatric disease may be eligible for a voucher that can be used to obtain a priority review for a subsequent human drug application after the date of approval of the rare pediatric disease drug product, referred to as a priority review voucher, or PRV. A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its NDA. A rare pediatric disease designation does not guarantee that a sponsor will receive a PRV upon approval of its NDA. Moreover, a sponsor who chooses not to submit a rare pediatric disease designation request may nonetheless receive a PRV upon approval of their marketing application if they request such a voucher in their original marketing application and meet all of the eligibility criteria. If a PRV is received, it may be sold or transferred an unlimited number of times. Congress has extended the PRV program through September 30, 2026, with the potential for PRVs to be granted through September 30, 2026.

#### ***Expedited development and review programs for drugs***

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs addressing unmet medical needs or for treating serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval. The purpose of these programs is to expedite either the development or the review of certain new drugs to get them to patients sooner than under standard FDA development and review procedures. TransCode anticipates seeking one or more of these qualifications or designations, but there is no assurance that any will be obtained.

A new drug is eligible for Fast Track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the agency may review portions of the marketing application before the sponsor submits the complete application, as well as Priority Review, discussed below. In addition, a new drug may be eligible for Breakthrough Therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient drug development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review and approval process, including Priority Review designation and accelerated approval. A product is eligible for Priority Review if it has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. Under priority review, the FDA must review an application in six months compared to ten months for a standard review. Additionally, products are eligible for accelerated approval if they can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality which is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

Accelerated approval is usually contingent on a sponsor’s agreement to conduct additional post-approval studies to verify and describe the product’s clinical benefit. The FDA may withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, unless otherwise informed by the FDA, the FDA currently requires, as a condition for accelerated approval, that all advertising and promotional

materials that are intended for dissemination or publication within 120 days following marketing approval be submitted to the agency for review during the pre-approval review period, and that after 120 days following marketing approval, all advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval but may expedite the development or review process.

### ***Pediatric information and pediatric exclusivity***

Under the Pediatric Research Equity Act, or PREA, certain NDAs and certain supplements to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The Food and Drug Administration Safety and Innovation Act, or FDASIA, amended the FD&C Act to require that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs.

A drug can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

### ***U.S. post-approval requirements for drugs***

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, reporting of adverse experiences with the product, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-market testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and their subcontractors involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose certain procedural and documentation requirements upon us and our contract manufacturers. Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing,

product seizures, injunctions, civil penalties or criminal prosecution. There is also a continuing, annual prescription drug product program user fee.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, requirements for post-market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs; or mandated modification of promotional materials and labeling and issuance of corrective information.

### ***FDA Regulation of In Vitro Diagnostics***

*In vitro* diagnostics, including companion diagnostics and complementary diagnostics, are regulated as medical devices by FDA. In the United States, the FD&C Act, and its implementing regulations and other federal and state statutes and regulations, govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption or FDA exercise of enforcement discretion applies, diagnostic tests generally require marketing clearance or approval from FDA prior to commercialization. The two primary types of FDA marketing authorization applicable to a medical device are clearance of a premarket notification, or 510(k), and approval of a premarket approval application, or PMA.

To obtain 510(k) clearance for a medical device, or for certain modifications to devices that have previously received 510(k) clearance, a manufacturer must submit a premarket notification demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or to a pre-amendment device that was in commercial distribution before May 28, 1976, or a predicate device, for which the FDA has not yet called for the submission of a PMA. In making a determination that the device is substantially equivalent to a predicate device, the FDA compares the proposed device to the predicate device and assesses whether the subject device is comparable to the predicate device with respect to intended use, technology, design and other features which could affect safety and effectiveness. If the FDA determines that the subject device is substantially equivalent to the predicate device, the subject device may be cleared for marketing. The 510(k) premarket notification pathway generally takes from three to twelve months from the date the application is completed, but can take significantly longer.

A PMA must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the quality system regulation, or QSR, which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. FDA's review of an initial PMA is required by statute to take between six to ten months, although the process typically takes longer, and may require

several years to complete. If FDA evaluations of both the PMA and the manufacturing facilities are favorable, FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If FDA's evaluation of the PMA or the manufacturing facilities is not favorable, FDA will deny the approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. Once granted, PMA approval may be withdrawn by FDA if compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

Companion diagnostics identify patients who are most likely to benefit from a particular therapeutic product; identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness. On July 31, 2014, FDA issued a final guidance document addressing the development and approval process for "*In Vitro* Companion Diagnostic Devices." According to the guidance document, for novel therapeutic products that depend on the use of a diagnostic test and where the diagnostic device could be essential for the safe and effective use of the corresponding therapeutic product, the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic, although FDA recognizes that there may be cases when contemporaneous development may not be possible. However, in cases where a drug cannot be used safely or effectively without the companion diagnostic, FDA's guidance indicates it will generally not approve the drug without the approval or clearance of the diagnostic device. FDA also issued draft guidance in July 2016 setting forth the principles for co-development of an *in vitro* companion diagnostic device with a therapeutic product. The draft guidance describes principles to guide the development and contemporaneous marketing authorization for the therapeutic product and its corresponding *in vitro* companion diagnostic. The use of the companion diagnostic device will be stipulated in the labeling of the therapeutic product. This is also true for a complementary diagnostic, although it is not a prerequisite for receiving approval of the therapeutic as is generally the case with companion diagnostics.

Once cleared or approved, an *in vitro* diagnostic device, including a companion diagnostic or complementary diagnostic, must adhere to post-marketing requirements including the requirements of FDA's quality system regulation, adverse event reporting, recalls and corrections along with product marketing requirements and limitations. Like drug makers, *in vitro* diagnostic makers are subject to unannounced FDA inspections at any time during which FDA will conduct an audit of the product(s) and the company's facilities for compliance with its authorities.

#### **Other regulatory matters**

Manufacturing, sales, promotion and other activities of therapeutic candidates following product approval, where applicable, or commercialization are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, which may include the Centers for Medicare & Medicaid Services, or CMS, other divisions of the Department of Health and Human Services, or HHS, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments and governmental agencies.

#### **Other healthcare laws**

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we develop, market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below.

- The federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid; a person or entity need not have actual

knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

- The federal civil and criminal false claims laws, including the civil False Claims Act, or FCA, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using, or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The FCA also permits a private individual acting as a “whistle-blower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil False Claims Act, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs.
- The federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary’s selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies.
- The Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for knowingly and willfully executing a scheme, or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, or falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, imposes, among other things, specified requirements on covered entities and their business associates relating to the privacy and security of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates in some cases, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions.
- The Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, imposed new annual reporting requirements for certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children’s Health Insurance Program, for certain payments and “transfers of value” provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. In addition, many states also require reporting of payments or other transfers of value, many of which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts.

- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.
- Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, which may be broader in scope and apply regardless of payor. These laws are enforced by various state agencies and through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant federal government compliance guidance, require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, and restrict marketing practices or require disclosure of marketing expenditures and pricing information. State and foreign laws also govern the privacy and security of health information in some circumstances. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts.

State and foreign laws also govern the privacy and security of health information in some circumstances. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts. California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA will require covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020, and the California Attorney General will commence enforcement actions against violators beginning July 1, 2020. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. The California Attorney General has proposed draft regulations, which have not been finalized to date, that may further impact our business activities if they are adopted. The uncertainty surrounding the implementation of CCPA exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to similar actions, penalties and sanctions. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

### ***Insurance Coverage and Reimbursement***

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a therapeutic candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. In the United States, the principal decisions about reimbursement for new medicines are typically made by the CMS, an agency within HHS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the



medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, therapeutic candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

### ***Current and future healthcare reform legislation***

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs. The Affordable Care Act includes provisions of importance to our potential therapeutic candidates that:

- created an annual, non-deductible fee on any entity that manufactures, or imports specified branded prescription drugs and biological products, apportioned among these entities according to their market share in certain government healthcare programs;
- expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide point-of-sale-discounts off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and
- created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the Affordable Care Act, or ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court and members of Congress have introduced several pieces of legislation aimed at significantly revising or repealing the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021, through August 15, 2021, for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. The implementation of the ACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Litigation and legislation related to the ACA are likely to continue, with unpredictable and uncertain results.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2029 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. On March 10, 2020, the former Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Further, the former Trump administration previously released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contained proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out-of-pocket costs of drug products paid by consumers. HHS implemented certain measures. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. However, it is unclear whether the Biden administration will challenge, reverse, revoke or otherwise modify these executive and administrative actions. More recently, at the federal level, President Biden signed an Executive Order on July 9, 2021, affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. In addition, individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product

access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, it is possible that additional governmental action is taken to address the COVID-19 pandemic.

On May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Outside the United States, ensuring coverage and adequate payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to government control in many countries. Pricing negotiations with government authorities can extend well beyond the receipt of regulatory approval for a product and may require a clinical trial that compares the cost-effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, or EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular therapeutic candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions.

Recently, many countries in the EU have increased the discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

#### ***Prescription Drug Pricing Reduction Act***

On August 16, 2022 the Inflation Reduction Act of 2022 was passed, which among other things, allows for CMS to negotiate prices for certain single-source drugs and biologics reimbursed under Medicare Part B and Part D, beginning with ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond.

The legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The legislation also caps Medicare beneficiaries’ annual out-of-pocket drug expenses at \$2,000. The effect of Inflation Reduction Act of 2022 on our business and the healthcare industry in general is not yet known.

#### ***Compliance with other federal and state laws or requirements; changing legal requirements***

If any products that we may develop are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, labeling, packaging, distribution, sales, promotion and

other activities also are potentially subject to federal and state consumer protection and unfair competition laws, among other requirements to we may be subject.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, exclusion from federal healthcare programs, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, relabeling or repackaging, or refusal to allow a firm to enter into supply contracts, including government contracts. Any claim or action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on marketing, sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling or packaging; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

#### ***Other U.S. environmental, health and safety laws and regulations***

We may be subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third-parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

#### ***Government regulation of drugs outside of the United States***

To market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization or identification of an alternate regulatory pathway, manufacturing, commercial sales and distribution of our products. For instance, in the United Kingdom and the European Economic Area, or the EEA (comprised of the 27 EU Member States plus Iceland, Liechtenstein and Norway), medicinal products must be authorized for marketing by using either the centralized authorization procedure or national authorization procedures.

- *Centralized procedure* — If pursuing marketing authorization of a therapeutic candidate for a therapeutic indication under the centralized procedure, following the opening of the European Medicines Agency's, or EMA, Committee for Medicinal Products for Human Use, or CHMP, the European Commission issues a single marketing authorization valid across the EEA. The centralized procedure is compulsory for human medicines derived from biotechnology processes or advanced therapy medicinal products (such as gene therapy, somatic cell therapy and tissue engineered products), products that contain

a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune diseases and other immune dysfunctions, viral diseases, and officially designated orphan medicines. For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the EMA, as long as the medicine concerned contains a new active substance not yet authorized in the EEA, is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health in the EEA. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding clock stops.

- *National authorization procedures* — There are also two other possible routes to authorize products for therapeutic indications in several countries, which are available for products that fall outside the scope of the centralized procedure:
- *Decentralized procedure* — Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure.
- *Mutual recognition procedure* — In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, additional marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned recognize the validity of the original, national marketing authorization.

In the EEA, new products for therapeutic indications that are authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial authorization of the reference product in the EU. The ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

The criteria for designating an “orphan medicinal product” in the EEA are similar in principle to those in the United States. In the EEA a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. During this ten-year orphan market exclusivity period, no marketing authorization application shall be accepted, and no marketing authorization shall be granted for a similar medicinal product for the same indication. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough orphan medicinal product.

Similar to the United States, the various phases of non-clinical and clinical research in the European Union are subject to significant regulatory controls.

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on GCP and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the European Union. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted. It is expected that the new Clinical Trials Regulation (EU) No 536/2014 will apply following confirmation of full functionality of the Clinical Trials Information System (CTIS), the centralized European Union portal and database for clinical trials foreseen by the regulation, through an independent audit. The regulation becomes applicable six months after the European Commission publishes notice of this confirmation. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC. Conduct of all clinical trials performed in the European Union will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial. The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single-entry point, the “EU portal”; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The collection and use of personal health data in the European Union, previously governed by the provisions of the Data Protection Directive, is now governed by the General Data Protection Regulation, or the GDPR, which became effective on May 25, 2018. While the Data Protection Directive did not apply to organizations based outside the EU, the GDPR has expanded its reach to include any business, regardless of its location, that provides goods or services to residents in the EU. This expansion would incorporate any clinical trial activities in EU members states. The GDPR imposes strict requirements on controllers and processors of personal data, including special protections for “sensitive information” which includes health and genetic information of data subjects residing in the EU. GDPR grants individuals the opportunity to object to the processing of their personal information, allows them to request deletion of personal information in certain circumstances, and provides the individual with an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Further, the GDPR imposes strict rules on the transfer of personal data out of the European Union to the United States or other regions that have not been deemed to offer “adequate” privacy protections. Failure to comply with the requirements of the GDPR and the related national data protection laws of the European Union Member States, which may deviate slightly from the GDPR, may result in fines of up to 4% of global revenues, or €20,000,000, whichever is greater. As a result of the implementation of the GDPR, we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules.

There is significant uncertainty related to the manner in which data protection authorities will seek to enforce compliance with GDPR. For example, it is not clear if the authorities will conduct random audits of companies doing business in the EU, or if the authorities will wait for complaints to be filed by individuals who claim their rights have been violated. Enforcement uncertainty and the costs associated with ensuring GDPR compliance are onerous and may adversely affect our business, financial condition, results of operations and prospects.

Should we utilize third-party distributors, compliance with such foreign governmental regulations would generally be the responsibility of such distributors, who may be independent contractors over whom we have limited control.

### ***Brexit and the Regulatory Framework in the United Kingdom***

In June 2016, the electorate in the United Kingdom voted in favor of leaving the EU (commonly referred to as “Brexit”). Thereafter, in March 2017, the country formally notified the European Union of its intention to EU withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom formally left the EU on January 31, 2020. A transition period began on February 1, 2020, during which EU pharmaceutical law remains applicable to the United Kingdom. This transition period ended on December 31, 2020. This means that since January 1, 2021, the United Kingdom operates under a distinct regulatory regime. EU pharmaceutical laws now only apply to the United Kingdom in respect of Northern Ireland (as laid out in the Protocol on Ireland and Northern Ireland). Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of therapeutic candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for therapeutic candidates and products in the United Kingdom. The Medicines and Healthcare products Regulatory Agency, or MHRA, the United Kingdom’s medicines and medical devices regulator, published detailed guidance for industry and organizations to follow from January 1, 2021, at the completion of the transition period, which will be updated as the United Kingdom’s regulatory position on medicinal products evolves over time.

### **EMPLOYEES AND HUMAN CAPITAL RESOURCES**

As of January 31, 2023, we had 19 employees, five of whom have Ph.D. degrees. All of our employees are full-time employees. Ten employees are engaged primarily in research and development, clinical and quality systems, and eight are engaged in business development, corporate strategy, finance, and general management and administration. We supplement the efforts of our employees by use of consultants and advisors. None of our employees is represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good. Our human capital is integral to helping us achieve our goal to change how cancer is treated both as a therapeutic modality and in terms of improving patient outcomes. Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and future employees. The principal purposes of our equity incentive plans are to attract, retain and motivate our employees, consultants and directors through the granting of stock-based compensation awards and cash-based performance bonus awards.

## MANAGEMENT

### Directors, Executive Officers, Significant Employees and Advisor

The following table and text set forth the names and ages of our current directors, executive officers, significant employees and an advisor as of January 30, 2023. Our board of directors comprises only one class. All directors serve until the next annual meeting of stockholders or until their successors are elected and qualified, or until their earlier death, retirement, resignation or removal. There are no family relationships among any of the directors and executive officers.

<u>Name</u>	<u>Age</u>	<u>Position</u>	<u>Committees</u>
<b>Executive Officers</b>			
Robert Michael Dudley	72	Co-Founder, President, Chief Executive Officer, Director	3
Thomas A. Fitzgerald, MBA	71	Vice President, Chief Financial Officer, Director	
<b>Significant Employees and Advisors</b>			
Zdravka Medarova, PhD	48	Co-Founder and Chief Technology Officer	
Qiyong Peter Liu, PhD	58	Chief Scientist	
Anna Moore, PhD	60	Co-Founder, Scientific Advisor	
<b>Non-Employee Directors</b>			
Philippe P. Calais, PhD	63	Independent Director, Chairman of the Board of Directors	1, 2
Erik Manting, PhD	51	Independent Director	1, 2, 3
Magda Marquet, PhD	64	Independent Director	1, 2, 3

(1) Member of the Audit Committee

(2) Member of the Compensation Committee

(3) Member of the Nomination and Corporate Governance Committee

#### **Executive Officers**

**Robert Michael Dudley** has served as Co-Founder, Chief Executive Officer and Director of TransCode since January 2016. Prior to founding TransCode, Mr. Dudley co-founded and was CEO and Chairman of Artemes Technologies, Inc. a Boston-based drug delivery technology company that specialized in customized drug delivery systems for injectable medications, from June 2012 to October 2015. Previously, he held executive level leadership positions with industry leaders in medical devices for imaging, drug delivery, and surgical applications. He has additional experience in the diagnostic industry and web based clinical trial applications as well as patient monitoring and information systems for hospitals. Mr. Dudley began his career as a Cancer Research Associate at Harvard Medical School conducting immunology and biochemistry research in the field of tumor-associated blocking factors in breast cancer from April 1973 to December 1975. Mr. Dudley obtained a B.S. degree in Biological Sciences with a concentration in Immunology and Chemistry from Kent State University in Kent, Ohio. We believe Mr. Dudley is qualified to serve on our board of directors because of the perspective and experience he brings as our Chief Executive Officer, his educational background and his strong scientific knowledge.

**Thomas A. Fitzgerald, MBA** has served as Chief Financial Officer and Director of TransCode since July 2018 (initially part-time and substantially full-time since January 2020). From August 2006 to December 2018 (the last 15 months on a half-time basis), he served as Chief Financial Officer of Velico Medical, Inc. Prior to Velico Medical, his experience included serving as founding Managing Director of the Corporate Finance/Investment Banking unit of SVB Securities LLC (f/k/a SVB Leerink LLC and, previously, Leerink Swann & Company), a healthcare investment banking firm. Mr. Fitzgerald served in the U.S. Army, including nearly two years as an airborne-qualified infantry officer. He received an A.B. in Economics with Honors from Stanford University and an M.B.A. from the Harvard University Graduate School of Business Administration. We believe Mr. Fitzgerald is qualified to serve on our board of directors because he brings extensive experience as a senior financial executive in the life sciences industry.



### **Key Employees and Advisor**

**Zdravka Medarova, PhD** has served as Scientific Co-Founder and a member of the advisory board of TransCode since January 2016 and is our chief technology officer. Dr. Medarova was on the Faculty of Harvard Medical School and MGH since June 2007 and has continued in that capacity on a part-time basis after joining TransCode. She has served as an Associate Professor of Radiology at Harvard Medical School from April 2016 and as an Assistant in Neuroimaging at the Athinoula A. Martinos Center for Biomedical Imaging at MGH since June 2007. Dr. Medarova is a geneticist/cancer biologist by training. Dr. Medarova is internationally recognized for her work on non-coding RNA for cancer therapy. She is one of the first to describe the design and application of nanoparticles as carriers of siRNA to tumors. Since then, her research has focused on developing nanotechnology and imaging tools to better understand cancer initiation and progression and applying this knowledge to design clinically relevant therapeutic and diagnostic agents against cancer. Dr. Medarova obtained a B.A. in pre-medicine from the University of Southern Maine in September 1998 and a Ph.D. in Genetics from the University of New Hampshire in December 2002.

**Qiyong Peter Liu, PhD** has served as a member of our science team since May 2020, originally on a part-time basis and full-time since November 2020. Effective January 1, 2022, Dr. Liu was promoted to VP of Research and Development and Chief Scientist for TransCode. Dr. Liu earned his doctoral degree in organic chemistry at Brown University and has over 25 years of R&D experience & leadership in the biopharma industry. He has in-depth knowledge and expertise in bioconjugation chemistry, nucleic acid chemistry, and blood product development. His scientific achievements include the co-discovery and development of novel enzymes for the production of universal red blood cells. He has co-invented over 20 US patents and applications on novel enzymes, xenotransplantation, platelet, plasma, and universal red blood cells. From October 2000 until October 2020, Dr. Liu was employed in various scientific positions at Velico Medical, Inc. His post-doctoral training was at Harvard University in the Department of Molecular and Cellular Biology focusing on biochemistry and molecular biology.

**Anna Moore, PhD** has served as our Co-Founder and Scientific Advisor since January 2016. Dr. Moore has served as a Professor of Radiology and Physiology; Director, Precision Health Program and Assistant Dean, College of Human Medicine at Michigan State University since January 1, 2018. Prior to joining Michigan State University, Dr. Moore was Professor of Radiology at Harvard Medical School from September 1991 to December 2017 and the Director of the Molecular Imaging Laboratory at the Athinoula A. Martinos Center for Biomedical Imaging at Massachusetts General Hospital from September 1991 to December 2017. She is a past member of the Board of Trustees of the World Molecular Imaging Society (WMIS) and a past member of the Executive Committee of WMIS. She has served as the Regional (US) Editor for Molecular Imaging and Biology, the official journal of WMIS, since July 2015. Dr. Moore holds a Ph.D. in Bioorganic Chemistry from the Russian Academy of Sciences, Moscow, Russia.

### **Non-Employee Directors**

**Philippe P. Calais, Pharm D, PhD** has served as a member of our board of directors since October 2018 and was elected chairman of the board in January 2021. Dr. Calais has over 30 years of biotech and pharmaceutical industry experience both in North America and Europe, and is the President, Chief Executive Officer and Director at MatriSys Bioscience, Inc. He is Chairman of the Board of Directors of Phileas Pharma, Inc., an oligonucleotide company he founded in May 2019. Previously, Dr. Calais served as the president and chief executive officer of Isarna Therapeutics B.V., a developer of oligonucleotide therapeutics in Germany, the Netherlands and the United States from March 2012 to June 2018. Dr. Calais was a director of CohBar, Inc. (Nasdaq: CWBR) from June 2018 to June 2020 and was the company's interim CEO from December 2019 to May 2019. Prior to Isarna Therapeutics, Dr. Calais was the President and CEO of Univalor, a Canadian technology transfer organization, from April 2011 to February 2012. He is also an Economic Advisor to the French government since 2013. Dr. Calais served as Chief Executive Officer, President and Director of Ambrilia Biopharma, Inc., (TSE: AMB) from January 2008 to July 2009. He served as President Global Business of Neurochem Inc from January 2003 to December 2007, focusing on corporate strategic positioning and company deployment. He served as Chairman of the Board of Neurochem International, a wholly owned subsidiary of Neurochem inc. (Nasdaq: NRMX) from March 2003 to December 2007. He was an Independent Director at Marina Biotech, Inc. (OTCBB: MRNX) from January 2017 until May 2018, and its Lead Independent Director since October 2017. He served as a board member of Autotelic Inc. from June 2016 to June 2018. He served as Director of Canada's Research Based Pharmaceutical Companies from 2002 to 2011; the Cité des Biotechs de Laval from February 2002 to February 2012; Cognisense from December 2010 to February 2012 and Medpharmgene from January 2011 to February 2012. Dr. Calais holds a bachelor's degree in pharmacy and a Doctor of Pharmacy from the Université François-Rabelais in Tours, France. We believe that Dr. Calais is qualified to serve on our board of directors due to his management experience in the pharmaceutical and biotherapeutics industries and his experience as an executive officer and board member of several biotechnology companies.

**Erik Manting, PhD** has served on our board of directors since December 2020. Dr. Manting served as Managing Director and Chief Executive Officer of DCPrime BV, an immuno-oncology company based in the Netherlands, from March 2018 until DCPrime's December 2020 merger with Immunicum AB, a listed Swedish biotechnology company. On June 23, 2022, Immunicum AB changed its name to Mendus AB. Dr. Manting currently serves as Chief Executive Officer of Mendus AB. He has also served as a supervisory board member of Synerkine Pharma BV, a biopharmaceutical company, since March 2019 and as founder of BioEntrepreneur BV, a consulting company, since September 2017. Prior to that, he served as executive director of life sciences and healthcare at Kempen & Co, an investment bank, from October 2012 to September 2017. We believe that Dr. Manting is qualified to serve on our board of directors due to his extensive commercial and managerial experience in banking and as an executive officer and board member of several biotechnology companies.

**Magda Marquet, PhD** has served on our board of directors since January 2021. Dr. Marquet is an experienced life sciences entrepreneur who has built, led and commercialized multiple life sciences companies. She has served as co-founder and co-chief executive officer of ALMA Life Sciences LLC, an early-stage healthcare investment firm, since 2013. Dr. Marquet also has been a co-founder of AltheaDx, a biotechnology company, from 2009 to 2022. Dr. Marquet previously served as the co-founder and chairman of Althea Technologies, a biotechnology company, from 2008 to 2019, and previously served as its co-president and co-chief executive officer from 1998 to 2008. Prior to starting Althea Technologies, Dr. Marquet held several positions in product development and pharmaceutical development in companies such as Vical and Amylin Pharmaceuticals. She currently serves on the board of directors of Arcturus Therapeutics (Nasdaq: ARCT), AnaptysBio (Nasdaq: ANAB) and Immix Biopharma (Nasdaq: IMMX). She also served on the board of Pfenex Inc. (Nasdaq: PFNX) from March 2019 until its acquisition by Ligand Pharmaceuticals in October 2020. In addition, she is the chairperson of the boards of Micronoma, Matrisys Biosciences and ProciseDx. Dr. Marquet holds a Ph.D in Biochemical Engineering from INSA/University of Toulouse, France. We believe that Dr. Marquet is qualified to serve on our board of directors due to her significant experience as an executive and director of a number of companies in the life sciences sector, and because of her management and clinical expertise.

### **Board Structure and Role in Risk Oversight**

The authorized number of our board of directors is set at five, and currently contains five members. Our board of directors has determined that Drs. Calais, Manting and Marquet do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of the director and that each of these directors is "independent" as that term is defined under the rules of the Nasdaq Capital Market. There are no family relationships among any of our directors or executive officers.

In accordance with our restated certificate of incorporation and amended and restated bylaws, our board of directors is elected once a year.

Our restated certificate of incorporation provides that the authorized number of directors may be changed only by resolution of the board of directors.

In selecting board members, our board may consider many factors, such as personal and professional integrity, ethics and values; experience in corporate management, such as serving as an officer or former officer of a publicly held company or a company comparable to ours; experience as a board member or executive officer of another publicly held company or a company comparable to ours; diversity of expertise and experience in substantive matters pertaining to our business relative to other board members; and diversity of background and perspective, including, but not limited to, with respect to age, gender, race, place of residence and specialized experience.

Our board of directors does not have a policy as to whether the roles of our chairman and chief executive officer should be separate. Instead, our board of directors makes this determination based on what best serves our company's needs at any given time. Currently, Mr. Dudley serves as our President and Chief Executive Officer while Dr. Calais serves as Chair of our board of directors.

In its governance role, and particularly in exercising its duty of care and diligence, the board of directors is responsible for ensuring that appropriate risk management policies and procedures are in place to protect the company's assets and business. Our board of directors has broad and ultimate oversight responsibility for our risk management processes and programs and executive management is responsible for the day-to-day evaluation and management of risks to the company.

### ***Director Independence***

Applicable Nasdaq Stock Market LLC, or Nasdaq, rules require that, within one year of listing, a majority of a listed company's board of directors comprise independent directors. In addition, Nasdaq rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Exchange Act and that compensation committee members satisfy independence criteria set forth in Rule 10C-1 under the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In addition, in affirmatively determining the independence of any director who will serve on a company's compensation committee, Rule 10C-1 under the Exchange Act requires that a company's board of directors must consider all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including the source of compensation to the director, including any consulting, advisory or other compensatory fee paid by such company to the director, and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

Our board of directors has determined that all members of the board of directors, except Robert Michael Dudley and Thomas A. Fitzgerald, are independent directors, including for purposes of the rules of Nasdaq and the SEC. In making such independence determination, our board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances that our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director. In considering the independence of the directors listed above, our board of directors considered the association of our directors with the holders of more than 5% of our common stock. There are no family relationships among any of our directors or executive officers. Messrs. Dudley and Fitzgerald are not independent directors under these rules because they are executive officers of the company.

### ***Legal Proceedings***

We are not aware of any of our directors or officers being involved in any legal proceedings in the past 10 years relating to bankruptcy, insolvency or criminal proceedings (other than traffic and other minor offenses) or being subject to any of the items set forth under Item 401(f) of Regulation S-K.

## EXECUTIVE COMPENSATION

Our named executive officers for the fiscal year ended December 31, 2022 are:

- Robert Michael Dudley, our Chief Executive Officer; and
- Thomas A. Fitzgerald, our Vice President and Chief Financial Officer.

### Summary Compensation Table

The following table provides information regarding the total compensation for services rendered in all capacities that was earned by our named executive officers during the fiscal years indicated.

<u>Name and principal position</u>	<u>Year</u>	<u>Salary (\$)<sup>(1)</sup></u>	<u>Bonus (\$)<sup>(2)</sup></u>	<u>Stock Awards (\$)</u>	<u>Option Awards (\$)<sup>(3)</sup></u>	<u>All Other Compensation (\$)</u>	<u>Total (\$)</u>
Robert Michael Dudley	2022	494,000	—	—	311,027	—	805,027
Chief Executive Officer	2021	240,000	255,484	—	—	—	495,484
	2020	—	—	—	42,978	—	42,978
Thomas A. Fitzgerald	2022	371,000	—	—	189,701	—	560,701
Vice President and Chief Financial Officer	2021	180,000	137,613	—	—	—	317,613
	2020	—	—	—	15,386	—	15,386

- (1) Prior to our completion of our IPO in July 2021, our named executive officers did not receive cash compensation. Effective upon completion of our IPO, the initial annualized base salaries for each of Mr. Dudley and Mr. Fitzgerald were \$480,000 and \$360,000, respectively.
- (2) The bonus amounts reported for 2021 reflect annual bonuses for 2021 performance which were paid in 2022, as well as a special bonus paid to each of Mr. Dudley and Mr. Fitzgerald following the IPO in the amount of \$15,484 and \$11,613, respectively.
- (3) The amounts reported represent the aggregate grant-date fair value of stock options, calculated in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718. Unlike the calculations contained in our financial statements, this calculation does not give effect to any estimate of forfeitures related to service-based vesting, but assumes that the executive will perform the requisite service for the award to vest in full.

### Narrative to Summary Compensation Table

Our board and compensation committee review compensation annually for our executive officers. In setting executive base salaries and annual incentives and granting equity incentive awards, we consider compensation for comparable positions in the market, the historical compensation levels of our executives, individual performance as compared to our expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our stockholders, and a long-term commitment to our Company. We target a general competitive position, based on independent third-party benchmark analytics to inform the mix of compensation of base salary, annual incentives, or long-term incentives.

Our compensation committee is responsible for reviewing and recommending to the Board the compensation for all of our executive officers. Our compensation committee and Board typically review and discuss management's proposed compensation with the Chief Executive Officer for executive officers and employees other than the Chief Executive Officer. Based on those discussions and its discretion, taking into account the factors noted above, the compensation committee recommends the compensation for the executive officers to our Board for approval. Our Board discusses the compensation committee's recommendation and ultimately approves the compensation of our executive officers.

Our compensation committee is authorized to retain the services of one or more executive compensation advisors, as it sees fit, in connection with the establishment of our executive compensation programs and related policies. Commencing in 2021, the compensation committee retained the services of Pay Governance, LLC (“Pay Governance”), as its external independent compensation consultant. During 2021 and 2022, Pay Governance did not provide services to us other than the services to our compensation committee described herein. Our compensation committee performs an annual assessment of its compensation consultants’ independence to determine whether the consultants are independent. Based on its evaluation, the compensation committee determined that Pay Governance is independent and that its work has not raised any conflicts of interest.

#### *Base Salary*

We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. Base salaries are reviewed annually, typically in connection with our annual performance review process, approved by our Board, and adjusted from time to time to realign salaries with market levels after taking into account individual responsibilities, performance and experience. For 2021, prior to our completion of our IPO, our named executive officers did not receive cash compensation. Effective upon completion of our IPO, the initial annualized base salaries for each of Mr. Dudley and Mr. Fitzgerald were \$480,000 and \$360,000, respectively.

#### *Bonuses*

During fiscal years 2021 and 2022, the named executive officers were eligible for incentive compensation opportunities based upon achievement of both corporate and individual goals determined by the Board. Each named executive officer may earn more or less than the target amount based on our company’s and his individual performance. For each of 2021 and 2022, Mr. Dudley’s target bonus was 50% of his annualized base salary, and Mr. Fitzgerald’s target bonus was 35% of his annualized base salary. For 2021, based upon achievement of corporate and individual performance, the Board determined that bonuses were earned at 100% of target levels. In addition to their annual performance bonuses, the Board approved the payment of a special bonus in 2021 to each of Mr. Dudley and Mr. Fitzgerald in recognition of their work on the IPO in the amounts of \$15,484 and \$11,613, respectively.

#### *Equity Compensation*

Although we do not have a formal policy with respect to the grant of equity incentive awards to our named executive officers, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incentivizes our executive officers to remain in our employment during the vesting period. Accordingly, our Board and Compensation Committee periodically review the equity incentive compensation of our named executive officers and may grant equity incentive awards to them from time to time.

#### *Employee Benefits.*

All of our full-time employees, including our named executive officers, are eligible to participate in certain medical, disability and life insurance benefit programs offered by us. We pay the premiums for term life insurance and short and long-term disability for all of our employees, including our named executive officers. We also provide all employees, including named executive officers, paid time off benefits including, vacation, sick time and holidays. We do not sponsor any qualified or non-qualified defined benefit plans for any of our employees or executives.

In the future, we may establish a defined contribution retirement plan, such as a 401(k) plan.

#### *Rule 10b5-1 Sales Plans*

Our directors and named executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. The director or officer may amend or terminate the plan in some circumstances. Our directors and named executive officers may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

*Executive Employment Agreements*

We have entered into written employment agreements with our named executive officers, each of whom has also executed our standard form of confidential information and invention assignment agreement. The term of each agreement is for three years with automatic renewal for additional 12 month periods on each anniversary of the agreement unless terminated by either party as provided in the agreement. Pursuant to the employment agreements, in the event that the named executive officer’s employment is terminated by the company without “cause” or the named executive officer resigns for “good reason,” as each such term is defined in the applicable employment agreement, subject to the named executive officer’s execution and non-revocation of a separation agreement, including a general release of claims, the named executive officer shall be entitled to a lump sum payment equal to the sum of (i) 18 months of the executive’s base salary and (ii) an amount equal to the greater of the incentive compensation paid to the executive in the year prior to the year of termination or 1.5 times the executive’s target bonus. If the named executive officer breaches any of the provisions of the confidential information and invention assignment agreement, all payments of the severance amount shall immediately cease. In addition, if the named executive officer’s employment is terminated by the company without cause or the named executive officer resigns for good reason, the company shall pay the premiums for the executive’s health, medical and dental insurance, including those incurred under COBRA, for a period of 12 months. In lieu of the severance payments and benefits set forth above, if the named executive officer’s employment is terminated by the company without cause or the named executive officer resigns for good reason and such termination or resignation occurs within three months prior to or 18 months following a “change in control,” as defined in the applicable employment agreement, absent the company obtaining an agreement from any successor to assume the employment agreement (which assumption shall be subject to the executive’s consent) and subject to the executive’s execution of a separation agreement, including a general release of claims, the named executive officer shall be entitled to:

- a lump sum payment equal to the sum of 24 months of the executive’s base salary plus the amount of bonus for which the executive would have been eligible during a 24-month period following the date of termination;
- vesting in full of any unvested equity awards or other unvested equity interests held by the executive that are outstanding on the date of termination; and
- reimbursement by the company for any expenses incurred by the executive for the executive’s health, medical and dental insurance, including those incurred under COBRA, for 24 months following termination.

***Outstanding Equity Awards at 2022 Fiscal Year-End***

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2022:

Name	Vesting Commencement Date	Option Awards				Stock Awards	
		Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price(\$)	Option Expiration Date	Number of Shares or Units of Stock that Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested (\$)
Robert Michael Dudley	12/1/2022	—	135,000	\$ 0.51	12/11/2032	—	—
	2/1/2022	—	135,000	\$ 2.45	1/31/2032		
	1/1/2020	818,852	—	\$ 0.09	6/18/2025		
Thomas A. Fitzgerald	12/1/2022	—	100,000	\$ 0.51	12/11/2032	—	—
	2/1/2022	—	52,000	\$ 2.12	2/28/2032		
	2/1/2022	—	33,000	\$ 2.45	1/31/2032		
	1/1/2020	242,622	—	\$ 0.08	6/18/2030		

- (1) Of the shares subject to this stock option, 33% vested as of the first anniversary of the vesting commencement date and the remainder vest in 24 equal monthly installments on the last day of each month beginning with the month of the first anniversary of the vesting commencement date, subject to the named executive officer’s continued service with us through the applicable vesting date.

### **Compensation Risk Assessment**

We believe that, although a portion of the compensation provided to our named executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking. This is primarily due to the fact that our compensation programs are designed to encourage our named executive officers and other employees to remain focused on both short-term and long-term strategic goals. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

### **Director Compensation**

The table below shows all compensation earned by or paid to our non-employee directors during the year ended December 31, 2022. Robert Michael Dudley, our Chief Executive Officer, and Thomas A. Fitzgerald, our Chief Financial Officer, do not receive any compensation for their services as directors and, consequently, are not included in this table. The compensation received by Mr. Dudley and Mr. Fitzgerald during 2022 is set forth above in the section of this prospectus captioned “Executive Compensation — Summary Compensation Table.”

The following table presents the total compensation for each person who served as a non-employee member of our Board and received compensation for such service during 2022. Other than as set forth in the table below, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any of the non-employee members of our Board in 2022.

<b>Name</b>	<b>Fees Earned or Paid in Cash (\$)</b>	<b>Option Awards \$(1)(2)</b>	<b>All Other Compensation(\$)</b>	<b>Total(\$)</b>
Philippe P. Calais, PhD	102,500	9,036	—	111,536
Erik Manting, PhD	60,500	9,036	—	69,536
Magda Marquet, PhD	62,500	9,036	—	71,536

- (1) The amounts reported in the “Option Awards” columns above represent the aggregate grant date fair value of the stock options granted during 2022 as computed in accordance with FASB ASC Topic 718, not including any estimates of forfeitures related to service-based vesting conditions.
- (2) As of December 31, 2022, the non-employee directors held the following number of shares underlying outstanding stock options: Dr. Calais held 45,893; Dr. Manting held 45,893; and Dr. Marquet held 45,893.

### **Non-Employee Director Compensation Policy**

We have adopted a non-employee director compensation policy. The policy is designed to enable us to attract and retain, on a long-term basis, highly qualified non-employee directors.

Under our non-employee director compensation policy, each director who is not an employee is paid cash compensation from and after the completion of the IPO, as set forth below. Annual cash retainers are generally paid in quarterly installments in advance and are pro-rated for any partial calendar quarter of service.

	<b>Annual Retainer</b>
<b>Board of Directors:</b>	
Members	\$ 40,000
Additional retainer for non-executive chair	\$ 40,000
<b>Audit Committee:</b>	
Members (other than chair)	\$ 7,500
Retainer for chair	\$ 15,000
<b>Compensation Committee:</b>	
Members (other than chair)	\$ 5,000
Retainer for chair	\$ 10,000
<b>Nominating and Corporate Governance Committee:</b>	
Members (other than chair)	\$ 5,000
Retainer for chair	\$ 8,000

In addition, the non-employee director compensation policy provides that, upon initial election to our board of directors, each non-employee director will be granted an equity award in the form of a non-qualified stock option to purchase 19,000 shares of common stock, or the Initial Grant. The Initial Grant vests in equal installments on the first, second and third anniversaries of the grant date, subject to continued service as a director through the applicable vesting date. Furthermore, on the date of each annual meeting of stockholders, beginning in 2022, each non-employee director who continues as a non-employee director following such meeting is granted an annual equity award in the form of a non-qualified stock option to purchase 9,500 shares of common stock, or the Annual Grant. The Annual Grant vests in full on the earlier of (i) the first anniversary of the grant date or (ii) our next annual meeting of stockholders, subject to continued service as a director through the applicable vesting date.

We reimburse all reasonable out-of-pocket expenses incurred by non-employee directors in attending meetings of the Board and committees.

#### ***Compensation Committee Interlocks and Insider Participation***

None of the members of our compensation committee is, or has been at any time during the prior three years, one of our officers or employees. None of our executive officers currently serves, or has served in the past fiscal year, as a member of the board of directors or compensation committee of any entity that has one or more of its executive officers serving as a member of our Board or our compensation committee.



## CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

### Certain Relationships and Transactions

Other than the compensation agreements and other arrangements described in this prospectus under “Executive Compensation” and “Director Compensation,” and the transactions described below, since January 1, 2022, there has not been and there is not currently proposed, any transaction or series of similar transactions to which we were, or will be, a party in which the amount involved exceeded, or will exceed, \$120,000 (or, if less, 1% of the average of our total assets amounts at December 31, 2022 and 2021) and in which any director, executive officer, holder of 5% or more of any class of our capital stock or any member of the immediate family of, or entities affiliated with, any of the foregoing persons, had, or will have, a direct or indirect material interest.

### Employment and Consulting Arrangements

We have entered into employment agreements with our executive officers. For more information regarding the agreements with our named executive officers, see “Executive Compensation — Employment Agreements.”

### Expenses Incurred by Related Parties

Between inception and mid-2018, our major stockholders and co-founders funded certain expenses of the Company. The aggregate amount of these expenses, \$35,525, was reimbursed during the fiscal year ended December 31, 2021.

### Indemnification Agreements

We have entered into agreements to indemnify our directors and executive officers. These agreements will, among other things, require us to indemnify these individuals for certain expenses (including attorneys’ fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on our behalf or in that person’s status as our executive officer or a member of our board of directors to the maximum extent allowed under Delaware law.

### Policies and Procedures for Related Party Transactions

Our board of directors reviews and approves transactions with directors, officers and holders of 5% or more of our voting securities and their affiliates, each a related party.

We have adopted a written related party transactions policy that provides that such transactions must be approved by our audit committee. Pursuant to this policy, the audit committee has the primary responsibility for reviewing and approving or disapproving “related party transactions,” which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed \$120,000 and in which a related person has or will have a direct or indirect material interest. For purposes of this policy, a related person is defined as a director, executive officer, nominee for director, or greater than 5% beneficial owner of our common stock, in each case since the beginning of the most recently completed year, and their immediate family members.

## PRINCIPAL STOCKHOLDERS

The following table sets forth information, to the extent known by us or ascertainable from public filings, with respect to the beneficial ownership of our common stock as of January 31, 2023, by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to be a beneficial owner of greater than 5.0% of our common stock.

The column entitled “Shares Beneficially Owned Prior to Offering — Percent” is based on 12,977,234 shares of our common stock outstanding as of January 31, 2023. The column entitled “Shares Beneficially Owned After Offering — Percent” is based on 24,977,234 shares of our common stock expected to be outstanding after this offering.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options that are currently exercisable or exercisable within 60 days of January 31, 2023, are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person, but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise indicated in the table below, addresses of named beneficial owners are in care of TransCode Therapeutics, Inc., 6 Liberty Square, #2382, Boston, MA 02109.

Name of Beneficial Owner	Shares Beneficially Owned Prior to Offering		Shares Beneficially Owned After Offering	
	Number	Percent	Number	Percent
<b>Greater-than-5% Stockholders</b>				
Zdravka Medarova, PhD, Chief Technology Officer <sup>(1)</sup>	1,664,182	12.7 %	1,664,182	6.6 %
Anna Moore, PhD, Co-Founder, Advisor <sup>(2)</sup>	1,602,069	12.3 %	1,602,069	6.4 %
<b>Named Executive Officers and Directors</b>				
Robert Michael Dudley, Chief Executive Officer, President, and Director <sup>(3)</sup>	1,764,461	12.7 %	1,764,461	6.8 %
Thomas A. Fitzgerald, Vice President, Chief Financial Officer <sup>(4)</sup>	415,048	3.1 %	415,048	1.6 %
Philippe Calais, PhD, Director <sup>(5)</sup>	155,682	1.2 %	155,682	0.6 %
Erik Manting, PhD, Director <sup>(6)</sup>	28,305	0.2 %	28,305	0.1 %
Magda Marquet, PhD, Director <sup>(7)</sup>	27,294	0.2 %	27,294	0.1 %
<b>All executive officers and directors as a group (5 persons)</b>	<b>2,390,790</b>	<b>16.8 %</b>	<b>2,390,790</b>	<b>9.1 %</b>

(1) Consists of (i) 1,552,787 shares of common stock and (ii) 111,395 shares of common stock underlying options exercisable within 60 days of January 31, 2023.

(2) Consists of (i) 1,552,787 shares of common stock and (ii) 49,282 shares of common stock underlying options exercisable within 60 days of January 31, 2023.

(3) Consists of (i) 893,114 shares of common stock and (ii) 871,347 shares of common stock underlying options exercisable within 60 days of January 31, 2023.

(4) Consists of (i) 139,377 shares of common stock and (ii) 275,671 shares of common stock underlying options exercisable within 60 days of January 31, 2023.

(5) Consists of (i) 127,377 shares of common stock and (ii) 28,305 shares of common stock underlying options exercisable within 60 days of January 31, 2023.

(6) Consists of 28,305 shares of common stock underlying options exercisable within 60 days of January 31, 2023.

(7) Consists of 27,294 shares of common stock underlying options exercisable within 60 days of January 31, 2023.

## DESCRIPTION OF CAPITAL STOCK

### General

The following description summarizes important terms of our capital stock, the rights of such stock, certain provisions of our Amended and Restated Certificate of Incorporation, our Amended and Restated Bylaws, certain provisions of Delaware General Corporation Law, and the pre-funded warrants. This summary does not purport to be complete and is qualified in its entirety by the provisions of our Amended and Restated Certificate of Incorporation, our Amended and Restated Bylaws, and applicable provisions of the Delaware General Corporation Law.

### Capital Stock

Our authorized capital stock consists of 290 million shares of common stock, par value \$0.0001 per share, and 10 million shares of preferred stock, par value \$0.0001 per share, all of which shares of preferred stock are undesignated. As of December 31, 2022, 12,977,234 shares of our common stock were outstanding and held by 20 stockholders of record. As of December 31, 2022, there were no shares of preferred stock outstanding.

### Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of our stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding convertible preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding convertible preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

### Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10 million shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments if we liquidate. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. As of December 31, 2022, there were no shares of preferred stock outstanding.

### Stock Options

In April 2020, the company adopted the 2020 Stock Option and Incentive Plan, or the 2020 Plan, which provided for awards to purchase up to 3,032,787 shares of our common stock. In March 2021, the company adopted its 2021 Stock Option and Incentive Plan, or the 2021 Plan, which provided for awards to purchase up to 2,500,000 shares of our common stock plus annual increases in such number of shares, and, with the 2020 Plan, the Plans. The purpose of the Plans is to encourage and enable our officers, employees, directors, consultants and other key persons (including prospective employees, but conditioned on their employment) upon whose judgment, initiative and efforts the company largely depends for the successful conduct of its business, to acquire a proprietary interest in the company. Upon completion of our IPO, our Board of Directors determined that no further awards under the 2020 Plan would be made. At that time, there were 1,792,672 shares subject to options outstanding under the 2020 Plan.

As of December 31, 2022, options to purchase an aggregate of 3,017,033 shares of our common stock were outstanding under the Plans, of which 1,489,065 were exercisable at that date.

## **Warrants**

In connection with the closing of our initial public offering, we agreed to issue as additional compensation to ThinkEquity, a division of Fordham Financial Management, Inc., warrants, or the ThinkEquity warrants, to purchase up to 312,500 shares of our common stock (5% of the aggregate number of shares of common stock sold in the initial closing of our initial public offering). The ThinkEquity warrants are exercisable at a per share exercise price equal \$5.00, subject to adjustment as described below. The ThinkEquity warrants are exercisable at any time and from time to time, in whole or in part, between January 8, 2022, and July 8, 2026 and remain outstanding in full as of the date of this prospectus. The exercise price and number of shares issuable upon exercise of the warrants may be adjusted in certain circumstances including in the event of a stock dividend or our recapitalization, reorganization, merger or consolidation. However, the warrant exercise price or underlying shares will not be adjusted for issuances of shares of common stock at a price below the warrant exercise price.

### **Pre-Funded Warrants**

The following summary of certain terms and provisions of the pre-funded warrants offered hereby in lieu of shares of common stock is not complete and is subject to, and qualified in its entirety by, the provisions of the pre-funded warrant, the form of which is filed as an exhibit to the registration statement of which this prospectus forms a part. Prospective investors should carefully review the terms and provisions of the form of pre-funded warrant for a complete description of the terms and conditions of the pre-funded warrants.

**Duration and Exercise Price.** Each pre-funded warrant offered hereby will have an initial exercise price per share equal to \$0.01. The pre-funded warrants will be immediately exercisable and may be exercised at any time. There is no expiration date for the pre-funded warrants. The exercise price and number of shares of common stock issuable upon exercise is subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock and the exercise price.

**Exercisability.** The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of the pre-funded warrant to the extent that the holder would own more than 4.99% (or at the election of the holder prior to the issuance of any pre-funded warrants, 9.99%) of the outstanding shares of common stock immediately after exercise. Any holder may increase such percentage to any percentage not in excess of 9.99% upon at least 61 days' prior notice to us. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares of common stock, we will pay the holder an amount in cash equal to the fractional amount multiplied by the exercise price of such pre-funded warrant or round up to the next whole share.

**Cashless Exercise.** In lieu of making the cash payment of the aggregate exercise price otherwise contemplated to be made to us upon such exercise, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the pre-funded warrants.

**Fundamental Transaction.** In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding shares of common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding shares of common stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction.

**Transferability.** Subject to applicable laws, a pre-funded warrant may be transferred at the option of the holder upon surrender of the pre-funded warrant to us together with the appropriate instruments of transfer.

**No Exchange Listing.** We do not intend to list the pre-funded warrants on any securities exchange or nationally recognized trading system.

No Rights as a Stockholder. Except as otherwise provided in the pre-funded warrants or by virtue of such holder's ownership of shares of our common stock, the holders of the pre-funded warrants do not have the rights or privileges of holders of our common stock, including any voting rights.

### **Registration Rights**

The ThinkEquity warrants provide for registration rights upon request in certain cases. Holders of a majority of registrable securities then outstanding have the right to demand that we file a registration statement covering registrable securities then outstanding subject to specified conditions and limitations. Upon such a request, we are required to effect the registration as soon as practicable, but in any event no later than 60 days after the receipt of such request. The demand registration right provided will terminate on July 8, 2026 and the demand registration right may only be exercised once at our expense. Additionally, if we propose to register any of our securities under the Securities Act either for our own account or for the account of other stockholders, the holders of registrable securities will each be entitled to notice of the registration and will be entitled to include their shares of common stock in the registration statement. These piggyback registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under specified circumstances. The piggyback registration right will terminate on January 8, 2024. We will bear all fees and expenses attendant to registering the securities issuable on exercise of the warrants other than underwriting commissions incurred and payable by the selling holders.

### **Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law**

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

#### ***Board Composition and Filling Vacancies***

Our certificate of incorporation provides that directors may be removed only for cause and then only by the affirmative vote of the holders of at least two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The limitations on removal of directors and treatment of vacancies have the effect of making it more difficult for stockholders to change the composition of our board of directors.

#### ***No Written Consent of Stockholders***

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

#### ***Meetings of Stockholders***

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws will limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

#### ***Advance Notice Requirements***

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content

of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

#### ***Amendment to Certificate of Incorporation and Bylaws***

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, and limitation of liability must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of a majority of the outstanding shares entitled to vote on the amendment, voting together as a single class, except that the amendment of the provisions relating to notice of stockholder business and nominations and special meetings must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

#### ***Undesignated Preferred Stock***

Our certificate of incorporation provides for 10 million authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

#### ***Choice of Forum***

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation and our amended and restated bylaws, (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or by-laws or (v) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein, or the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Unless we consent in writing to the selection of an alternate forum, the United States District Court for the District of Massachusetts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision, as our principal business address is in Boston, Massachusetts. These forum provisions may impose additional costs on stockholders, may limit our stockholders' ability to bring a claim in a forum they find favorable, and the designated courts may reach different judgments or results than other courts. In addition, there is uncertainty as to whether the Federal Forum Provision will be enforced, which may impose additional costs on us and stockholders.

## **Section 203 of the Delaware General Corporation Law**

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

## **Market Listing**

Our common stock is traded on the Nasdaq Capital Market under the trading symbol “RNAZ.” See “Risk Factors” on pages 64 and 65 under the caption “We could lose our listing on the Nasdaq Capital Market if the closing bid price of our common stock does not return to above \$1.00 for ten consecutive days during the 180 days ending July 7, 2023. The loss of the Nasdaq listing would make our common stock significantly less liquid and would adversely affect its value.”

## **Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is Vstock Transfer, LLC.

## **MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS TO NON-U.S. HOLDERS**

The following discussion is a summary of certain material U.S. federal income tax consequences of (i) the purchase, ownership and disposition of shares of our common stock issued pursuant to this offering, or the Shares and (ii) the purchase, ownership and disposition of the pre-funded warrants. The Shares and pre-funded warrants are referred to collectively herein as our securities. This summary does not purport to be a complete analysis of all potential tax consequences relating to the purchase, ownership, exercise, lapse and disposition of our securities. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable U.S. state or local or non-U.S. tax laws are not discussed, nor is the potential application of the alternative minimum tax, the Medicare contribution tax on net investment income, or the special tax accounting rules under Section 451(b) of the U.S. Internal Revenue Code of 1986, as amended, or the Code. This discussion is based on the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or the IRS, in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a holder. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership, exercise, lapse and disposition (as applicable) of our securities.

This discussion is limited to holders that hold our securities as “capital assets” within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a holder’s particular circumstances. In addition, it does not address consequences relevant to holders subject to special rules, including, without limitation:

- holders that own or are deemed to own more than 5% of our capital stock;
- certain former citizens or long-term residents of the United States;
- persons for whom shares of our common stock or pre-funded warrants constitute “qualified small business stock” within the meaning of Section 1202 of the Code;
- persons holding our securities as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- persons deemed to sell our securities under the constructive sale provisions of the Code;
- banks, insurance companies, and other financial institutions;
- brokers, dealers or traders in securities or currencies;
- “controlled foreign corporations,” “passive foreign investment companies,” and corporations that accumulate earnings to avoid U.S. federal income tax;
- S corporations, partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);



- tax-exempt organizations or governmental organizations;
- tax-qualified retirement plans;
- holders who hold or receive our securities pursuant to the exercise of employee stock options or otherwise as compensation; and
- “qualified foreign pension funds” as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by one or more qualified foreign pension funds.

If an entity or arrangement treated as a partnership for U.S. federal income tax purposes holds our securities, the tax treatment of a partner in such partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding securities and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

**THIS DISCUSSION IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP, EXERCISE, LAPSE AND DISPOSITION OF OUR SECURITIES ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY U.S. STATE OR LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.**

#### **Treatment of Pre-Funded Warrants**

Although it is not entirely free from doubt, a pre-funded warrant should be treated as a share of our common stock for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of such shares, as described below. Accordingly, no gain or loss should be recognized upon the exercise of a pre-funded warrant and, upon exercise, the holding period of a pre-funded warrant should carry over to the share received. Similarly, the tax basis of the pre-funded warrant should carry over to the share received upon exercise, increased by the exercise price of \$0.0001 per share. If a pre-funded warrant expires without being exercised, the holder should recognize a capital loss in an amount equal to such holder’s tax basis in the pre-funded warrant. This loss will be long-term capital loss if, at the time of the expiration, the holder’s holding period in the pre-funded warrant is more than one year. The deductibility of capital losses is subject to limitations.

Our characterization is not binding on the IRS, and the IRS may treat our pre-funded warrants as warrants to acquire shares of our common stock. In that case, the amount and character of your gain with respect to an investment in our pre-funded warrants could be materially different than the discussion set forth below. Accordingly, each holder should consult his, her or its tax advisor regarding the risks associated with the acquisition of pre-funded warrants pursuant to this offering (including potential alternative characterizations). The balance of this discussion generally assumes that a pre-funded warrant is treated as a share of our common stock for U.S. federal income tax purposes.

#### **Tax Considerations Applicable to U.S. Holders**

##### ***Definition of U.S. Holder***

In general, a “U.S. holder” means a beneficial owner of our securities (other than a partnership or an entity or arrangement treated as a partnership for U.S. federal income tax purposes) that is, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or an entity treated as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States or of any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or

- a trust if (a) a U.S. court can exercise primary supervision over the trust's administration and one or more U.S. persons have the authority to control all of the trust's substantial decisions or (b) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

### ***Distributions on the Shares***

As described in the section titled "Dividend Policy," we do not anticipate declaring any cash dividends to holders of common stock in the foreseeable future. However, if we do make distributions (including constructive distributions as described below) on our Shares, such distributions will constitute dividends to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles, and will be includible in your income as ordinary income when received. However, with respect to dividends received by individuals, such dividends generally are taxed under current law at applicable long-term capital gains rates, provided certain holding period requirements are satisfied. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the U.S. holder's investment, up to such U.S. holder's adjusted tax basis in the Shares. Any remaining excess will be treated as capital gain from the sale or exchange of such Shares, as applicable, subject to the tax treatment described below in "— Sale or Other Taxable Disposition of Our Securities."

### ***Constructive Dividends on Pre-Funded Warrants***

Under Section 305 of the Code, an adjustment to (or failure to adjust) the number of shares that will be issued on the exercise of the pre-funded warrants, or an adjustment to (or failure to adjust) the exercise price of the pre-funded warrants, may be treated as a constructive distribution to a U.S. holder of the pre-funded warrants if, and to the extent that, such adjustment (or failure to adjust) has the effect of increasing such U.S. holder's proportionate interest in our assets or earnings and profits as determined under U.S. federal income tax principles, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders). U.S. holders should consult their tax advisors as to (i) whether a constructive dividend deemed paid to a non-corporate U.S. holder would be eligible for the preferential rates of U.S. federal income tax applicable in respect of certain dividends received, (ii) whether corporate holders would be entitled to claim the dividends received deduction with respect to any such constructive dividends, and (iii) the general treatment of constructive distributions under their particular circumstances. Because a constructive dividend deemed received by a U.S. holder would not give rise to any cash from which any applicable withholding could be satisfied, if backup withholding is paid on behalf of a U.S. holder (because such U.S. holder failed to establish an exemption from backup withholding), such backup withholding may be set off against payments on the pre-funded warrants or Shares, or offset against other assets of such U.S. holder. Generally, a U.S. holder's adjusted tax basis in pre-funded warrant should be increased to the extent any such constructive distribution is treated as a dividend. U.S. holders should consult their tax advisors on the impact a constructive distribution may have on their holding period in the securities.

### ***Sale or Other Taxable Disposition of Our Securities***

Upon the sale, exchange or other taxable disposition of the Shares or pre-funded warrants, a U.S. holder will generally recognize capital gain or loss equal to the difference between the amount of cash and the fair market value of any property received upon the sale, exchange or other taxable disposition and such U.S. holder's adjusted tax basis in such securities. This capital gain or loss will be long-term capital gain or loss if the U.S. holder's holding period in such securities is more than one year at the time of the sale, exchange or other taxable disposition. Long-term capital gains recognized by certain non-corporate U.S. holders, including individuals, generally will be subject to reduced rates of U.S. federal income tax. The deductibility of capital losses is subject to limitations.

### ***Backup Withholding and Information Reporting***

A U.S. holder may be subject to information reporting and backup withholding when such holder receives payments on our securities (including constructive dividends) or receives proceeds from the sale or other taxable disposition of our securities. Certain U.S. holders are exempt from backup withholding, including C corporations and certain tax-exempt organizations. A U.S. holder will be subject to backup withholding if such holder is not otherwise exempt and such holder:

- fails to furnish the holder's taxpayer identification number, which for an individual is ordinarily his or her social security number;

- furnishes an incorrect taxpayer identification number;
- is notified by the IRS that the holder previously failed to properly report payments of interest or dividends; or
- fails to certify under penalties of perjury that the holder has furnished a correct taxpayer identification number and that the IRS has not notified the holder that the holder is subject to backup withholding.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a U.S. holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS. U.S. holders should consult their tax advisors regarding their qualification for an exemption from backup withholding and the procedures for obtaining such an exemption.

## **Tax Considerations Applicable to Non-U.S. Holders**

### ***Definition of Non-U.S. Holder***

For purposes of this discussion, a "non-U.S. holder" is a beneficial owner of our securities that is neither a U.S. holder (nor a partnership or an entity or arrangement treated as a partnership) for U.S. federal income tax purposes.

### ***Distributions and Constructive Distributions***

As described in the section titled "Dividend Policy," we do not anticipate declaring any cash dividends to holders of Common Stock in the foreseeable future. However, if we do make distributions of cash or property on the Shares, or if any deemed dividends result from certain adjustments, or failure to make adjustments, to the conversion rate or exercise price of the pre-funded warrants, as described above under "Tax Considerations Applicable to U.S. Holders — Constructive Dividends on Pre-Funded Warrants," such actual or deemed distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a non-U.S. holder's adjusted tax basis in its Shares or pre-funded warrants, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "— Sale or Other Taxable Disposition of Our Securities."

Subject to the discussion below on effectively connected income, backup withholding and FATCA, dividends paid or deemed paid to a non-U.S. holder will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the actual or deemed dividends (or such lower rate specified by an applicable income tax treaty, provided the non-U.S. holder furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate). Because a constructive dividend deemed received by a non-U.S. holder would not give rise to any cash from which any applicable withholding tax could be satisfied, if withholding taxes are paid on behalf of a non-U.S. holder, those withholding taxes may be set off against payments of cash on the Shares or pre-funded warrants or sales proceeds received by or other funds or assets of such non-U.S. holder. A non-U.S. holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate of U.S. federal withholding tax, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaties.

If dividends paid or deemed paid to a non-U.S. holder are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such dividends are attributable), the non-U.S. holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the non-U.S. holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States. Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular rates. A non-U.S. holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items.

Non-U.S. holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

### ***Sale or Other Taxable Disposition of Our Securities***

Subject to the discussions below regarding backup withholding and FATCA, a non-U.S. holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our securities unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such gain is attributable);
- the non-U.S. holder is a nonresident alien individual present in the United States for a period or periods aggregating 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation", or USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular rates applicable to United States persons (as defined in the Code). A non-U.S. holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty), which may be offset by certain U.S. source capital losses of the non-U.S. holder (even though the individual is not considered a resident of the United States), provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our worldwide real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or that we will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition of the shares or common stock by a non-U.S. holder will not be subject to U.S. federal income tax if our common stock is (and assuming that our pre-funded warrants are not) "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and such non-U.S. holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the non-U.S. holder's holding period. It is unclear how a non-U.S. holder's ownership of pre-funded warrants impacts the determination of the 5% threshold with respect to such non-U.S. holder's actual or constructive ownership of our common stock. There can be no assurance that our common stock will be or continue to be regularly traded on an established securities market. Our pre-funded warrants are not expected to be regularly traded on an established securities market. Dispositions by a non-U.S. holder of pre-funded warrants also may not be subject to U.S. federal income tax, even if we are treated as a U.S. real property holding corporation, if on the date such pre-funded warrants were acquired by such non-U.S. holder, such holdings had a fair market value no greater than the fair market value on that date of 5% of our common stock (if it is regularly traded on an established securities market), provided that, if such non-U.S. holder subsequently acquires additional pre-funded warrants, then such interests would be aggregated and valued as of the date of the subsequent acquisition to apply this 5% limitation.

Non-U.S. holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

### ***Information Reporting and Backup Withholding***

Payments of distributions on our securities (and constructive distributions deemed paid) will not be subject to backup withholding, provided the non-U.S. holder certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any distributions paid or deemed paid to the non-U.S. holder, regardless of whether any tax was actually withheld. In addition, proceeds of the sale or other taxable disposition of our securities within the United States or conducted through certain U.S. — related

brokers generally will not be subject to backup withholding or information reporting if the applicable withholding agent receives the certification described above or the non-U.S. holder otherwise establishes an exemption. Proceeds of a disposition of our common stock or pre-funded warrants conducted through a non-U.S. office of a non-U.S. broker that does not have certain enumerated relationships with the United States generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the non-U.S. holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

#### ***Additional Withholding Tax on Payments Made to Foreign Accounts***

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on actual or deemed dividends on, or (subject to the proposed Treasury Regulations discussed below) gross proceeds from the sale or other disposition of, our securities paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of actual or deemed dividends on our securities. Proposed Treasury Regulations eliminate FATCA withholding on payments of gross proceeds from the sale or other disposition of our securities. Taxpayers generally may rely on these proposed Treasury Regulations until final Treasury Regulations are issued.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our securities.

**EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS TAX ADVISOR REGARDING THE PARTICULAR U.S. FEDERAL, STATE AND LOCAL AND NON-U.S. TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP, EXERCISE, LAPSE AND DISPOSITION OF OUR SECURITIES, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAWS.**

## UNDERWRITING

EF Hutton, division of Benchmark Investments, LLC, is acting as the sole underwriter of this offering. We have entered into an underwriting agreement on , 2023, with respect to the offering of shares of our common stock. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase, at the public offering price less the underwriting discount set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

<b>Underwriter</b>	<b>Number of Shares</b>	<b>Number of Pre-Funded Warrants</b>
EF Hutton, division of Benchmark Investments, LLC	—	—
Total	—	—

The underwriting agreement provides that the obligations of the underwriter to pay for and accept delivery of the shares of common stock and pre-funded warrants offered by this prospectus are subject to various conditions and representations and warranties, including the approval of certain legal matters by their counsel and other conditions specified in the underwriting agreement. The shares of common stock and pre-funded warrants are offered by the underwriter, subject to prior sale, when, as and if issued to and accepted by them.

We have agreed to indemnify the underwriter against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriter may be required to make in respect thereof.

### Over-Allotment Option

We have granted a 45-day option to the underwriter to purchase up to an aggregate of 1,800,000 additional shares of our common stock and/or pre-funded warrants (equal to 15% of the common stock and pre-funded warrants sold in this offering) at the public offering price per share, less underwriting discounts and commissions, set forth on the cover page of this prospectus, solely to cover over-allotments, if any. If the underwriter exercises its option in whole or in part, then they will be committed, subject to the conditions described in the underwriting agreement, to purchase the additional shares of common stock.

### Discounts, Commissions and Reimbursement

The underwriter has advised us that the underwriter proposes to offer the shares of common stock and pre-funded warrants to the public at the public offering price set forth on the cover page of this prospectus. The underwriter may offer shares and/or pre-funded warrants to dealers at that price less a concession not in excess of \$ per share and/or pre-funded warrant, as applicable, of which up to \$ per share and/or pre-funded warrant, as applicable, may be reallocated to other dealers. After the initial offering to the public, the underwriter may change the offering price and other selling terms.

The following table summarizes the underwriting discount and commissions and proceeds to us before deducting our other offering expenses. This information assumes either no exercise or full exercise of the over- allotment option we granted to the underwriter.

	<u>Per Share</u>	<u>Per Pre-Funded Warrant</u>	<u>With No Over-Allotment</u>	<u>With Full Over-Allotment</u>
Public offering price	\$ —	\$ —	\$ —	\$ —
Underwriting discount (7%)	\$ —	\$ —	\$ —	\$ —
Proceeds, before expenses, to us	\$ —	\$ —	\$ —	\$ —

We have agreed to pay certain expenses of the underwriter relating to this offering as set forth in the underwriting agreement, including the fees and expenses of the underwriter’s legal counsel, in an amount not to exceed \$125,000.

We estimate that our total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding underwriting discounts and commissions and expenses, will be approximately \$450,000.

### **Discretionary Accounts**

The underwriter does not intend to confirm sales of the securities offered hereby to any accounts over which they have discretionary authority.

### **Lock-Up Agreements**

The company and our directors, officers and certain of our stockholders have agreed, subject to certain exceptions, for a period of 90 days with respect to the company, and for a period of 180 days with respect to our directors, officers and certain of our stockholders, after the date of this prospectus, without the prior written consent of the underwriter, not to directly or indirectly:

- in the case of us, issue, offer, pledge, assign, encumber, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of capital stock of the company or any securities convertible into or exercisable or exchangeable for shares of capital stock of the company;
- in the case of us, file or cause the filing of any registration statement under the Securities Act with respect to any shares of common stock or other capital stock or any securities convertible into or exercisable or exchangeable for our common stock or other capital stock;
- complete any offering of debt securities of the company, other than entering into a line of credit, term loan arrangement or other debt instrument with a traditional bank;
- enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the company's securities, whether any such transaction is to be settled by delivery of shares of our common stock or such other securities, in cash or otherwise;
- sell, agree to sell, offer or sell, solicit offers to purchase, grant any call option, warrant or other right to purchase, purchase any put option or other right to sell, pledge, borrow or otherwise dispose of company's securities
- establish or increase any "put equivalent position" or liquidate or decrease any "call equivalent position" (in each case within the meaning of Section 16 of the Exchange Act) with respect to any company security;
- make any demand for or exercise any right with respect to the registration of any company security;
- otherwise enter into any swap, derivative or other transaction or arrangement that transfers to another, in whole or in part, any economic consequence of ownership of a company security, whether or not such transaction is to be settled by delivery of company securities, other securities, cash or other consideration; or
- publicly announce an intention to do any of the foregoing.

### **Market Listing**

Our common stock is traded on the Nasdaq Capital Market under the symbol "RNAZ." See "Risk Factors" on pages 64 and 65 under the caption "We could lose our listing on the Nasdaq Capital Market if the closing bid price of our common stock does not return to above \$1.00 for ten consecutive days during the 180 days ending July 7, 2023. The loss of the Nasdaq listing would make our common stock significantly less liquid and would adversely affect its value." There is no established trading market for the pre-funded warrants nor do we expect a market for such securities to develop. In addition, we do not intend to apply to list the pre-funded

warrants on any national securities exchange or other trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited.

### **Price Stabilization, Short Positions and Penalty Bids**

In connection with this offering, the underwriter may engage in stabilizing transactions, over-allotment transactions, syndicate-covering transactions, penalty bids and purchase to cover positions created by short sales. Stabilizing transactions permit bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the shares while this offering is in progress.

Over-allotment transactions involve sales by the underwriter of shares in excess of the number of shares the underwriter is obligated to purchase. This creates a syndicate short position in our common stock which may be either a covered short position or a “naked” short position. In a covered short position, the number of shares of common stock over-allotted by the underwriter is not greater than the number of shares of common stock that it may purchase through exercise of the over-allotment option. In a naked short position, the number of shares of common stock involved is greater than the number of shares common stock in the over-allotment option. To close out a syndicate short position, the underwriter may elect to exercise all or part of the over-allotment option. The underwriter may also elect to stabilize the price of our common stock or reduce any syndicate short position by bidding for, and purchasing, common stock in the open market.

Syndicate short covering transactions may involve purchases of shares in the open market after the distribution has been completed. In determining the source of shares to close out the short position, the underwriter will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which it may purchase shares through exercise of the over-allotment option. If the underwriter sells more shares than could be covered by exercise of the over-allotment option and, therefore, has a naked short position, the naked short position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriter is concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in this offering.

The underwriter may also impose a penalty bid. Penalty bids permit an underwriter to reclaim a selling concession from a syndicate member when the shares originally sold by that syndicate member are purchased in stabilizing or syndicate-covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate short covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than the price that might otherwise exist absent these activities. Neither we nor the underwriter make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected in the over-the-counter market and otherwise and, if commenced, may be discontinued at any time.

### **Other Relationships**

From time to time, the underwriter and/or its affiliates may in the future provide investment banking, commercial banking and other various financial services for us for which they may receive customary fees. In the course of their businesses, the underwriter and its affiliates may actively trade our securities or loans for their own account or for the accounts of customers, and, accordingly, the underwriter and its affiliates may at any time hold long or short positions in such securities or loans. Except for services provided in connection with this offering, no underwriter has provided any investment banking or other financial services to us during the 180-day period preceding the date of this prospectus and we do not expect to retain any underwriter to perform any investment banking or other financial services for at least 90 days after the date of this prospectus.

### **Indemnification**

We have agreed to indemnify the underwriter against liabilities relating to this offering arising under the Securities Act and the Exchange Act, liabilities arising from breaches of some or all of the representations and warranties contained in the underwriting agreement, and to contribute to payments that the underwriter may be required to make for these liabilities.



## **Electronic Offer, Sale and Distribution of Securities**

This prospectus in electronic format may be made available on websites or through other online services maintained by one or more of the underwriter or selling group members. The underwriter may agree to allocate a number of securities to selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriter and selling group members making internet distributions on the same basis as other allocations. Other than this prospectus in electronic format, the information on the website of any underwriter or selling group member and any information contained in any other website maintained by an underwriter or selling group member is not part of, nor incorporated by reference into, this prospectus or the registration statement of which this prospectus forms a part, has not been approved and/or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

## **Selling Restrictions**

No action has been taken in any jurisdiction (except in the United States) that would permit a public offering of our common stock or the possession, circulation or distribution of this prospectus or any other material relating to us or our common stock in any jurisdiction where action for that purpose is required. Accordingly, our common stock may not be offered or sold, directly or indirectly, and this prospectus or any other offering material or advertisements in connection with our common stock may not be distributed or published, in or from any country or jurisdiction except in compliance with applicable rules and regulations of any such country or jurisdiction.

## ***European Economic Area***

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive, each a “Relevant Member State,” with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, or the “Relevant Implementation Date,” our securities will not be offered to the public in that Relevant Member State prior to the publication of a prospectus related to those securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that, with effect from and including the Relevant Implementation Date, an offer of our securities may be made to the public in that Relevant Member State at any time:

- to any legal entity that is a qualified investor as defined in the Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriter for any such offer; or
- in any other circumstances which do not require the publication by the issuer of a prospectus pursuant to Article 3(2) of the Prospectus Directive, provided that no such offer of the securities shall require the issuer or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an “offer of securities to the public” in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and securities to be offered so as to enable an investor to decide to purchase or subscribe for securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State, and the expression “Prospectus Directive” means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in each Relevant Member State and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

## ***United Kingdom***

In the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion)

Order 2005, as amended, or the Order, and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together, the relevant persons). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates may be made or taken exclusively by relevant persons.

### **Canada**

The offering of our common stock in Canada is being made on a private placement basis in reliance on exemptions from the prospectus requirements under the securities laws of each applicable Canadian province and territory where our common stock may be offered and sold, and therein may only be made with investors that are purchasing, or deemed to be purchasing, as principal and that qualify as both an “accredited investor” as such term is defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario) and as a “permitted client” as such term is defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any offer and sale of our common stock in any province or territory of Canada may only be made through a dealer that is properly registered under the securities legislation of the applicable province or territory wherein our common stock is offered and/or sold or, alternatively, where such registration is not required.

Any resale of our common stock by an investor resident in Canada must be made in accordance with applicable Canadian securities laws, which require resales be made in accordance with an exemption from, or in a transaction not subject to, prospectus requirements under applicable Canadian securities laws. These resale restrictions may under certain circumstances apply to resales of the common stock outside of Canada.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment hereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non- Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (“NI 33-105”), the underwriter is not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Upon receipt of this prospectus, each Québec investor hereby confirms that it has expressly requested that all documents evidencing or relating in any way to the sale of the securities described herein (including for greater certainty any purchase confirmation or any notice) be drawn up in the English language only. *Par la réception de ce document, chaque investisseur québécois confirme par les présentes qu’il a expressément exigé que tous les documents faisant foi ou se rapportant de quelque manière que ce soit à la vente des valeurs mobilières décrites aux présentes (incluant, pour plus de certitude, toute confirmation d’achat ou tout avis) soient rédigés en anglais seulement.*

## **LEGAL MATTERS**

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Goodwin Procter LLP. Certain legal matters will be passed upon for the underwriter by McGuireWoods LLP.

## **EXPERTS**

Our financial statements as of and for the years ended December 31, 2021 and 2020, included in this registration statement, of which this prospectus forms a part, have been audited by Withum Smith+Brown, PC, independent registered public accounting firm, as stated in their report appearing herein (which report includes an explanatory paragraph about the existence of substantial doubt concerning the company's ability to continue as a going concern). Such financial statements have been so included in reliance upon the authority of said firm as experts in accounting and auditing.

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## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of TransCode Therapeutics, Inc.

### Opinion on the Financial Statements

We have audited the accompanying balance sheets of TransCode Therapeutics, Inc. the “Company”), as of December 31, 2021 and 2020, and the related statements of operations, stockholders’ equity (deficit) and cash flows for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the “financial statements”). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

### Substantial Doubt Regarding Going Concern

The accompanying financial statements have been prepared assuming that the entity will continue as a going concern. As discussed in Note 1 to the financial statements, the entity has suffered recurring losses from operations, has experienced cash used from operations, and has an accumulated deficit, that raise substantial doubt about its ability to continue as a going concern. Management’s plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. Our opinion is not modified with respect to this matter.

### Basis for Opinion

These financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (“PCAOB”) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ WithumSmith+Brown, PC

We have served as the Company’s auditor since 2020.

East Brunswick, New Jersey

March 31, 2022

PCAOB ID Number 100

## TRANSCODE THERAPEUTICS, INC.

## BALANCE SHEETS

	December 31,	
	2021	2020
<b>Assets</b>		
Current assets:		
Cash	\$ 20,825,860	\$ 828,016
Prepaid expenses and other current assets	1,906,315	3,199
Total current assets	22,732,175	831,215
Fixed assets, net of depreciation	206,268	—
Deferred offering costs	—	224,153
Total assets	<u>\$ 22,938,443</u>	<u>\$ 1,055,368</u>
<b>Liabilities and Stockholders' Equity (Deficit)</b>		
Current liabilities		
Accounts payable and accrued expenses	\$ 2,503,569	\$ 369,177
Due to related parties	—	35,685
Deferred grant income	30,528	—
Total current liabilities	2,534,097	404,862
Long-term liabilities		
Convertible promissory notes, net of debt issuance costs and debt discount	—	2,086,675
Accrued interest – convertible promissory notes	—	191,687
Derivative liability	—	1,751,000
Warrant liability	—	29,376
Total long-term liabilities	—	4,058,737
Total liabilities	2,534,097	4,463,600
Commitments and contingencies (Note 8)		
Stockholders' equity (deficit)		
Preferred stock – \$0.0001 par value; 10,000,000 and 5,000,000 shares authorized at December 31, 2021 and 2020, respectively; -0- shares issued or outstanding at December 31, 2021 and 2020	—	—
Common stock – \$0.0001 par value, 290,000,000 shares authorized at December 31, 2021, and 20,000,000 shares authorized at December 31, 2020; 12,904,574 and 4,636,216 shares issued and outstanding at December 31, 2021 and 2020, respectively	1,291	464
Additional paid-in capital	30,708,336	65,949
Subscription receivable	—	(12,763)
Accumulated deficit	(10,305,281)	(3,461,882)
Total stockholders' equity (deficit)	20,404,346	(3,408,232)
Total liabilities and stockholders' equity (deficit)	<u>\$ 22,938,443</u>	<u>\$ 1,055,368</u>

The accompanying notes are an integral part of these financial statements.

## TRANSCODE THERAPEUTICS, INC.

## STATEMENTS OF OPERATIONS

	Years ended December 31,	
	2021	2020
<b>Operating Expenses</b>		
Research and development	\$ 2,753,966	\$ 284,459
General and administrative	3,397,169	442,145
Total operating expenses	6,151,135	726,604
<b>Operating loss</b>	<b>(6,151,135)</b>	<b>(726,604)</b>
<b>Other income (expense)</b>		
Change in fair value of derivative liabilities	(867,000)	(1,208,000)
Change in fair value of warrant liability	(6,109)	(14,852)
Grant income	278,333	—
Loss on sale of equipment	(3,082)	—
Interest expense	(95,070)	(394,573)
Interest income	664	136
Total other income (expense)	(692,264)	(1,617,289)
<b>Net loss</b>	<b>\$ (6,843,399)</b>	<b>\$ (2,343,893)</b>
<b>Basic and diluted net loss per share</b>		
Net loss	\$ (6,843,399)	\$ (2,343,893)
Weighted-average common shares outstanding	8,425,880	4,636,216
Net loss per share	\$ (0.81)	\$ (0.51)

The accompanying notes are an integral part of these financial statements.

TRANSCODE THERAPEUTICS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)  
Years ended December 31, 2021 and 2020

	Common Stock		Additional Paid-In Capital	Subscription Receivable	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balance, December 31, 2019	4,636,216	\$ 464	\$ 20,014	\$ (12,272)	\$ (1,117,989)	\$ (1,109,783)
Interest on subscription receivable	—	—	491	(491)	—	—
Share based compensation	—	—	45,444	—	—	45,444
Net loss from operations	—	—	—	—	(2,343,893)	(2,343,893)
Balance, December 31, 2020	4,636,216	464	65,949	(12,763)	(3,461,882)	(3,408,232)
Issuance of common stock in initial public offering, net of offering costs	7,187,500	719	25,399,954	—	—	25,400,673
Conversion of convertible promissory notes, including embedded derivative, to common stock upon completion of initial public offering	1,068,135	107	4,991,324	—	—	4,991,431
Exercise of warrants	12,723	1	64,751	—	—	64,752
Proceeds from subscription receivable	—	—	—	13,125	—	13,125
Interest on subscription receivable	—	—	362	(362)	—	—
Share based compensation	—	—	185,996	—	—	185,996
Net loss from operations	—	—	—	—	(6,843,399)	(6,843,399)
Balance, December 31, 2021	12,904,574	\$ 1,291	\$ 30,708,336	\$ —	\$ (10,305,281)	\$ 20,404,346

The accompanying notes are an integral part of these financial statements.



TRANSCODE THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS

	Years ended December 31,	
	2021	2020
Cash flows from operating activities:		
Net loss	\$ (6,843,399)	\$ (2,343,893)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation	42,470	—
Share-based compensation expense	185,996	45,444
Loss on sale of equipment	3,082	—
Change in fair value of derivative liabilities	867,000	1,208,000
Non-cash interest expense	39,471	272,864
Change in fair value of warrant liability	6,109	14,852
Due to related parties	(35,685)	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,903,114)	(3,199)
Accounts payable and accrued expenses	2,285,059	191,253
Deferred grant income	30,528	—
Accrued interest on convertible promissory notes	55,598	121,709
Net cash used in operating activities	(5,266,885)	(492,971)
Cash flows from investing activities:		
Purchase of equipment	(254,820)	—
Proceeds from sale of equipment	3,000	—
Net cash used in investing activities	(251,820)	—
Cash flows from financing activities:		
Proceeds from initial public offering of common stock, net of offering costs	26,335,100	—
Proceeds from convertible promissory notes	—	1,190,000
Proceeds from escrow for warrant exercise advances	29,267	—
Proceeds from subscription receivable	13,125	—
Payments of deferred offering costs - additions	(860,943)	(73,484)
Net cash provided by financing activities	25,516,549	1,116,516
Net change in cash	19,997,844	623,545
Cash, beginning of year	828,016	204,471
Cash, end of year	\$ 20,825,860	\$ 828,016
Supplemental disclosure of cash flows		
Cash paid during the year for		
Interest	\$ 17,870	\$ —
Income taxes	\$ —	\$ —
Supplemental disclosure of non-cash investing and financing activities		
Accrued interest on subscriptions receivable	\$ 362	\$ 491
Debt discounts associated with derivative liabilities of convertible promissory notes	\$ —	\$ 304,000
Deferred offering costs included in accounts payable and accrued expenses	\$ —	\$ 150,669
Conversion of convertible promissory notes, including embedded derivative, to common stock	\$ 4,991,431	\$ —
Deferred offering costs adjusted into additional paid-in capital in connection with IPO	\$ 73,484	\$ —
Fair value of warrant liability associated with warrant exercise	\$ 35,485	\$ —
Underwriting discounts and commissions paid from gross proceeds of IPO	\$ 2,414,900	\$ —

The accompanying notes are an integral part of these financial statements.

**TRANSCODE THERAPEUTICS, INC.**  
**NOTES TO FINANCIAL STATEMENTS**  
**December 31, 2021 and 2020**

**(1) Nature of Business and Liquidity**

TransCode Therapeutics, Inc. (the “Company” or “TransCode”) was incorporated on January 11, 2016, under the laws of the State of Delaware. TransCode is a biopharmaceutical company focused primarily on developing and commercializing innovative drugs and diagnostics for treating and identifying metastatic disease. TransCode is preparing for its first clinical trial. The Company’s lead therapeutic candidate, TTX-MC138, is an oligonucleotide conjugated to an iron oxide nanoparticle designed to be administered by infusion to inhibit the ability of metastatic tumor cells to survive. The goal of the therapy, if approved, is to achieve lifelong regression and long-term patient survival.

From its founding until mid-2021, the Company was engaged in organizational activities, including raising capital, and limited research and development (“R&D”) activities. On July 13, 2021, the Company completed the initial public offering (“IPO”) of its common stock raising \$28.75 million in gross proceeds. Since the IPO, the Company has increased its R&D activities, hired additional employees, and begun more traditional operations.

The Company has not generated revenues and has not yet achieved profitable operations, nor has it ever generated positive cash flows from operations. There is no assurance that profitable operations, if achieved, could be sustained on a continuing basis. The Company is subject to those risks associated with any early-stage biopharmaceutical company that requires substantial expenditures for research and development. There can be no assurance that the Company’s research and development projects will be successful, that products developed will obtain necessary regulatory approvals, or that any approved product will be commercially viable. In addition, the Company operates in an environment of rapid technological change and is largely dependent on the services of its employees and consultants. Further, the Company’s future operations are dependent on the success of the Company’s efforts to raise additional capital.

Following the IPO, the Company’s common stock commenced trading on the Nasdaq Capital Market under the ticker symbol “RNAZ”. The Company issued 7,187,500 shares of common stock in connection with the IPO, including exercise of the underwriter’s over-allotment option, at an initial offering price of \$4.00 per share. The net proceeds from the IPO were approximately \$25.4 million after deducting underwriting discounts, commissions and estimated offering expenses payable by the Company, including offering costs paid in 2020. In connection with the IPO, the Company also granted the underwriters warrants to purchase up to 312,500 shares of Company common stock at an exercise price of \$5.00 per share (125% of the initial public offering price). Upon the closing of the IPO, outstanding convertible promissory notes converted into 1,068,135 shares of Company common stock.

***Going Concern***

These financial statements have been prepared under the assumption that the Company will continue as a going concern which contemplates the continuation of operations, realization of assets and liquidation of liabilities in the ordinary course of business. Due to the Company’s recurring and expected continuing losses from operations, the Company has concluded there is substantial doubt concerning its ability to continue as a going concern within one year of the issuance of these financial statements without additional capital becoming available. These financial statements do not include any adjustments that might result from the outcome of this uncertainty.

To date, the Company has incurred substantial losses and negative cash flows from operations. It expects to continue to incur operating losses for the foreseeable future as it pursues development of its lead therapeutic candidate and other programs. Operating losses are expected to continue until such time, if ever, that the Company can generate significant revenue from product candidates currently in development. The Company is unable to predict the extent of any future losses or when the Company will become profitable, if ever.

For the year ended December 31, 2021, net cash used in operating activities was \$5,266,885 and the Company’s net loss was \$6,843,399. As of December 31, 2021, the Company had an accumulated deficit of \$10,305,281 and \$20,825,860 in cash.

The Company plans to expand development of its lead therapeutic candidate and other candidates, and explore strategic partnerships. Management believes that current cash is sufficient to fund operations and capital requirements into the first quarter of

**TRANSCODE THERAPEUTICS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
**December 31, 2021 and 2020**

2023, but does not believe that existing cash will be sufficient to fund requirements for a full 12 months from the date of these financial statements.

To support its planned expanded operations, the Company will require additional capital; however, the Company cannot be certain that additional funding will be available on acceptable terms, or at all. Through December 31, 2021, the Company's primary source of capital was from the sale of convertible promissory notes and equity securities in the IPO. For the foreseeable future, the Company plans to fund its operations by continuing to raise additional capital through sales of equity or additional debt.

To the extent the Company raises additional funds by issuing equity securities, its stockholders may experience significant dilution. Any debt financing, if available, may include potentially dilutive features and include restrictive covenants that impact the Company's ability to conduct business. If the Company is unable to raise additional capital when required or on acceptable terms, the Company may have to (i) significantly scale back its planned operations or (ii) relinquish or otherwise dispose of rights to technologies on unfavorable terms.

**(2) Summary of Significant Accounting Policies**

**(a) Basis of Presentation**

These financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") and the rules and regulations of the U.S. Securities and Exchange Commission ("SEC"). Any reference in these notes to applicable guidance is meant to refer to U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB"). In the opinion of management, these statements include all adjustments, consisting only of normal, recurring adjustments, necessary for a fair presentation of the financial position of TransCode Therapeutics, Inc. at December 31, 2021 and 2020, and its results of operations and its cash flows for the years ended December 31, 2021 and 2020.

**(b) Use of Estimates**

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, including disclosure of contingent assets and liabilities, at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Significant items subject to such estimates and assumptions include but are not limited to the valuation of share-based compensation, income from grants, derivative liabilities, and warrant liability. Future events and their effects cannot be predicted with certainty; accordingly, accounting estimates require the exercise of judgment. Accounting estimates used in the preparation of these financial statements change as new events occur, as more experience is acquired, as additional information is obtained and as the operating environment changes. Due to the uncertainty of factors surrounding the estimates or judgments used in the preparation of the financial statements, actual results may vary materially from these estimates.

**(c) Basic and Diluted Earnings (Loss) per Share**

Basic net earnings (loss) per share is determined by dividing the net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period. Diluted net earnings (loss) per share includes the effect, if any, from the potential conversion, vesting or exercise of securities (Contingent Securities) such as convertible promissory notes, stock options and warrants, which would result in the issuance of additional shares of common stock. The computation of diluted net earnings (loss) per shares does not include the conversion or exercise of Contingent Securities that would be antidilutive. The basic and dilutive computations of the Company's net earnings (loss) per share for the years ended December 31, 2021 and 2020, are the same because the effect of including Contingent Securities was antidilutive.

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**(d) Cash**

The Company classifies deposits in banks, money market funds and cash invested temporarily in various instruments with original maturities of three months or less as cash. At times, the Company's cash balances in U.S. banks may exceed the levels of insured amounts under the Federal Deposit Insurance Corporation (FDIC). The Company's cash balance at December 31, 2021, was \$20,825,860.

**(e) Fair Value of Financial Instruments**

The Company's financial instruments at December 31, 2021 and 2020, included cash, accounts payable, accrued expenses, convertible notes, and derivative liabilities related to the convertible notes. Cash and the derivative liabilities are reported at fair value. The recorded carrying amount of accounts payable and accrued expenses reflect their fair value due to their short-term nature. The carrying value of the interest-bearing convertible notes approximates fair value based upon the borrowing rates currently available to the Company for loans with similar terms and maturities.

**(f) Research and Development**

Research and development costs are expensed as incurred and primarily comprise expenses to discover, research and develop therapeutic candidates. These expenses may include personnel costs, stock-based compensation expense, materials and supplies, allocated facility-related and depreciation expenses, third-party license fees, and costs under arrangements with third party vendors, such as contract research organizations ("CROs"), contract manufacturing organizations ("CMOs"), and consultants. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are recorded as prepaid expenses. Such amounts are recognized as expenses as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered. At December 31, 2021 and 2020, the Company's outstanding payables to CROs or CMOs were \$386,057 and \$31,346, respectively.

The Company has entered into various research and development-related contracts with companies both inside and outside of the United States. The related costs are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ materially from the Company's estimates.

*Patent Costs*

All legal fees and expenses and costs related to patent-related filings with governmental authorities incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses. Other patent costs are classified as R&D expenses.

**(g) Grant Income**

Funds from grants are recognized as grant income in the statements of operations as and when earned for the specific research and development projects for which the grants are designated. Since there is no transfer of ownership of the work performed under the Award, and we do not lose control over the work performed under the Award, we deemed the Award funds as a contribution. Grant payments received are recorded as deferred grant income on the Company's balance sheet until the related income has been earned. Grant income earned in excess of grant payments received is recorded as grant receivable on the Company's balance sheet.

**(h) Share-Based Compensation**

Share based compensation, if any, for employees and non-employees is measured at the grant date based on the fair value of the award. The Company recognizes compensation expense, if any, for awards to employees and directors over the requisite service

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period, which is generally the vesting period of the respective award, and for awards to non-employees over the period during which services are rendered by such non-employees until completed. Generally, the Company issues awards with only service-based vesting conditions and records the expense for these awards using the straight-line method. The Company classifies stock-based compensation expense in its statements of operations in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified. Forfeitures are accounted for as they occur.

Because prior to the IPO, there was no public market for the Company's common stock, the estimated fair value of the common stock was determined by the Company's board of directors (the "Board") as of the date of each award, with input from management, considering, when available, third-party valuations of the Company's common stock as well as the Board's assessment of additional objective and subjective factors that it believed were relevant and which may have changed between the date of the then most recent third-party valuation and the date of the grant. The assumptions used in calculating the fair value of share-based awards represent management's best estimates and involve inherent uncertainties and the application of management's judgment. As a result, if factors were to change and management were to use different assumptions, share-based compensation expense could be materially different.

Certain stock appraisal methodologies utilize, among other variables, the volatility of the stock price. As an historically private company, the Company lacked company-specific historical and implied volatility information for its stock. Therefore, it estimated its expected stock price volatility based on the historical volatility of publicly-traded peer companies and expects to continue to do so until such time, if ever, as it has adequate historical data regarding the volatility of its own publicly-traded stock price. The expected life of options awarded was estimated using the simplified method because the Company has limited historical information on which to base reasonable expectations about future exercise patterns and post-vesting employment. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends on its common stock and does not expect to pay cash dividends in the foreseeable future.

**(i) Property and equipment**

Property and equipment are recorded at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset as follows:

	<b>Estimated useful life</b>
Laboratory equipment	3 years
Furniture and fixtures	5 years
Computer and office equipment	3 years
Leasehold improvements	Shorter of the useful life or remaining lease term

When assets are retired or otherwise disposed of, the cost of assets disposed of and the related accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the statements of operations in the period of disposal. Expenditures for repairs and maintenance are charged to expense as incurred.

**(j) Income Taxes**

The Company provides for income taxes using the asset and liability approach. Deferred tax assets and liabilities are recorded based on the differences between the financial statement and tax bases of assets and liabilities and the tax rates in effect when these differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. As of December 31, 2021 and 2020, the Company had a full valuation allowance against deferred tax assets.

The Company is subject to the provisions of ASC 740-10-25, Income Taxes (ASC 740). ASC 740 prescribes a more likely-than-not threshold for the financial statement recognition of uncertain tax positions. ASC 740 clarifies the accounting for income taxes by prescribing a minimum recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return.

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There are currently no open Federal or State tax audits. The Company has not recorded any liability for uncertain tax positions at December 31, 2021 or 2020.

**(k) Concentrations of Credit Risk**

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash. The Company generally maintains balances in various accounts at one or more U.S. banks in amounts that may exceed federally insured limits. The Company has not experienced any losses related to its cash and does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking balances.

**(l) Derivative Liabilities**

The Company does not use derivative instruments to hedge exposures to interest rate, market, or foreign currency risks. The Company evaluates all of its financial instruments, including convertible promissory notes, to determine if such instruments contain features that meet the definition of embedded derivatives.

Embedded derivatives must be separately measured from the host contract if all the requirements for bifurcation are met. The assessment of the conditions surrounding the bifurcation of embedded derivatives depends on the nature of the host contract. Bifurcated embedded derivatives are recognized at fair value, with changes in fair value recognized in the statements of operations each period. Bifurcated embedded derivatives are classified with the related host contract in the Company's balance sheets.

In connection with the Company's convertible promissory notes, the Company identified certain embedded and freestanding derivatives which it recorded as liabilities on the balance sheets and remeasured to fair value at each reporting date until the derivative was settled. Changes in the fair value of the derivative liabilities are recognized in the statements of operations.

**(m) Deferred Offering Costs**

The Company capitalizes certain legal, professional accounting and other third-party fees directly associated with in-process capital stock financings as deferred offering costs until such financings are consummated. After consummation of the financing, these costs are recorded in stockholders' equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering. Should a planned equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the statements of operations. As of December 31, 2021 and 2020, the Company had recorded deferred offering costs of \$0 and \$224,153, respectively, incurred in connection with the Company's IPO and reported as long-term assets on the Company's balance sheets. Deferred offering costs of \$934,427 were offset against proceeds received in the IPO and charged to additional paid-in capital.

**(n) Emerging Growth Company Status**

The Company is an "emerging growth company" ("EGC") as defined in the Jumpstart Our Business Startups Act ("JOBS Act") and may take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not EGCs. The Company may take advantage of these exemptions until it is no longer an EGC under Section 107 of the JOBS Act and has elected to use the extended transition period for complying with new or revised accounting standards. As a result of this election, the Company's financial statements may not be comparable to companies that comply with public company Financial Accounting Standards Board ("FASB") standards' effective dates. The Company may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of a public offering or such earlier time that it is no longer an EGC.

**(o) Recent Accounting Pronouncements**

In November 2021, the Financial Accounting Standards Board (the "FASB"), issued Accounting Standards Update No. 2021-10 entitled "Government Assistance (Topic 832), Disclosures by Business Entities about Government Assistance" (the "ASU"). This ASU will require enhanced disclosures related to the Company's contracts with the U.S. Government that are accounted for by

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applying a grant or contribution accounting model by analogy. The new disclosure requirements include information about the nature of the transactions and the related accounting policy used to account for the transactions; the line items on the balance sheet and income statement that are affected by the transactions, and the amounts applicable to each financial statement line item; and significant terms and conditions of the transactions, including commitments and contingencies. The ASU is effective for annual periods beginning after December 15, 2021. The Company is currently evaluating ASU 2021-10 and assessing the impact of its adoption on its financial statements, but does not believe the adoption of this standard will have a significant impact on its financial statements.

In August 2020, the FASB issued ASU No. 2020-06, Debt — Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging — Contracts in Entity’s Own Equity (Subtopic 815-40). ASU 2020-06 simplifies accounting for convertible instruments by removing major separation models required under current GAAP. The ASU also simplifies the diluted earnings per share (EPS) calculation in certain areas. The ASU is effective for public business entities that meet the definition of a Securities and Exchange Commission (SEC) filer, excluding entities eligible to be smaller reporting companies as defined by the SEC, for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. For all other entities, the standard will be effective for fiscal years beginning after December 15, 2023, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating ASU 2020-06 and assessing the impact of its adoption on its financial statements.

**(p) Reverse Stock Split**

On March 22, 2021, the Board and shareholders of the Company approved a reverse split of the Company’s common stock at a ratio of one share for every 1.6486484 shares previously held. All common stock share and per share data and conversion or exercise price data for applicable common stock equivalents included in these financial statements have been retroactively adjusted to reflect the reverse stock split.

**(3) Fair Value Measurements**

ASC 820, Fair Value Measurements, provides guidance on the development and disclosure of fair value measurements. The Company follows this guidance for fair value measurements, which defines fair value, establishes a framework for measuring fair value under U.S. GAAP, and expands disclosures about fair value measurements. The guidance requires fair value measurements be classified and disclosed in one of the following three categories:

Level 1: Quoted prices (unadjusted) in active markets that are accessible at the measurement date for identical assets or liabilities.

Level 2: Observable prices that are based on inputs not quoted on active markets but corroborated by market data.

Level 3: Unobservable inputs which are supported by little or no market activity with values determined using pricing models, discounted cash flow methodologies, or similar techniques, as well as instruments for which the determination of fair value requires significant judgment or estimation.

Fair value measurements discussed herein are based upon certain market assumptions and pertinent information available to management as of December 31, 2021 and 2020. The carrying amount of cash and accounts payable and accrued liabilities approximated fair value as they are short term in nature. The guidance in ASC 815, Derivatives and Hedging, required that we mark the fair value of our common stock warrant liability to market and recognize the change in valuation in our statements of operations each reporting period. Determining the warrant liability to be recorded required us to develop estimates to be used in calculating the fair value of the related warrant. The fair value of the related warrants was estimated based on a Black-Scholes model at the reporting date. The estimated fair value of the warrant liability and the derivative liability (“embedded put features”) included in the convertible

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promissory notes represent Level 3 measurements. The following table details the fair value measurement within the fair value hierarchy of the Company's financial instruments, which includes the Level 3 liabilities:

	Fair value measurements as of December 31, 2020, using:			
	Level 1	Level 2	Level 3	Total
<b>Liabilities</b>				
Derivative liabilities	\$ —	\$ —	\$ 1,751,000	\$ 1,751,000
Warrant liability	—	—	29,376	29,376
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 1,780,376</u>	<u>\$ 1,780,376</u>

	Fair value measurements as of December 31, 2021, using:			
	Level 1	Level 2	Level 3	Total
<b>Liabilities</b>				
Derivative liabilities	\$ —	\$ —	\$ —	\$ —
Warrant liability	—	—	—	—
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>

During the years ended December 31, 2021 and 2020, there were no transfers between Level 1, Level 2 and Level 3.

A summary of the changes in the fair value of Level 3 financial instruments for the year ended December 31, 2021, is as follows:

<b>Balance, December 31, 2020</b>	\$ 1,780,376
Changes in fair value of derivative liability	867,000
Extinguishment of liability on conversion of Notes	(2,647,376)
Changes in fair value of warrant liability	6,109
Extinguishment of liability on exercise of warrants	(6,109)
<b>Balance, December 31, 2021</b>	<u>\$ —</u>

For further discussion of the derivative liabilities, see Note 9. For further discussion of the warrant liability, see Note 11.

**(4) Prepaid Expenses and Other Current Assets**

Prepaid expenses and other current assets consisted of the following:

	December 31, 2021	December 31, 2020
Contract manufacturers and research organizations	\$ 441,593	\$ —
Insurance premiums	1,393,853	—
Prepaid operating expenses	61,459	—
Deposits	9,410	3,199
	<u>\$ 1,906,315</u>	<u>\$ 3,199</u>



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**(5) Property and Equipment**

Property and equipment, net consisted of the following:

	December 31, 2021	December 31, 2020
Laboratory equipment	\$ 247,522	\$ —
Less accumulated depreciation	(41,254)	—
Total property and equipment, net	<u>\$ 206,268</u>	<u>\$ —</u>

Depreciation expense for the years ended December 31, 2021 and 2020, was \$42,470 and \$0, respectively.

**(6) Accounts Payable and Accrued Expenses**

Accounts payable and accrued expenses consisted of the following:

	December 31, 2021	December 31, 2020
Professional fees	\$ 91,985	\$ 193,281
General consulting fees	126,491	80,013
R&D billings – CMOs, CROs, Supplies, Equipment and Consulting	595,465	51,806
General expenses	256,463	1,778
Insurance premiums	945,928	—
Payroll and benefits	482,237	—
Accrued license payments	5,000	42,300
	<u>\$ 2,503,569</u>	<u>\$ 369,178</u>

See Note 8 for further information regarding the accrued license payments.

**(7) Deferred Grant Income**

In April 2021, the Company received a Fast-Track Small Business Innovation Research, or SBIR, Award from the National Cancer Institute of the National Institutes of Health (“NIH”). The Award is expected to provide \$2,392,845 over three years to fund a two-phased research partnership between the Company and Massachusetts General Hospital. In May 2021, the Company received the first-year funding of \$308,861 which it recorded as deferred grant income. Income under the grant is recognized as work under the grant is completed. The Company recognized \$278,333 and \$0 of grant income for the years ended December 31, 2021 and 2020, respectively, resulting in deferred grant income of \$30,528 and \$0 at December 31, 2021 and 2020, respectively.

**(8) Commitments and Contingencies**

**(a) Leases**

In March 2021, the Company entered into an agreement with Massachusetts Biomedical Initiatives, Inc. (“MBI”) whereby the Company subleased approximately 2,484 square feet of laboratory space with room for minor administrative functions. The Company may also use shared laboratory equipment at the facility. The monthly rental is \$6,210 and the Company pays an additional amount for its allocated share of operating expenses currently assessed at \$15 per square foot or \$3,105 per month. The agreement is for one year, includes an option to extend the agreement upon the mutual agreement of the parties, and is cancelable anytime upon 90 days’ notice. The lease commitment as of December 31, 2021, through February 28, 2022, amounts to \$18,630. See Note 16 — “Subsequent Events.” In March 2020, the Company entered into an agreement with the Pagliuca Harvard Life Lab whereby the Company rented one laboratory bench and the right to use certain common facilities at the Life Lab. In March 2021, the Company terminated the Life Lab arrangement.

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**(b) License Agreement**

In November 2018, the Company licensed the exclusive rights to certain intellectual property to support development of its therapeutic candidates (“License”). The intellectual property licensed by the Company is owned by The General Hospital Corporation, d/b/a Massachusetts General Hospital, (“Licensor”). Payments by the Company under the license agreement included a one-time non-refundable fee of \$50,000 paid after execution of the License; reimbursement of Licensor’s patent costs which, at execution of the License, were approximately \$145,000; a minimum annual license fee of \$25,000 payable within 60 days of each anniversary of the effective date of the License prior to the first commercial sale of a product or process covered by the License; milestone payments upon attainment of certain milestone events; royalties based on net sales of products covered by the patent-related rights; and a portion of any sublicense income received by the Company. The Company is responsible for the development and commercialization of the licensed assets and for meeting certain milestones set forth in the License.

At December 31, 2021 and 2020, the Company had accrued \$0 and \$42,300, respectively, in license payments under the terms of the License, included in accounts payable and accrued expenses. The amount due at December 31, 2020, has been paid.

The milestone payments the Company is obligated to pay to Licensor shall not exceed \$1,550,000 based upon and subject to the attainment of each event indicated below. These payments are generally due within 60 days of achievement of the milestone.

<u>Milestone Event</u>	<u>Amount</u>
Enrollment of first patient in a phase II clinical trial of a therapeutic product or process	\$ 100,000
Enrollment of first patient in a phase III clinical trial of a therapeutic product or process	\$ 200,000
First commercial sale of a therapeutic product or process	\$ 1,000,000
Filing of an application for regulatory approval of a clinical diagnostic product or process	\$ 100,000
First regulatory approval of a clinical diagnostic product or process	\$ 150,000

As of December 31, 2021 and 2020, no milestone events had been achieved.

In addition to milestone payments, royalties shall be paid to Licensor assessed on net sales of licensed products on a country-by-country basis in an amount equal to 3.0% for therapeutic products or processes and 6.0% for clinical diagnostic products and processes. The Company shall pay Licensor 30% of any and all sublicense income.

The Company has the right to terminate the License at any time by giving 90 days advance notice subject to the payment of any amounts due under the License at that time. The License may also be terminated for cause by either party upon the breach of the material obligations of the other party or the bankruptcy or liquidation of the other party. If the License does not terminate, its term shall continue until the latest of (i) the date on which all issued patents and filed patent applications subject to the License have expired or been abandoned; (ii) expiration of the last to expire regulatory exclusivity covering a covered product or process; or (iii) 10 years after the first commercial sale. The License requires the Company to make royalty payments beyond the term of the License at 1.5%.

In November 2020, the Company and Licensor amended the November 2018 license. Under the amendment, the intellectual property licensed in 2018 was categorized as “Patent Family 1” and a provisional patent filing related to the Company’s nanoparticle technology was added to Patent Family 1. A second patent family (“Patent Family 2”) was created which includes Licensor intellectual property targeting PD-L1.

The minimum annual license fee prior to the first commercial sale of a product or process covered by the License was increased from \$25,000 per year to \$30,000 per year for Patent Family 1 and a minimum annual license fee of \$10,000 per year was added related to Patent Family 2. All other terms of the License, including milestone payments, royalties and payment terms related to sublicense income received by the Company, remain the same as in the original License.

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***Option Agreement***

The Company signed an Exclusive Option And Internal Evaluation License Agreement (the “Option”) with the Licensor effective February 15, 2021. Under the Option, the Company has (1) the exclusive right to negotiate a license of a certain technology patented by the Licensor and (2) a non-exclusive internal evaluation license to allow the Company to evaluate the technology. The Option provided for a six-month term at a cost of \$5,000 with a right to extend, upon the mutual agreement of the parties, for an additional six months for a second \$5,000 payment. In August 2021, the Licensor agreed to extend the initial term of the Option until November 15, 2021, at no cost to the Company. On November 8, 2021, the Company exercised its right to extend the Option to May 15, 2022, in consideration of the payment of the second \$5,000. The Company is also responsible for patent costs related to the subject technology incurred by Licensor during the Option period. Patent costs incurred by the Licensor prior to the effective date will not be reimbursed under the Option. At December 31, 2021, the Company had accrued \$5,000 due under the terms of the Option, included in accounts payable and accrued expenses, which amount has since been paid.

***(c) Employment Agreements***

Prior to the IPO, the Company entered into employment agreements with its executive officers which became effective on completion of the IPO. The employment agreements provide the employee with, among other things, severance payments upon termination of the agreement by the Company for any reason other than for cause, death or disability or by the employee for good reason (as such terms are defined in the agreements). At December 31, 2021, the maximum aggregate severance payments under the agreements, which arise in the event of termination involving a Change of Control (as defined in the agreements), are approximately \$2,412,000.

***(d) Litigation***

The Company may from time to time be subject to claims by others under various legal disputes. The defense of such claims, or any adverse outcome relating to any such claims, could have a material adverse effect on the Company’s liquidity, financial condition, and cash flows. At December 31, 2021 and 2020, the Company did not have any pending legal actions.

***(e) Indemnification Agreements***

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners, and other parties with respect to certain matters including, but not limited to, losses arising out of certain events occurring under such agreements, breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and executive officers that require the Company, among other things, to indemnify the parties against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any costs as a result of payments required by such indemnifications. The Company is not aware of any demands under indemnification arrangements that could have a material adverse effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its financial statements, as of December 31, 2021 and 2020.

***(f) Risks and Uncertainties***

The extent to which the COVID-19 pandemic could have a material impact on the Company’s current or future operations including planned clinical trials is dependent on the spread of the disease and government and healthcare system responses to such spread, which are presently highly uncertain. Management continues to evaluate the potential impact. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

In July 2021, the Company was subject to what it believes was a computer-based phishing attack. Management believes this incident had an immaterial impact on the Company’s financial condition but has implemented certain changes with respect to

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computer operations and continues to review the Company’s computer-related policies and implement additional defenses. There is no assurance that any preventative actions will not be thwarted by malicious actions.

**(9) Convertible Promissory Notes**

From May 2018 through May 2020, the Company issued 14 convertible promissory notes (“Notes”) having an aggregate principal amount of \$2,240,000 with an interest rate of 6% per annum. These Notes and accrued interest thereon converted into 1,068,135 shares of the Company’s common stock in connection with the Company’s IPO. As of the IPO and at December 31, 2020, total accrued interest on the Notes was \$247,285 and \$191,687, respectively.

Convertible promissory notes at the time of the IPO comprised the following:

<b>Note Identifier</b>	<b>Issue Date</b>	<b>Principal Amount</b>	<b>Accrued Interest at July 13, 2021</b>	<b>Accrued Interest at December 31, 2020</b>
Note One	May 2, 2018	\$ 500,000	\$ 92,548	\$ 80,137
Note Two	June 26, 2018	\$ 50,000	\$ 8,803	\$ 7,562
Note Three	March 2, 2019	\$ 100,000	\$ 13,249	\$ 10,767
Note Four	March 5, 2019	\$ 50,000	\$ 6,625	\$ 5,466
Note Five	March 8, 2019	\$ 50,000	\$ 6,707	\$ 5,384
Note Six	March 15, 2019	\$ 50,000	\$ 6,567	\$ 5,326
Note Seven	March 20, 2019	\$ 50,000	\$ 6,534	\$ 5,293
Note Eight	November 7, 2019	\$ 100,000	\$ 9,205	\$ 6,723
Note Nine	November 7, 2019	\$ 100,000	\$ 8,942	\$ 6,460
Note Ten	February 17, 2020	\$ 1,000,000	\$ 75,806	\$ 50,984
Note Eleven	April 3, 2020	\$ 40,000	\$ 2,780	\$ 1,790
Note Twelve	May 8, 2020	\$ 50,000	\$ 3,192	\$ 1,951
Note Thirteen	May 8, 2020	\$ 50,000	\$ 3,192	\$ 1,951
Note Fourteen	May 15, 2020	\$ 50,000	\$ 3,135	\$ 1,893

The unamortized amounts of debt issuance costs and debt discounts deducted from the principal amounts of the convertible promissory notes to calculate convertible promissory notes, net at the IPO and December 31, 2020, were:

	<b>July 13, 2021</b>	<b>December 31, 2020</b>
Principal amount of convertible promissory notes	\$ 2,240,000	\$ 2,240,000
Less unamortized debt issuance costs	(6,002)	(8,002)
Less unamortized debt discounts	(107,851)	(145,323)
Convertible promissory notes, net	<u>\$ 2,126,147</u>	<u>\$ 2,086,675</u>

Settlement of the Notes required that, at the closing of a Qualified Financing (as defined), the Company provide the holder with a variable number of shares with an aggregate fair value determined by reference to the debt principal and accrued but unpaid interest. In this scenario, the value that the holder receives at settlement does not vary with the value of the Company’s common stock, so the settlement provision was not a typical conversion option. Rather, the share settlement feature was considered a contingent redemption provision (i.e., a contingent embedded put). The Company evaluated the embedded put features in accordance with ASC 815-15-25. The embedded puts are not clearly and closely related to the debt host instrument and therefore were separately measured at fair value with subsequent changes in fair value recognized in the statements of operations.

Management used a scenario-based analysis to estimate the fair value of the embedded put features upon issuance of the Notes. The original values of the embedded put features were recorded as a debt discount to the Notes which discount was amortized over the life of the Notes as non-cash interest expense during the reporting periods.

**TRANSCODE THERAPEUTICS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
**December 31, 2021 and 2020**

The IPO constituted a Qualified Financing. At the IPO and at December 31, 2020, the fair value of the derivative liability was \$2,618,000 and \$1,751,000, respectively. Between December 31, 2020, and the IPO, the Company recorded an increase in fair value of the derivative liability of \$867,000.

Between December 31, 2020, and the IPO, the Company amortized debt issuance costs of \$10,538 to interest expense.

**(10) Stockholders' Equity**

**(a) Overview**

The Company's Certificate of Incorporation, originally filed on January 11, 2016, was amended on April 15, 2020, to increase the number of shares of common stock authorized and to authorize the issuance of Preferred Stock. The Company's Certificate of Incorporation was further amended and restated on April 27, 2021. The total number of shares which the Company is authorized to issue is 300,000,000, each with a par value of \$0.0001 per share. Of these shares, 290,000,000 shall be common stock and 10,000,000 shall be Preferred Stock. At December 31, 2021, the Company had issued and outstanding 12,904,574 shares all of which were free of vesting restrictions. As of December 31, 2020, the Company had issued and outstanding 4,636,216 shares of restricted common stock which, at issuance, were subject to forfeiture until vested. At December 31, 2020, 4,489,738 shares of restricted common stock had vested. Of shares sold in 2018, an aggregate of 292,250 shares were issued to two purchasers in exchange for subscriptions receivable bearing interest at 4% per annum and secured by the underlying restricted shares. One subscription receivable in the principal amount of \$3,290 and accumulated interest was repaid in full in April 2021. The second subscription receivable and accrued interest was repaid in full during the fourth quarter of 2021. The Preferred Stock is undesignated; no shares of Preferred Stock have been issued.

At the IPO and at December 31, 2020, the Company had reserved 1,080,858 shares and 1,050,694 shares, respectively, of common stock for the conversion of outstanding convertible promissory notes (see Note 9) and the exercise of outstanding warrants to purchase shares of common stock (see Note 11).

The following table lists information about unvested restricted common stock.

Unvested restricted common stock at December 31, 2020	146,483
Shares issued	—
Shares vested	(146,483)
Unvested restricted common stock at December 31, 2021	<u>—</u>

Our IPO was completed on July 13, 2021, in which we sold 7,187,500 shares at a public offering price of \$4.00 per share. The gross proceeds from the IPO were \$28,750,000 from which we paid \$2,415,000 of underwriting commissions and expenses and \$934,427 of other offering expenses. The underwriter also paid \$100 in aggregate for the underwriter warrants issued in connection with the IPO.

**(b) Common Stock**

i. Dividends

Subject to the rights of holders of any Preferred Stock, holders of common stock are entitled to receive dividends as may be declared from time to time by the Board. No cash dividends were declared or paid during the years ended December 31, 2021 and 2020, or at any other time through the date of these financial statements.

ii. Liquidation

Subject to the rights of holders of any Preferred Stock as to liquidation, upon the liquidation, dissolution or winding up of the Company, the remaining assets of the Company will be distributed to holders of common stock.

**TRANSCODE THERAPEUTICS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
**December 31, 2021 and 2020**

iii. Voting

Holders of Common Stock are entitled to one vote for each share of common stock held but shall not be entitled to vote on any amendment to the Certificate of Incorporation that relates solely to the terms of any series of Preferred Stock. There is no cumulative voting.

**(11) Warrants**

In connection with the May 2, 2018, issuance of the Convertible Promissory Note designated as “Note One” (see Note 9), the Company agreed to pay a cash fee to the finder involved in the sale and to issue to the finder warrants to purchase shares of the Company’s common stock. The number of shares of common stock subject to the warrants was equal to five percent of the number of shares of common stock into which Note One converted. The exercise price was the conversion price applicable on conversion of Note One. The number of shares of common stock to be issued to the holder of Note One on conversion of the Note is equal to the principal amount of the Note, plus accrued but unpaid interest to the date of conversion, divided by the applicable conversion price. The applicable conversion price was equal to the price paid for the Company’s equity securities in a Qualified Financing (as defined) less a discount. The discount ranged from 20% to 30% depending on the length of time after the investment was made to complete the Qualified Financing. Regardless of the applicable conversion price resulting from application of the foregoing process, the applicable conversion price could not exceed that price per share that equated to a \$15 million pre-money valuation. The Warrants were exercised in full, representing 12,723 shares, the day prior to the IPO at an exercise price of \$2.32 per share.

Pursuant to ASC 718, the obligation to issue the Warrants was accounted for as a liability until issuance as they were an award that embodied an unconditional obligation to issue an undeterminable number of shares for a fixed monetary amount known at inception. Upon issuance, the liability was reclassified to equity.

The obligation to issue Warrants was recorded at fair value on inception date and was remeasured at each reporting period until issuance. The compensation cost recognized for a liability-classified award equals the amount for which the award is settled. Therefore, the Company measured the obligation to issue the Warrants at fair value on May 2, 2018, and remeasured fair value at each reporting period until the Warrants were issued. At the time of exercise, in addition to recording the aggregate exercise price of the warrants, the Company also extinguished the balance of the warrant liability.

A summary regarding the fair value of the warrant liability is as follows:

	<b>Warrant Liability</b>
Fair value at December 31, 2020	\$ 29,376
Change in fair value	6,109
Fair value at July 12, 2021 (date of exercise)	35,485
Extinguishment of warrant liability on warrant exercise	(35,485)
Fair value at December 31, 2021	\$ —

The fair value of the Company’s warrant liability was calculated using the Black-Scholes model and the following assumptions:

	As of July 12, 2021	As of December 31, 2020
Fair value per share of Company’s common stock	\$ 4.00	\$ 3.91
Dividend yield	0.0 %	0.0 %
Expected volatility	89.0 %	84.0 %
Risk free interest rate	0.5 %	0.3 %
Expected life (years)	3.40	4.67
Fair value of warrants	\$ 35,485	\$ 29,376

**TRANSCODE THERAPEUTICS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
**December 31, 2021 and 2020**

*Underwriter Warrants*

In connection with the IPO, the Company granted the underwriters warrants to purchase up to 312,500 shares of Company common stock at an exercise price of \$5.00 per share, which amount is 125% of the initial public offering price. The warrants have a five-year term and are exercisable beginning January 9, 2022. All of these warrants were outstanding at December 31, 2021.

**(12) Share-Based Compensation**

Since inception, the Company has sold shares of restricted stock to co-founders, directors, managers, and advisors generally at prices believed to be fair market value at the time of the sale. Shares of restricted stock were reserved at the time of issue. To the extent that the sale price was less than the estimated fair market value at the grant date, a charge was recorded for the periods in which such shares vested. The vesting period for restricted stock was generally two to three years.

In April 2020, the Board and stockholders approved the TransCode Therapeutics, Inc. 2020 Stock Option and Incentive Plan (the “2020 Plan”) providing for the issuance of options or other awards to purchase up to 3,032,787 shares of the Company’s common stock. The Board has determined not to make any further awards under the 2020 Plan following the closing of the IPO. In March 2021, our 2021 Stock Option and Incentive Plan (the “2021 Plan”) was approved by our Board and our stockholders and became effective upon the effectiveness of our IPO. The 2021 Plan provides for the issuance of options or other awards to purchase up to 2,500,000 shares of the Company’s common stock.

Both Plans provide for grants of equity in the form of stock awards, stock options and other instruments to employees, members of the Board, officers and consultants of and advisors to the Company. The Plans are administered by the Board or, at the discretion of the Board, by a committee of the Board. The amount and terms of grants are determined by the Board. The terms of options granted under the Plans generally are for ten (10) years after date of grant and are exercisable in cash or as otherwise determined by the Board. The vesting period for equity-based awards is determined at the discretion of the Board and is generally two to four years. If stock options granted under the 2021 Plan terminate, expire, or are surrendered or cancelled, the shares subject to such grants will again be available under the 2021 Plan.

The exercise price for incentive stock options is determined at the discretion of the Board but for grants to any person possessing less than 10% of the total combined voting power of all classes of stock may not have an exercise price less than 100% of the fair market value of the common stock on the grant date (110% for grants to any person possessing more than 10% or more of the total combined voting power of all classes of stock). The option term for incentive stock option awards may not be greater than ten years from the date of the grant (five years for grants to any person possessing 10% or more of the total combined voting power of all classes of stock).

In 2020, the Board awarded options to purchase 1,756,279 shares of common stock under the 2020 Plan. Options to purchase 78,979 shares awarded under the 2020 Plan were forfeited during the year ended December 31, 2021, resulting in 1,713,693 options outstanding under the 2020 Plan at December 31, 2021. In January 2021, the Board awarded options to purchase 36,393 shares of common stock under the 2020 Plan, all of which were outstanding at December 31, 2021. During the year ended December 31, 2021, no awards were made under the 2021 Plan.

**TRANSCODE THERAPEUTICS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
**December 31, 2021 and 2020**

At December 31, 2021, there were 1,042,534 options outstanding under the 2020 Plan that were vested and exercisable. Information about options to purchase common stock of the Company under the 2020 Plan is as follows:

	Number of shares	Weighted average exercise price per share	Weighted average contractual term (years)
Outstanding at December 31, 2019	—	—	—
Granted	1,756,279	\$ 0.25	5.9
Exercised	—	—	—
Forfeited	—	—	—
Outstanding at December 31, 2020	<u>1,756,279</u>	<u>\$ 0.25</u>	<u>5.9</u>
Granted	36,393	\$ 3.91	5.5
Exercised	—	—	—
Forfeited	78,979	—	—
Outstanding at December 31, 2021	<u>1,713,693</u>	<u>\$ 0.33</u>	<u>5.2</u>

The intrinsic value of the outstanding options as of December 31, 2021, was \$3,787,262.

*Option valuation*

The assumptions that the Company used to determine the grant-date fair value of options granted during the year ended December 31, 2021, were as follows:

	Years ended December 31,	
	2021	2020
Risk-free interest rate	0.59 %	0.25% – 0.55 %
Expected term (in years)	6.0	3.5 – 6.25
Expected volatility	97.20 %	95.83% – 97.20 %
Expected dividend yield	— %	— %
Fair value per share of underlying stock	\$ 3.91	\$ 0.08 – \$3.91

The weighted average grant date fair value of the options granted in 2021 was \$3.01 per share.

The Company recorded stock-based compensation expense of \$185,996 and \$45,444 during the years ended December 31, 2021 and 2020, respectively. Stock-based compensation in the year ended December 31, 2021, comprised \$184,599 related to stock options and \$1,397 related to restricted stock. Stock-based compensation in the year ended December 31, 2020, comprised \$42,651 related to stock options and \$2,793 related to restricted stock. Compensation costs on stock options remaining to be recognized at December 31, 2021, is \$192,000 over approximately 1.9 years.

**(13) Net Loss Per Share**

The Company reported net losses for the years ended December 31, 2021 and 2020. Basic and diluted net loss per share attributable to common stockholders are the same for all periods in which the Company reported losses because inclusion of shares issuable on conversion of all convertible promissory notes, upon exercise of all warrants, and upon exercise of vested stock options into the computation of diluted weighted-average shares outstanding would have an antidilutive impact.



**TRANSCODE THERAPEUTICS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
**December 31, 2021 and 2020**

The following table sets forth the computation of basic and diluted net earnings (loss) per share:

	Years Ended December 31,	
	2021	2020
<b>Basic and diluted net loss per share</b>		
Numerator		
Net loss	\$ (6,843,399)	\$ (2,343,893)
Denominator		
Weighted-average common shares outstanding	8,425,880	4,636,216
Net loss per share	\$ (0.81)	\$ (0.51)

**(14) Income Taxes**

The Company's federal and state provision (benefit) for income taxes were \$53,051 and \$0 for the years ended December 31, 2021 and 2020, respectively. The Company believes that the provision for the year ended December 31, 2021, will be fully offset by research and development credits.

A reconciliation of income tax provision (benefit) computed at the statutory federal income tax rate to income taxes as reflected in the financial statements is as follows:

	Years Ended December 31,	
	2021	2020
Federal income tax benefit at statutory rate	21.0 %	21.0 %
State and local tax, net of federal benefit	4.5 %	1.9 %
Permanent differences	(3.2)%	(14.8)%
Deferred true-up	— %	(0.6)%
Change in valuation allowance	(23.1)%	(7.5)%
Effective income tax rate	(0.8)%	0.0 %

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets comprise the following:

Net operating loss carryforwards	\$ 1,353,293	\$ 421,000
Capitalized research and development	666,145	10,000
Capitalized patent and other costs	4,829	4,000
Stock-based compensation	35,123	—
Accrued expenses	16,798	—
Subtotal deferred tax assets before valuation allowance	2,076,188	435,000
Less valuation allowance	(2,019,835)	(435,000)
Deferred tax assets	56,353	—
Deferred tax liability		
Fixed assets	(56,353)	—
Net deferred taxes	\$ —	\$ —

The Company had U.S. federal net operating loss ("NOL") carryforwards of \$5,025,481 and \$1,294,914 for the years ended December 31, 2021 and 2020, respectively, which may be available to offset future income tax liabilities. Federal NOL carryforwards generated in 2017 and prior of \$38,297 will expire beginning in 2036. The remaining federal NOL carryforwards generated in 2018 and later do not expire. However, they are subject to the 80% limitation when utilized. The Company also had U.S. state NOL

**TRANSCODE THERAPEUTICS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
**December 31, 2021 and 2020**

carryforwards of \$4,714,271 and \$1,291,575 for the years ended December 31, 2021 and 2020, respectively, which may be available to offset future income tax liabilities and will expire beginning in 2036.

The Company has recorded a full valuation allowance against its net deferred tax assets as of December 31, 2021 and 2020, because the Company has determined that it is more likely than not that these assets will not be fully realized due to the significant uncertainty about the realization of the deferred tax asset until the Company can operate profitably. The Company experienced a net change in valuation allowance of \$1,584,835 and \$175,000 in the years ended December 31, 2021 and 2020, respectively.

Under the provisions of the Internal Revenue Code, the NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed financings since its inception and completed its IPO in 2021 which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future. The Company has not analyzed the historical or potential impact of its financings on beneficial ownership, and therefore, no determination has been made whether the net operating loss carryforward is subject to any Internal Revenue Code Section 382 limitation. To the extent there is a limitation, there could be a reduction in the deferred tax asset with an offsetting reduction in the valuation allowance.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. The Company's tax years from 2018 to the present remain open for review. All open years may be examined to the extent that tax credits or NOL carryforwards are used in future periods. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") was signed into law. The Act contains several new or changed income tax provisions, including but not limited to the following: increased limitation threshold for determining deductible interest expense, class life changes to qualified improvements (in general, from 39 years to 15 years), and the ability to carry back net operating losses incurred from tax years 2018 through 2020 up to the five preceding tax years. The Company has evaluated the new tax provisions of the CARES Act and determined the impact to be either immaterial or not applicable.

As of December 31, 2021 and 2020, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations.

**(15) Related -Party Transactions**

Between inception and mid-2018, major shareholders and co-founders funded certain expenses of the Company. The aggregate amount of these expenses remaining unreimbursed at December 31, 2021 and 2020, is \$0 and \$35,685, respectively. The Company reimbursed these obligations in 2021.

On approximately April 26, 2021, three members of the Company's management advanced an aggregate of \$31,500 to the Company to enable it to pay certain Company IPO expenses. These advances were repaid in full, without interest, on May 13, 2021.

**TRANSCODE THERAPEUTICS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
**December 31, 2021 and 2020**

**(16) Subsequent Events**

For its financial statements as of December 31, 2021, the Company evaluated subsequent events through March 31, 2022, the date on which those financial statements were issued.

In February 2022, the Company extended its agreement with Massachusetts Biomedical Initiatives, Inc. (“MBI”) through December 31, 2022. See Note 8(a). Beginning March 1, 2022, the Company’s base rent will increase 5.0% to \$6,520.50 per month. While MBI has not yet provided the amount of the Company’s allocated share of operating expenses, which amount was \$3,105 during the first 12 months of the lease, MBI indicated that the Company’s portion of total operating expenses would remain the same. If operating expenses increase 5%, the amount of the Company’s allocated share of operating expenses would increase to \$3,260.25 per month and its total monthly rent would be \$9,780.75. Based on the foregoing, the Company’s total lease commitment from March 1, 2022, through December 31, 2022, would be \$97,807.50.

On February 1, 2022, the Company made awards of 259,000 stock options under its 2021 Stock Option and Incentive Plan (the “2021 Plan”) at an exercise price of \$2.45 per share, the closing price per share of the Company’s common stock on the date of grant. On March 1, 2022, the Company made awards of 192,000 stock options under the 2021 Plan at an exercise price of \$2.12 per share, the closing price per share of the Company’s common stock on the date of grant.

## TRANSCODE THERAPEUTICS, INC.

## BALANCE SHEETS

	September 30, 2022	December 31, 2021
	(Unaudited)	
<b>Assets</b>		
Current assets:		
Cash	\$ 8,790,540	\$ 20,825,860
Grant receivable	487,879	—
Prepaid expenses and other current assets	2,291,466	1,906,315
Total current assets	11,569,885	22,732,175
Property and equipment, net of depreciation	209,871	206,268
Deferred offering costs	235,817	—
Total assets	<u>\$ 12,015,573</u>	<u>\$ 22,938,443</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable and accrued expenses	\$ 3,747,838	\$ 2,503,569
Deferred grant income	23,538	30,528
Total current liabilities	3,771,376	2,534,097
Total liabilities	<u>3,771,376</u>	<u>2,534,097</u>
Stockholders' equity:		
Preferred stock – \$0.0001 par value; 10,000,000 and 5,000,000 shares authorized at September 30, 2022, and December 31, 2021, respectively; - 0- shares issued and outstanding at September 30, 2022 and December 31, 2021	—	—
Common stock – \$0.0001 par value, 290,000,000 shares authorized at September 30, 2022, and December 31, 2021; 12,977,234 and 12,904,574 shares issued and outstanding at September 30, 2022, and December 31, 2021, respectively	1,298	1,291
Additional paid-in capital	30,979,092	30,708,336
Accumulated deficit	(22,736,193)	(10,305,281)
Total stockholders' equity	8,244,197	20,404,346
Total liabilities and stockholders' equity	<u>\$ 12,015,573</u>	<u>\$ 22,938,443</u>

See accompanying notes to financial statements.

TRANSCODE THERAPEUTICS, INC.

STATEMENTS OF OPERATIONS  
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
<b>Operating expenses</b>				
Research and development	\$ 3,044,024	\$ 992,946	\$ 7,545,628	\$ 1,468,457
General and administrative	1,909,536	1,366,963	5,592,727	1,696,444
Total operating expenses	4,953,560	2,359,909	13,138,355	3,164,901
<b>Operating loss</b>	(4,953,560)	(2,359,909)	(13,138,355)	(3,164,901)
<b>Other income (expense)</b>				
Change in fair value of derivative liabilities	—	—	—	(867,000)
Change in fair value of warrant liability	—	(1,340)	—	(6,109)
Grant income	654,949	31,735	696,669	88,786
Interest expense	—	(333)	—	(95,070)
Interest income	9,001	141	10,774	154
Total other income (expense)	663,950	30,203	707,443	(879,239)
<b>Net loss</b>	<u>\$ (4,289,610)</u>	<u>\$ (2,329,706)</u>	<u>\$ (12,430,912)</u>	<u>\$ (4,044,140)</u>
<b>Basic and diluted loss per share</b>				
Net loss	<u>\$ (4,289,610)</u>	<u>\$ (2,329,706)</u>	<u>\$ (12,430,912)</u>	<u>\$ (4,044,140)</u>
Weighted-average common shares outstanding	<u>12,977,234</u>	<u>11,526,514</u>	<u>12,977,234</u>	<u>6,932,982</u>
Net loss per share	<u>\$ (0.33)</u>	<u>\$ (0.20)</u>	<u>\$ (0.96)</u>	<u>\$ (0.58)</u>

See accompanying notes to financial statements.

**TRANSCODE THERAPEUTICS, INC.**  
**STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)**  
**(Unaudited)**

	Common Stock		Additional Paid-In Capital	Subscription Receivable	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
<b>Three and nine months ended</b>						
<b>September 30, 2022</b>						
Balance, December 31, 2021	12,904,574	\$ 1,291	\$ 30,708,336	\$ —	\$ (10,305,281)	\$ 20,404,346
Net loss	—	—	—	—	(3,470,070)	(3,470,070)
Exercise of stock options	72,660	7	5,982	—	—	5,989
Share based compensation	—	—	60,573	—	—	60,573
Balance, March 31, 2022	12,977,234	1,298	30,774,891	—	(13,775,351)	17,000,838
Net loss	—	—	—	—	(4,671,232)	(4,671,232)
Share based compensation	—	—	98,599	—	—	98,599
Balance, June 30, 2022	12,977,234	1,298	30,873,490	—	(18,446,583)	12,428,205
Net loss	—	—	—	—	(4,289,610)	(4,289,610)
Share based compensation	—	—	105,602	—	—	105,602
Balance, September 30, 2022	<u>12,977,234</u>	<u>\$ 1,298</u>	<u>\$ 30,979,092</u>	<u>\$ —</u>	<u>\$ (22,736,193)</u>	<u>\$ 8,244,197</u>
<b>Three and nine months ended</b>						
<b>September 30, 2021</b>						
Balance, December 31, 2020	4,636,216	\$ 464	\$ 65,949	\$ (12,763)	\$ (3,461,882)	\$ (3,408,232)
Net loss	—	—	—	—	(4,485,338)	(4,485,338)
Interest on subscription receivable	—	—	128	(128)	—	—
Share based compensation	—	—	48,431	—	—	48,431
Balance, March 31, 2021	4,636,216	464	114,508	(12,891)	(7,947,220)	(7,845,139)
Net income	—	—	—	—	2,770,904	2,770,904
Interest on subscription receivable	—	—	103	(103)	—	—
Proceeds from subscription receivable	—	—	—	3,640	—	3,640
Share based compensation	—	—	34,514	—	—	34,514
Balance, June 30, 2021	4,636,216	464	149,125	(9,354)	(5,176,316)	(5,036,081)
Net loss	—	—	—	—	(2,329,706)	(2,329,706)
Issuance of common stock in initial public offering, net of offering costs	7,187,500	719	25,399,954	—	—	25,400,673
Conversion of convertible promissory notes, including embedded derivative, to common stock upon completion of initial public offering	1,068,135	107	4,991,324	—	—	4,991,431
Exercise of warrants	12,723	1	64,751	—	—	64,752
Interest on subscription receivable	—	—	92	(92)	—	—
Share based compensation	—	—	64,051	—	—	64,051
Balance, September 30, 2021	<u>12,904,574</u>	<u>\$ 1,291</u>	<u>\$ 30,669,297</u>	<u>\$ (9,446)</u>	<u>\$ (7,506,022)</u>	<u>\$ 23,155,120</u>

See accompanying notes to financial statements.

TRANSCODE THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS  
(Unaudited)

	Nine Months Ended September 30,	
	2022	2021
Cash flows from operating activities:		
Net loss	\$ (12,430,912)	\$ (4,044,140)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation	69,101	13,482
Share-based compensation expense	264,774	146,996
Change in fair market value of derivative liabilities	—	867,000
Non-cash interest expense	—	39,471
Change in fair market value of warrant liability	—	6,109
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(385,152)	(2,701,186)
Accounts payable and accrued expenses	1,234,270	1,766,148
Deferred grant income	(6,990)	220,075
Grants receivable	(487,879)	—
Payment of amount due to related parties	—	(35,685)
Accrued interest on convertible promissory notes	—	55,598
Net cash used in operating activities	<u>(11,742,788)</u>	<u>(3,666,132)</u>
Cash flows from investing activities:		
Purchase of equipment	(72,704)	(169,092)
Net cash used in investing activities	<u>(72,704)</u>	<u>(169,092)</u>
Cash flows from financing activities:		
Proceeds from initial public offering (IPO) of common stock, net of offering costs	—	26,335,100
Proceeds from exercise of stock options	5,989	—
Proceeds from subscription receivable	—	3,640
Proceeds from exercise of warrants	—	29,267
Payments of deferred offering costs	(225,817)	(860,943)
Net cash provided by (used in) financing activities	<u>(219,828)</u>	<u>25,507,064</u>
Net change in cash	<u>(12,035,320)</u>	<u>21,671,840</u>
Cash, beginning of period	20,825,860	828,016
Cash, end of period	<u>\$ 8,790,540</u>	<u>\$ 22,499,856</u>
Supplemental disclosure of cash flow		
Cash paid during the year for:		
Interest	\$ 20,623	\$ —
Supplemental disclosure of non-cash investing and financing activities:		
Accrued interest on subscriptions receivable	\$ —	\$ 323
Debt discounts associated with derivative liabilities of convertible promissory notes	\$ —	\$ 37,471
Conversion of convertible promissory notes, including embedded derivative, to common stock	\$ —	\$ 4,991,431
Deferred offering costs included in accounts payable and accrued expenses	\$ 10,000	\$ —
Deferred offering costs adjusted into additional paid-in capital in connection with IPO	\$ —	\$ 73,484
Fair value of warrant liability associated with warrant exercise	\$ —	\$ 35,485
Underwriting discounts and commissions paid from gross proceeds of IPO	\$ —	\$ 2,414,900

See accompanying notes to financial statements.

**TRANSCODE THERAPEUTICS, INC.**

**NOTES TO FINANCIAL STATEMENTS  
(Unaudited)**

**(1) Nature of Business and Liquidity**

TransCode Therapeutics, Inc. (the “Company” or “TransCode”) was incorporated on January 11, 2016, under the laws of the State of Delaware. TransCode is a biopharmaceutical company focused primarily on developing and commercializing innovative drugs and diagnostics for treating and identifying cancer. TransCode is preparing for its first clinical trial. The Company’s lead therapeutic candidate, TTX-MC138, comprises an oligonucleotide conjugated to an iron oxide nanoparticle designed to be administered by infusion to inhibit the ability of metastatic tumor cells to survive. The goal of the therapy, if approved, is to achieve lifelong regression and long-term patient survival.

From its founding until mid-2021, the Company was engaged in organizational activities, including raising capital, and limited research and development (“R&D”) activities. On July 13, 2021, the Company completed the initial public offering (“IPO”) of its common stock raising \$28.75 million in gross proceeds. Since the IPO, the Company has increased its R&D activities, hired additional employees, and begun more traditional operations.

The Company has not generated revenues and has not yet achieved profitable operations, nor has it ever generated positive cash flows from operations. There is no assurance that profitable operations, if achieved, could be sustained on a continuing basis. The Company is subject to those risks associated with any early-stage biopharmaceutical company that requires substantial expenditures for research and development. There can be no assurance that the Company’s research and development projects will be successful, that products developed will obtain necessary regulatory approvals, or that any approved product will be commercially viable. In addition, the Company operates in an environment of rapid technological change and is largely dependent on the services of its employees and consultants. Further, the Company’s future operations are dependent on the success of the Company’s efforts to raise additional capital.

Following the IPO, the Company’s common stock commenced trading on the Nasdaq Capital Market under the ticker symbol “RNAZ.” The Company issued 7,187,500 shares of common stock in connection with the IPO, including exercise of the underwriter’s over-allotment option, at an initial offering price of \$4.00 per share. The net proceeds from the IPO were approximately \$25.4 million after deducting underwriting discounts, commissions and estimated offering expenses payable by the Company, including offering costs paid in 2020. In connection with the IPO, the Company also granted the underwriters warrants to purchase up to 312,500 shares of Company common stock at an exercise price of \$5.00 per share (125% of the initial public offering price). Upon the closing of the IPO, outstanding convertible promissory notes converted into 1,068,135 shares of Company common stock.

***Going Concern***

These financial statements have been prepared under the assumption that the Company will continue as a going concern which contemplates the continuation of operations, realization of assets and liquidation of liabilities in the ordinary course of business. Due to the Company’s recurring and expected continuing losses from operations, the Company has concluded there is substantial doubt concerning its ability to continue as a going concern within one year of the issuance of these financial statements without additional capital becoming available. These financial statements do not include any adjustments that might result from the outcome of this uncertainty.

To date, the Company has incurred substantial losses and negative cash flows from operations. It expects to continue to incur operating losses for the foreseeable future as it pursues development of its lead therapeutic candidate and other programs. Operating losses are expected to continue until such time, if ever, that the Company can generate significant revenue from product candidates currently in development. The Company is unable to predict the extent of any future losses or when the Company will become profitable, if ever.

For the nine months ended September 30, 2022, net cash used in operating activities was approximately \$11.7 million and the Company’s net loss was approximately \$12.4 million. As of September 30, 2022, the Company had an accumulated deficit of approximately \$22.7 million and approximately \$8.8 million in cash.



**TRANSCODE THERAPEUTICS, INC.**

**NOTES TO FINANCIAL STATEMENTS  
(Unaudited)**

The Company plans to expand development of its lead therapeutic candidate and other candidates, and explore strategic partnerships. Management believes that current cash along with the approximately \$928 thousand it expects to receive under year-two of the Company's SBIR Award (see Note 7) are sufficient to fund operations and capital requirements through the first quarter of 2023, but does not believe that existing cash will be sufficient to fund requirements for a full 12 months from the date of these financial statements.

To support its planned expanded operations, the Company will require additional capital; however, the Company cannot be certain that additional funding will be available on acceptable terms, or at all. Through September 30, 2022, the Company's primary source of capital was from the sale of equity securities in the IPO, previous sales of convertible promissory notes and funds received under the SBIR Award. For the foreseeable future, the Company plans to fund its operations by continuing to raise additional capital, primarily through sales of equity or debt, and from funds expected under the SBIR Award.

To the extent the Company raises additional funds by issuing equity securities, its stockholders may experience significant dilution. Any debt financing, if available, may include potentially dilutive features and include restrictive covenants that impact the Company's ability to conduct business. If the Company is unable to raise additional capital when required or on acceptable terms, the Company may have to (i) significantly scale back its planned operations or (ii) relinquish or otherwise dispose of rights to technologies on unfavorable terms.

**(2) Summary of Significant Accounting Policies**

**(a) Basis of Presentation**

The interim financial statements included herein are unaudited. These financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") and the rules and regulations of the U.S. Securities and Exchange Commission ("SEC"). Any reference in these notes to applicable guidance is meant to refer to U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB"). In the opinion of management, these statements include all adjustments, consisting only of normal, recurring adjustments, necessary for a fair presentation of the financial position of TransCode Therapeutics, Inc. at September 30, 2022, its results of operations for the three and nine months ended September 30, 2022 and 2021, and its cash flows for the nine months ended September 30, 2022 and 2021. The interim results of operations are not necessarily indicative of the results to be expected for a full year. These interim financial statements should be read in conjunction with the audited financial statements for the year ended December 31, 2021, and notes thereto contained in the Company's Annual Report on Form 10-K, filed with the SEC. Certain information and note disclosures normally included in financial statements prepared in accordance with U.S. GAAP have been omitted pursuant to such rules and regulations relating to interim financial statements.

**(b) Use of Estimates**

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, including disclosure of contingent assets and liabilities, at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Due to the uncertainty of factors surrounding the estimates or judgments used in the preparation of the financial statements, actual results may materially vary from these estimates.

Significant items subject to such estimates and assumptions include but are not limited to the valuation of share-based compensation, income from grants, derivative liabilities, and warrant liability. Future events and their effects cannot be predicted with certainty; accordingly, accounting estimates require the exercise of judgment. Accounting estimates used in the preparation of these financial statements change as new events occur, as more experience is acquired, as additional information is obtained and as the operating environment changes.

**TRANSCODE THERAPEUTICS, INC.**

**NOTES TO FINANCIAL STATEMENTS  
(Unaudited)**

**(c) Basic and Diluted Earnings (Loss) per Share**

Basic net earnings (loss) per share is determined by dividing the net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period. Diluted net earnings (loss) per share includes the effect, if any, from the potential conversion, vesting or exercise of securities (Contingent Securities) such as convertible promissory notes, stock options and warrants, which would result in the issuance of additional shares of common stock. The computation of diluted net earnings (loss) per shares does not include the conversion or exercise of Contingent Securities when the effect of doing so would be antidilutive.

**(d) Cash**

The Company classifies deposits in banks, money market funds and cash invested temporarily in various instruments with original maturities of three months or less as cash and cash equivalents. To date, the Company has not held any funds in money market funds or instruments with original maturities of three months or less. At times, the Company's cash balances in U.S. banks may exceed the levels of insured amounts under the Federal Deposit Insurance Corporation (FDIC).

**(e) Fair Value of Financial Instruments**

The Company's financial instruments at September 30, 2022, and December 31, 2021, included cash, accounts payable, and accrued expenses. Cash is reported at fair value. The recorded carrying amount of accounts payable and accrued expenses approximate their fair value due to their short-term nature.

**(f) Research and Development**

Research and development costs generally are expensed as incurred and primarily comprise expenses to discover, research and develop therapeutic candidates. These expenses may include personnel costs, stock-based compensation expense, materials and supplies, allocated facility-related and depreciation expenses, third-party license fees, and costs under arrangements with third party vendors, such as contract research organizations ("CROs"), contract manufacturing organizations ("CMOs"), and consultants. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are recorded as prepaid expenses. Such amounts are recognized as expenses as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

The Company has entered into various research and development-related contracts with companies both inside and outside the United States. The related costs are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ materially from the Company's estimates.

*Patent Costs*

All legal fees and expenses and costs related to patent-related filings with governmental authorities incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses. Other patent costs are classified as R&D expenses.

**TRANSCODE THERAPEUTICS, INC.**

**NOTES TO FINANCIAL STATEMENTS  
(Unaudited)**

**(g) Grant Income**

Funds from grants are recognized as grant income in the statements of operations as and when earned for the specific research and development projects for which the grants are designated. In April 2021, the Company received an award (the “Award”) from the National Cancer Institute in support of the Company’s lead therapeutic candidate. Since there is no transfer of ownership of the work performed under the Award, and the Company does not lose control over the work performed under the Award, the Company deems the Award funds as a contribution. Grant payments received in excess of grant income earned are recorded as deferred grant income on the Company’s balance sheet until the related income has been earned. Grant income earned in excess of grant payments received is recorded as grant receivable on the Company’s balance sheet.

**(h) Share-Based Compensation**

Share based compensation, if any, for employees and non-employees is measured at the grant date based on the fair value of the award. The Company recognizes compensation expense, if any, for awards to employees and directors over the requisite service period, which is generally the vesting period of the respective award, and for awards to non-employees over the period during which services are rendered by such non-employees until completed. Generally, the Company issues awards with only service-based vesting conditions and records the expense for these awards using the straight-line method. The Company classifies stock-based compensation expense in its statements of operations in the same manner in which the award recipient’s payroll costs are classified or in which the award recipient’s service payments are classified. Forfeitures are accounted for as they occur.

Because prior to the IPO, there was no public market for the Company’s common stock, the estimated fair value of the common stock was determined by the Company’s board of directors (the “Board”) as of the date of each award, with input from management, considering, when available, third-party valuations of the Company’s common stock as well as the Board’s assessment of additional objective and subjective factors that it believed were relevant and which may have changed between the date of the then most recent third-party valuation, if any, and the date of the grant. The assumptions used in calculating the fair value of share-based awards represented management’s best estimates and involved inherent uncertainties and the application of management’s judgment. As a result, if factors were to change and management were to use different assumptions, share-based compensation expense could be materially different. The fair value of awards made subsequent to the IPO are determined using the closing price of the Company’s common stock on the date of grant.

Certain stock appraisal methodologies utilize, among other variables, the volatility of the stock price. When private, the Company lacked Company-specific historical and implied volatility information for its stock. Therefore, it estimated its expected stock price volatility based on the historical volatility of publicly-traded peer companies and expects to continue to do so until such time, if ever, as it has adequate historical data regarding the volatility of its own publicly-traded stock price. The expected life of options awarded was estimated using the simplified method because the Company has limited historical information on which to base reasonable expectations about future exercise patterns and post-vesting employment. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends on its common stock and does not expect to pay cash dividends in the foreseeable future.

**TRANSCODE THERAPEUTICS, INC.**

**NOTES TO FINANCIAL STATEMENTS  
(Unaudited)**

**(i) Property and Equipment**

Property and equipment are recorded at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset as follows:

	<u>Estimated useful life</u>
Laboratory equipment	3 years
Furniture and fixtures	5 years
Computer and office equipment	3 years
Leasehold improvements	Shorter of the useful life or remaining lease term

When assets are retired or otherwise disposed of, the cost of assets disposed of and the related accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the statements of operations in the period of disposal. Expenditures for repairs and maintenance are charged to expense as incurred.

**(j) Income Taxes**

The Company provides for income taxes using the asset and liability approach. Deferred tax assets and liabilities are recorded based on the differences between the financial statement and tax bases of assets and liabilities and the tax rates in effect when these differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. As of the dates of the Company's balance sheets herein, the Company had a full valuation allowance against deferred tax assets.

The Company is subject to the provisions of ASC 740-10-25, "Income Taxes" (ASC 740). ASC 740 prescribes a more likely-than-not threshold for the financial statement recognition of uncertain tax positions. ASC 740 clarifies the accounting for income taxes by prescribing a minimum recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return.

There are currently no open federal or state tax audits. The Company has not recorded any liability for uncertain tax positions at the dates of the Company's balance sheets herein.

**(k) Concentrations of Credit Risk**

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash. The Company generally maintains balances in various accounts at one or more U.S. banks in amounts that may exceed federally insured limits. The Company has not experienced any losses related to its cash and does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking balances.

**(l) Emerging Growth Company Status**

The Company is an "emerging growth company" ("EGC") as defined in the Jumpstart Our Business Startups Act ("JOBS Act") and may take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not EGCs. The Company may take advantage of these exemptions until it is no longer an EGC under Section 107 of the JOBS Act and has elected to use the extended transition period for complying with new or revised accounting standards. As a result of this election, the Company's financial statements may not be comparable to companies that comply with public company FASB standards' effective dates. The Company may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of a public offering or such earlier time that it is no longer an EGC.

**TRANSCODE THERAPEUTICS, INC.****NOTES TO FINANCIAL STATEMENTS  
(Unaudited)****(m) Recent Accounting Pronouncements**

In November 2021, the FASB, issued Accounting Standards Update No. 2021-10 entitled “Government Assistance (Topic 832), Disclosures by Business Entities about Government Assistance”. This ASU requires enhanced disclosures related to the Company’s contracts with the U.S. Government that are accounted for by applying a grant or contribution accounting model by analogy. The new disclosure requirements include information about the nature of the transactions and the related accounting policy used to account for the transactions; the line items on the balance sheet and income statement that are affected by the transactions, and the amounts applicable to each financial statement line item; and significant terms and conditions of the transactions, including commitments and contingencies. The ASU is effective for annual periods beginning after December 15, 2021. The Company’s adoption of this standard on January 1, 2022, did not have a significant effect on its financial statements.

**(n) Reverse Stock Split**

On March 22, 2021, the Board and shareholders of the Company approved a reverse split of the Company’s common stock at a ratio of one share for every 1.6486484 shares previously held. All common stock share and per share data, and exercise price data for applicable common stock equivalents, included in these financial statements have been retroactively adjusted to reflect the reverse stock split.

**(3) Fair Value Measurements**

ASC 820, “Fair Value Measurements”, provides guidance on the development and disclosure of fair value measurements. The Company follows this guidance for fair value measurements, which defines fair value, establishes a framework for measuring fair value under U.S. GAAP, and expands disclosures about fair value measurements. The guidance requires fair value measurements be classified and disclosed in one of the following three categories:

Level 1: Quoted prices (unadjusted) in active markets that are accessible at the measurement date for identical assets or liabilities.

Level 2: Observable prices that are based on inputs not quoted on active markets but corroborated by market data.

Level 3: Unobservable inputs which are supported by little or no market activity with values determined using pricing models, discounted cash flow methodologies, or similar techniques, as well as instruments for which the determination of fair value requires significant judgment or estimation.

Fair value measurements discussed herein are based upon certain market assumptions and pertinent information available to management as of the dates of the Company’s balance sheets herein. The carrying amount of cash and accounts payable and accrued liabilities approximated fair value as they are short term in nature.

**(4) Prepaid Expenses and Other Current Assets**

Prepaid expenses and other current assets consisted of the following:

	September 30, 2022	December 31, 2021
Prepaid operating expenses	\$ 172,652	\$ 61,459
Contract manufacturers and research organizations	295,023	441,593
Insurance premiums	1,814,381	1,393,853
Deposits	9,410	9,410
	<u>\$ 2,291,466</u>	<u>\$ 1,906,315</u>

**TRANSCODE THERAPEUTICS, INC.****NOTES TO FINANCIAL STATEMENTS  
(Unaudited)****(5) Property and Equipment**

Property and equipment, net consisted of the following:

	September 30, 2022	December 31, 2021
Laboratory and computer equipment	\$ 320,226	\$ 247,522
Less accumulated depreciation	(110,355)	(41,254)
Total property and equipment, net	<u>\$ 209,871</u>	<u>\$ 206,268</u>

Depreciation expense for the nine months ended September 30, 2022 and 2021, was \$69,101 and \$13,482, respectively.

**(6) Accounts Payable and Accrued Expenses**

Accounts payable and accrued expenses consisted of the following:

	September 30, 2022	December 31, 2021
Professional and general consulting fees	\$ 299,378	\$ 218,476
R&D-related – CMOs, CROs, supplies, equipment and consulting	1,687,011	595,465
General expenses	167,357	256,463
Insurance premiums	1,438,901	945,928
Payroll and benefits	134,704	482,237
Accrued license payments	20,487	5,000
	<u>\$ 3,747,838</u>	<u>\$ 2,503,569</u>

At September 30, 2022, and December 31, 2021, the Company's outstanding payables to CROs or CMOs included above were \$1,334,632 and \$386,057, respectively.

See Note 8 for further information regarding the accrued license payments.

**(7) Grant Income**

In April 2021, the Company received a Fast-Track Small Business Innovation Research, or SBIR, Award from the National Cancer Institute of the National Institutes of Health (the "NIH"). The Award is expected to provide up to \$2,392,845 over three years to fund a two-phased research partnership between the Company and Massachusetts General Hospital. In May 2021, the Company received first-year funding of \$308,861 which it recorded as deferred grant income. In May 2022, second-year funding of \$1,129,316 was made available to the Company. Income under the grant's first year funding was recognized as work under the grant was completed. In the second year of the grant, the Company will draw available funds in arrears. The Company recognized grant income of \$654,949 and \$696,669, respectively, for the three and nine months ended September 30, 2022, and \$31,735 and \$88,786 for the three and nine months ended September 30, 2021, respectively. The Company recorded grant income receivable of \$487,879 at September 30, 2022, and \$0 at December 31, 2021. The Company had deferred grant income of \$23,538 and \$30,528 at September 30, 2022, and December 31, 2021, respectively.

**TRANSCODE THERAPEUTICS, INC.****NOTES TO FINANCIAL STATEMENTS  
(Unaudited)****(8) Commitments and Contingencies****(a) Leases**

In March 2021, the Company entered into an agreement with Massachusetts Biomedical Initiatives, Inc. (“MBI”) whereby the Company has subleased approximately 2,484 square feet of laboratory space with room for minor administrative functions. The Company may also use shared laboratory equipment at the facility. The monthly rental is \$6,521 and the Company pays an additional amount for its allocated share of operating expenses, currently \$3,105 per month. In 2022, the Company added the right to use cubicle space outside its laboratory area to its sublease for an additional \$650 per month, resulting in total monthly rental of \$10,276. The sublease extends through December 31, 2022, includes an option to extend the sublease upon the mutual agreement of the parties, and is cancelable anytime upon 90 days’ notice. Based on the foregoing, the Company’s total sublease commitment from October 1, 2022, through December 31, 2022, is \$30,828. The Company and MBI intend to extend the sublease after December 31, 2022, on a month-to-month basis.

**(b) License Agreements**

In November 2018, the Company licensed the exclusive rights to certain intellectual property to support development of its therapeutic candidates (“License”). The intellectual property licensed by the Company is owned by The General Hospital Corporation, d/b/a Massachusetts General Hospital, (“Licensor”). Payments by the Company under the license agreement included a one-time non-refundable fee of \$50,000 paid after execution of the License; reimbursement of Licensor’s patent costs which, at execution of the License, were approximately \$145,000; a minimum annual license fee of \$25,000 payable within 60 days of each anniversary of the effective date of the License prior to the first commercial sale of a product or process covered by the License; milestone payments upon attainment of certain milestone events; royalties based on net sales of products covered by the patent-related rights; and a portion of any sublicense income received by the Company. The Company is responsible for the development and commercialization of the licensed assets and for meeting certain milestones set forth in the License.

The milestone payments the Company shall pay to Licensor shall not exceed \$1,550,000 based upon and subject to the attainment of each milestone event indicated below. These payments are generally due within 60 days of achievement of the milestone.

<u>Milestone Event</u>	<u>Amount</u>
Enrollment of first patient in a phase II clinical trial of a therapeutic product or process	\$ 100,000
Enrollment of first patient in a phase III clinical trial of a therapeutic product or process	\$ 200,000
First commercial sale of a therapeutic product or process	\$ 1,000,000
Filing of an application for regulatory approval of a clinical diagnostic product or process	\$ 100,000
First regulatory approval of a clinical diagnostic product or process	\$ 150,000

As of September 30, 2022, and December 31, 2021, no milestone events had been achieved.

The royalties to be paid to Licensor shall be assessed on net sales of licensed products on a country-by-country basis in an amount equal to 3.0% for therapeutic products or processes, and 6.0% for clinical diagnostic products and processes. The Company shall pay Licensor 30% of any and all sublicense income.

The Company has the right to terminate the License at any time by giving 90 days’ advance notice subject to the payment of any amounts due under the License at that time. The License may also be terminated for cause by either party upon the breach of the material obligations of the other party or the bankruptcy or liquidation of the other party. If the Company does not terminate the License, the term of the License shall continue until the latest of (i) the date on which all issued patents and filed patent applications subject to the License have expired or been abandoned; (ii) expiration of the last to expire regulatory exclusivity covering a covered product or process; or (iii) 10 years after the first commercial sale. The License requires the Company to make royalty payments beyond the term of the License at 1.5%.

**TRANSCODE THERAPEUTICS, INC.**

**NOTES TO FINANCIAL STATEMENTS  
(Unaudited)**

In November 2020, the Company and Licensor amended the November 2018 license. Under the amendment, the intellectual property licensed in 2018 was categorized as “Patent Family 1” and a provisional patent filing related to the Company’s nanoparticle technology was added to Patent Family 1. A second patent family (“Patent Family 2”) was created which includes Licensor intellectual property targeting PD-L1.

The minimum annual license fee prior to the first commercial sale of a product or process covered by the License was increased from \$25,000 per year to \$30,000 per year for Patent Family 1 and a minimum annual license fee of \$10,000 per year was added related to Patent Family 2. All other terms of the License including milestone payments, royalties and payment terms related to sublicense income received by the Company remain the same as in the original License.

***Option Agreement – LIN28B***

The Company signed an Exclusive Option And Internal Evaluation License Agreement (the “Option”) with the Licensor effective February 15, 2021. Under the Option, the Company has (1) the exclusive right to negotiate a license of a certain technology patented by the Licensor and (2) a non-exclusive internal evaluation license to allow the Company to evaluate the technology. The Option provided for a six-month term at a cost of \$5,000 with a right to extend, upon the mutual agreement of the parties, for an additional six months for a second \$5,000 payment. In August 2021, the Licensor agreed to extend the initial term of the Option until November 15, 2021, at no cost to the Company. Effective November 8, 2021, the Company and the Licensor agreed to extend the Option through May 22, 2022, at a cost to the Company of \$5,000. Effective September 28, 2022, the Company and the Licensor agreed to further extend the Option through June 30, 2023, at a cost to the Company of \$10,000. The Company is also responsible for patent costs related to the subject technology incurred by Licensor during the Option period. Patent costs incurred by the Licensor prior to the effective date will not be reimbursed under the Option.

***Option Agreement – Radiolabeled Nanoparticles***

The Company signed an Exclusive Option Agreement (the “Radiolabeled Option”) with the Licensor effective April 15, 2022. Under the Radiolabeled Option, the Company has the exclusive right to negotiate a license of technology patented by the Licensor pertaining to Therapeutic, Radiolabeled Nanoparticles and Methods of Use Thereof, described and claimed in Patent Application PCT/US2021/057912. The Radiolabeled Option provides for a one-year term at a cost of \$7,500 with a right to extend, upon the mutual agreement of the parties, for an additional six months for an additional payment of \$5,000. The Company is also responsible for patent costs related to the subject technology incurred by Licensor during the Radiolabeled Option period. Patent costs incurred by the Licensor prior to the effective date will not be reimbursed.

***Accrued License Obligations***

At September 30, 2022, and December 31, 2021, the Company had accrued \$20,487 and \$5,000, respectively, in license payments under the foregoing arrangements included in accounts payable and accrued expenses. All amounts due at September 30, 2022, and December 31, 2021, have been paid.

***(c) Collaboration Agreement***

On July 29, 2022, the Company signed a five-year strategic collaboration agreement with The University of Texas M. D. Anderson Cancer Center (“MD Anderson”). Under this alliance, the Company anticipates making certain expenditures with respect to Phase I and Phase II clinical trials which it expects will be conducted in part by MD Anderson as a primary investigator site. MD Anderson will also provide preclinical work under the alliance. The details of clinical and preclinical work are to be mutually agreed by the parties prior to commencing work. The Company has committed to fund up to \$10 million over the term of the collaboration, with \$500,000 payable within the first year. Subsequent payments are \$2 million on the first anniversary of the effective date of the agreement and \$2.5 million on each of the second, third and fourth anniversaries thereof. Activities conducted under the arrangement with MD Anderson are research and development activities. Therefore, the Company records all costs incurred under the arrangement



**TRANSCODE THERAPEUTICS, INC.**

**NOTES TO FINANCIAL STATEMENTS  
(Unaudited)**

as research and development costs in its Statements of Operations. Total expenses incurred under the arrangement for the nine months ended September 30, 2022 and 2021, were \$250,000 and \$0, respectively.

**(d) Employment Agreements**

Prior to the IPO, the Company entered into employment agreements with its executive officers which became effective on completion of the IPO. The employment agreements provide the employee with, among other things, severance payments upon termination of the agreement by the Company for any reason other than for cause, death or disability or by the employee for good reason. The maximum aggregate severance payments under the agreements, which arise in the event of termination involving a Change of Control (as defined in the agreements), are approximately \$2,483,700.

**(e) Litigation**

The Company may from time to time be subject to claims by others under various legal disputes. The defense of such claims, or any adverse outcome relating to any such claims, could have a material adverse effect on the Company's liquidity, financial condition, and cash flows. At September 30, 2022, and December 31, 2021, the Company did not have any pending legal actions.

**(f) Indemnification Agreements**

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners, and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and executive officers that require the Company, among other things, to indemnify the parties against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any costs as a result of payments required by such indemnifications. The Company is not aware of any indemnification arrangements that could have a material adverse effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its financial statements, as of September 30, 2022, and December 31, 2021.

**(g) Risks and Uncertainties**

As SARS-CoV-2, or the coronavirus, continues to evolve, the extent to which it affects the Company's operations directly or through parties on whom the Company depends is highly uncertain and cannot be predicted with confidence. The outcomes resulting from these events could delay the Company's plans, increase its operating expenses and have a material adverse effect on its financial condition or results of operations.

In July 2021, the Company was subject to what it believes was a sophisticated computer-based phishing attack involving \$526,435 of which \$45,682 was recovered in five days while the \$480,753 balance was recovered on October 15, 2021. Management believes this incident had an immaterial impact on the Company's financial condition and continues to review its computer-related policies to implement additional defenses.

**(9) Stockholders' Equity**

**(a) Overview**

The Company's Certificate of Incorporation, originally filed on January 11, 2016, was amended on April 15, 2020, to increase the number of shares of common stock authorized and to authorize the issuance of preferred stock. The Company's Certificate of Incorporation was further amended and restated on April 27, 2021. The total number of shares which the Company is authorized to issue is 300,000,000, each with a par value of \$0.0001 per share. Of these shares, 290,000,000 shall be common stock and 10,000,000

**TRANSCODE THERAPEUTICS, INC.**

**NOTES TO FINANCIAL STATEMENTS  
(Unaudited)**

shall be preferred stock. At September 30, 2022, and December 31, 2021, the Company had 12,977,234 and 12,904,574 shares of common stock issued and outstanding, respectively. Of shares sold in 2018, an aggregate of 292,250 shares were issued to two purchasers in exchange for subscriptions receivable bearing interest at 4% per annum and secured by the underlying restricted shares. Both subscriptions receivable and accumulated interest were repaid in 2021. The preferred stock is undesignated; no shares of preferred stock have been issued.

The Company's IPO was completed on July 13, 2021, in which it sold 7,187,500 shares at a public offering price of \$4.00 per share. The gross proceeds from the IPO were \$28,750,000 from which the Company paid \$2,415,000 of underwriting commissions and expenses and \$934,427 of other offering expenses. The underwriter also paid \$100 in aggregate for the underwriter warrants issued in connection with the IPO. See Note 10.

**(b) Common Stock**

i. Dividends

Subject to the rights of holders of any preferred stock, holders of common stock are entitled to receive dividends as may be declared from time to time by the Board. No cash dividends were declared or paid during the three and nine months ended September 30, 2022, nor at any other time through the date of these financial statements.

ii. Liquidation

Subject to the rights of holders of any preferred stock as to liquidation, upon the liquidation, dissolution or winding up of the Company, the remaining assets of the Company will be distributed to holders of common stock.

iii. Voting

Holders of common stock are entitled to one vote for each share of common stock held but shall not be entitled to vote on any amendment to the Certificate of Incorporation that relates solely to the terms of any series of preferred stock. There is no cumulative voting.

**(10) Warrants**

In connection with the IPO, the Company granted the underwriters warrants to purchase up to 312,500 shares of Company common stock at an exercise price of \$5.00 per share, which amount is 125% of the initial public offering price. The warrants have a five-year term and became exercisable on January 9, 2022. All of the warrants were outstanding at September 30, 2022, and December 31, 2021. The Company accounts for these warrants as a component of stockholders' equity.

**(11) Share-Based Compensation**

From inception through October 2018, the Company sold shares of restricted stock to co-founders, directors, managers, and advisors generally at prices believed to be fair market value at the time of the sale. Shares of restricted stock were reserved at the time of issue. To the extent that the sale price was less than the estimated fair market value at the grant date, a charge was recorded for the periods in which such shares vested. The vesting period for restricted stock was generally two to three years. All shares of restricted stock had vested by December 31, 2021.

In April 2020, the Board approved the TransCode Therapeutics, Inc. 2020 Stock Option and Incentive Plan (the "2020 Plan") providing for the issuance of options or other awards to purchase up to 3,032,787 shares of the Company's common stock. The Board determined not to make any further awards under the 2020 Plan following the closing of the IPO. In March 2021, the Company's 2021 Stock Option and Incentive Plan (the "2021 Plan") was approved by the Company's Board and stockholders and became effective upon the effectiveness of the IPO. The 2021 Plan initially provided for the issuance of options or other awards to purchase up to

**TRANSCODE THERAPEUTICS, INC.**

**NOTES TO FINANCIAL STATEMENTS  
(Unaudited)**

2,500,000 shares of the Company's common stock. The number of options or other awards available under the 2021 Plan increased 645,228 shares in January 2022.

Both Plans provide for grants of equity in the form of stock awards, stock options and other instruments to employees, members of the Board, officers and consultants of and advisors to the Company. The Plans are administered by the Board or, at the discretion of the Board, by a committee of the Board. The amount and terms of grants are determined by the Board. The terms of options granted under the Plans generally are for ten (10) years after date of grant and are exercisable in cash or as otherwise determined by the Board. The vesting period for equity-based awards is determined at the discretion of the Board and is generally two to four years. If stock options granted under the 2021 Plan terminate, expire, or are surrendered or cancelled, the shares subject to such grants will again be available under the 2021 Plan.

The exercise price for incentive stock options is determined at the discretion of the Board but for grants to any person possessing less than 10% of the total combined voting power of all classes of stock may not have an exercise price less than 100% of the fair market value of the Common Stock on the grant date (110% for grants to any person possessing more than 10% of the total combined voting power of all classes of stock). The option term for incentive stock option awards may not be greater than ten years from the date of the grant (five years for grants to any person possessing more than 10% of the total combined voting power of all classes of stock).

In 2020, the Board awarded options to purchase 1,756,279 shares of common stock under the 2020 Plan. In 2021, the Board awarded options to purchase 36,393 shares of common stock under the 2020 Plan. Of the options issued under the 2020 Plan, options for 72,660 shares were exercised in January 2022 and options for 78,979 shares terminated in December 2021. In 2022, the Board awarded options to purchase 259,000 shares of common stock in February at an exercise price of \$2.45 per share, 194,000 shares of common stock in March at an exercise price of \$2.12 per share, and 28,500 shares in June at an exercise price of \$1.24 per share under the 2021 Plan, all of which were outstanding at September 30, 2022. In September 2022, the Board approved an award of options to purchase 242,500 shares of common stock for which the date of grant was October 3, 2022, at an exercise price of \$1.07 per share.

At September 30, 2022, there were 1,362,107 options outstanding that were vested and exercisable. All options vested at that date, had been awarded under the 2020 Plan; no options awarded under the 2021 Plan had vested. Information about options to purchase common stock of the Company under both Plans is as follows:

	<u>Number of shares</u>	<u>Weighted average exercise price per share</u>	<u>Weighted average contractual term (years)</u>
Outstanding at December 31, 2020	1,756,279	\$ 0.25	5.9
Granted	36,393	3.91	5.5
Exercised	—	—	—
Forfeited	78,979	—	—
Outstanding at December 31, 2021	1,713,693	0.33	5.2
Granted	481,500	2.27	9.6
Exercised	72,660	0.08	—
Forfeited	—	—	—
Outstanding at September 30, 2022	<u>2,122,533</u>	<u>\$ 0.77</u>	<u>5.8</u>

The intrinsic value of the outstanding options as of September 30, 2022, was \$700,436.

**TRANSCODE THERAPEUTICS, INC.****NOTES TO FINANCIAL STATEMENTS  
(Unaudited)***Option valuation*

The assumptions that the Company used to determine the grant-date fair value of options granted in the nine months ended September 30, 2022 and 2021, were as follows:

	<u>Nine months ended September 30,</u>	
	<u>2021</u>	<u>2022</u>
Risk-free interest rate	0.59%	1.38% - 2.79%
Expected term (in years)	6.0	3.5 - 6.0
Expected volatility	97.2%	93.2%
Expected dividend yield	—	—
Fair value per share of underlying stock	\$3.91	\$1.24 - \$2.45

The weighted average grant date fair value per share of the options granted was \$1.81 for those granted in February 2022, \$1.61 for those granted in March 2022, and \$0.95 for those granted in June 2022.

The Company recorded share-based compensation expense of \$105,602 and \$264,774 during the three months and nine months ended September 30, 2022, respectively, and \$64,052 and \$146,996 during the three months and nine months ended September 30, 2021, respectively. Share-based compensation in the three and nine months ended September 30, 2022, was entirely related to stock options. In the three months ended September 30, 2021, share-based compensation expense was entirely related to stock options while in the nine months ended September 30, 2021, it included \$1,397 related to restricted stock. The remaining share-based compensation expense to be recognized in the future is \$778,581 over approximately 2.1 years.

**(12) Employee Stock Purchase Plan**

In 2021, the Company adopted an Employee Stock Purchase Plan (the "ESPP") to provide eligible employees of the Company with opportunities to purchase shares of the Company's common stock. The ESPP initially provided for the purchase of an aggregate of up to 150,000 shares of common stock. The number of shares of common stock available through the ESPP increased by 90,000 shares in January 2022 and may be increased each subsequent year by up to 90,000 shares.

**(13) Net Loss Per Share**

The Company reported net losses for the three months and nine months ended September 30, 2022 and 2021, respectively. Basic and diluted net loss per share attributable to common stockholders are the same for all periods because shares issuable in connection with Contingent Securities have been excluded from the computation of diluted weighted-average shares outstanding. The effect of their inclusion would have been antidilutive.

**TRANSCODE THERAPEUTICS, INC.**

**NOTES TO FINANCIAL STATEMENTS  
(Unaudited)**

The following table sets forth the computation of basic and diluted loss per share:

	<b>Three months ended September 30,</b>		<b>Nine months ended September 30,</b>	
	<b>2022</b>	<b>2021</b>	<b>2022</b>	<b>2021</b>
<b>Basic loss per share</b>				
Net loss	\$ (4,289,610)	\$ (2,329,706)	\$ (12,430,912)	\$ (4,044,140)
Weighted-average common shares outstanding	12,977,234	11,526,514	12,977,234	6,932,982
Net loss per share	\$ (0.33)	\$ (0.20)	\$ (0.96)	\$ (0.58)
<b>Diluted loss per share</b>				
Net loss	\$ (4,289,610)	\$ (2,329,706)	\$ (12,430,912)	\$ (4,044,140)
Weighted-average common shares outstanding	14,651,841	12,611,893	14,651,841	7,844,750
Net loss per share	\$ (0.29)	\$ (0.18)	\$ (0.85)	\$ (0.52)

Shares issuable upon the exercise of stock options shown in the computation of diluted earnings (loss) per weighted-average share outstanding are assumed as follows:

	<b>Three Months Ended September 30,</b>		<b>Nine Months Ended September 30,</b>	
	<b>2022</b>	<b>2021</b>	<b>2022</b>	<b>2021</b>
<b>Shares issuable on exercise of:</b>				
Vested options	1,362,107	824,962	1,362,107	824,962
Underwriter warrants	312,500	260,417	312,500	86,806

**(14) Income Taxes**

The Company's income tax benefit (expense) was \$0 for the three and nine months ended September 30, 2022 and 2021. The Company has recorded a full valuation allowance against its net deferred tax assets as of September 30, 2022, and December 31, 2021, because the Company has determined that it is more likely than not that these assets will not be fully realized due to historic net operating losses incurred. Accordingly, the benefit of the net operating loss that would have been recognized in the three and nine months ended September 30, 2022 and 2021, was fully offset by changes in the valuation allowance.

As of September 30, 2022, and December 31, 2021, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations.

**(15) Related-Party Transactions**

Between inception and mid-2018, major shareholders and co-founders funded certain expenses of the Company. The aggregate amount of these expenses, \$35,685, was reimbursed by the Company during 2021.

In April 2021, three members of the Company's management advanced an aggregate of \$31,500 to the Company to enable it to pay certain Company IPO expenses. These advances were repaid in full, without interest, on May 13, 2021.

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12,000,000 Shares of Common Stock  
Up to 12,000,000 Pre-Funded Warrants to Purchase Shares of Common Stock

TRANSCODE  
THERAPEUTICS™

TransCode Therapeutics, Inc.

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PRELIMINARY PROSPECTUS

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**EF HUTTON**  
division of Benchmark Investments, LLC

, 2023

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## Part II

### Information Not Required in Prospectus

#### Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the fees and expenses, other than underwriting discounts and commissions, payable in connection with the registration of the common stock hereunder. All amounts are estimates except the SEC registration fee and the FINRA filing fee.

	Amount Paid or to Be Paid
SEC registration fee	\$ 1,268
FINRA filing fee	2,225
Printing and mailing	75,000
Legal fees and expenses	275,000
Accounting fees and expenses	60,000
Miscellaneous	36,507
Total	<u>\$ 450,000</u>

#### Item 14. Indemnification of Directors and Officers.

Section 145 of the DGCL authorizes a corporation to indemnify its directors and officers against liabilities arising out of actions, suits and proceedings to which they are made or threatened to be made a party by reason of the fact that they have served or are currently serving as a director or officer to a corporation. The indemnity may cover expenses (including attorneys' fees) judgments, fines and amounts paid in settlement actually and reasonably incurred by the director or officer in connection with any such action, suit or proceeding. Section 145 permits corporations to pay expenses (including attorneys' fees) incurred by directors and officers in advance of the final disposition of such action, suit or proceeding. In addition, Section 145 provides that a corporation has the power to purchase and maintain insurance on behalf of its directors and officers against any liability asserted against them and incurred by them in their capacity as a director or officer, or arising out of their status as such, whether or not the corporation would have the power to indemnify the director or officer against such liability under Section 145.

We have adopted provisions in our amended and restated certificate of incorporation and amended and restated bylaws to be in effect immediately prior to the completion of this offering that limit or eliminate the personal liability of our directors to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for any breach of the director's duty of loyalty to us or our stockholders; any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law; any unlawful payments related to dividends or unlawful stock purchases, redemptions or other distributions; or any transaction from which the director derived an improper personal benefit.

These limitations of liability do not alter director liability under the federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, our bylaws provide that:

- we will indemnify our directors, officers and, in the discretion of our board of directors, certain employees to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended; and
- we will advance reasonable expenses, including attorneys' fees, to our directors and, in the discretion of our board of directors, to our officers and certain employees, in connection with legal proceedings relating to their service for or on behalf of us, subject to limited exceptions.

We intend to enter into indemnification agreements with each of our directors, executive officers, and other officers as determined from time to time by our board of directors or our remuneration committee. These agreements will provide that we will indemnify each of our directors, officers with whom we have entered into indemnification agreements, and, at times, their affiliates to the fullest extent permitted by Delaware law. We will advance expenses, including attorneys' fees (but excluding judgments, fines and settlement amounts), to each indemnified director, executive officer or affiliate in connection with any proceeding in which indemnification is available and we will indemnify our directors and officers for certain actions or proceedings arising out of that person's services as a director or officer brought on behalf of us or in furtherance of our rights. Additionally, certain of our directors or officers may have certain rights to indemnification, advancement of expenses or insurance provided by their affiliates or other third-parties, which indemnification relates to and might apply to the same proceedings arising out of such director's or officer's services as a director referenced herein. Nonetheless, we will agree in the indemnification agreements that our obligations to those same directors or officers are primary and any obligation of such affiliates or other third-parties to advance expenses or to provide indemnification for the expenses or liabilities incurred by those directors are secondary.

We will maintain general liability insurance which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act of 1933, as amended, or the Securities Act.

The underwriting agreement filed as Exhibit 1.1 to this registration statement provides for indemnification of us and our directors and officers by the underwriter against certain liabilities under the Securities Act and the Securities Exchange Act of 1934.

#### **Item 15. Recent Sales of Unregistered Securities.**

In the three years preceding the filing of this registration statement, we have issued the following securities that were not registered under the Securities Act. No underwriters were involved in the sales and the certificates representing the securities sold and issued contain legends restricting transfer of the securities without registration under the Securities Act or an applicable exemption from registration.

(a) Between May 2018 and May 2020, we sold \$2,240,000 of interest-bearing, unsecured convertible notes, or Notes, to nine investors. The interest rate on the Notes was 6% per annum. At the closing of our IPO on July 13, 2021, all of our outstanding convertible promissory notes plus accrued interest converted into 1,068,135 shares of our common stock.

(b) In June and July 2020, we granted to our directors, officers, employees, consultants and other service providers stock options to purchase an aggregate of 1,683,493 shares of common stock upon the exercise of options under our 2020 Plan at exercise prices per share of \$0.08 and \$0.09.

(c) In December 2020, we granted to our independent directors stock options to purchase an aggregate of 72,786 shares of common stock upon the exercise of options under our 2020 Plan at an exercise price per share of \$3.91.

(d) In January 2021, we granted to an independent director stock options to purchase an aggregate of 36,393 shares of common stock at an exercise price of \$3.91 per share pursuant to our 2020 Plan.

The issuances of certain of the securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act or Rule 701 promulgated under the Securities Act as transactions pursuant to compensatory benefit plans. The shares of common stock issued upon the exercise of options are deemed to be restricted securities for purposes of the Securities Act.



**Item 16. Exhibits and financial statement schedules.**

(a) Exhibits

The Exhibit Index set forth below is incorporated by reference in response to this Item.

<b>Exhibit number</b>	<b>Description</b>
1.1*	<a href="#">Form of Underwriting Agreement.</a>
3.1	<a href="#">Amended and Restated Certificate of Incorporation of TransCode Therapeutics, Inc. (Incorporated by reference to Exhibit 3.3 to the Registrant's Registration Statement on Form S-1, filed on February 26, 2021 (File No. 333-253599)).</a>
3.2	<a href="#">Amended and Restated Bylaws of TransCode Therapeutics, Inc. (Incorporated by reference to Exhibit 3.5 to the Registrant's Registration Statement on Form S-1, filed on February 26, 2021 (File No. 333-253599)).</a>
4.1	<a href="#">Specimen Common Stock Certificate (Incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1, filed on April 8, 2021 (File No. 333-253599)).</a>
4.2*	<a href="#">Form of Pre-funded Warrant.</a>
5.1*	<a href="#">Opinion of Goodwin Procter LLP.</a>
10.1#	<a href="#">2020 Stock Option and Incentive Plan and form of award agreements thereunder (Incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1, filed on February 26, 2021 (File No. 333-253599)).</a>
10.2#	<a href="#">2021 Stock Option and Incentive Plan and form of award agreements thereunder (Incorporated by reference to Exhibit 10.2 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1, filed on March 24, 2021 (File No. 333-253599)).</a>
10.3#	<a href="#">Senior Executive Cash Incentive Bonus Plan (Incorporated by reference to Exhibit 10.3 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1, filed on March 24, 2021 (File No. 333-253599)).</a>
10.4#	<a href="#">Form of Indemnification Agreement between the Registrant and each of its executive officers (Incorporated by reference to Exhibit 10.4 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1, filed on March 24, 2021 (File No. 333-253599)).</a>
10.5#	<a href="#">Form of Indemnification Agreement between the Registrant and each of its directors (Incorporated by reference to Exhibit 10.5 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1, filed on March 24, 2021 (File No. 333-253599)).</a>
10.6	<a href="#">Exclusive Patent License Agreement by and between TransCode Therapeutics, Inc. and The General Hospital Corporation, d/b/a Massachusetts General Hospital, dated as of October 26, 2018 (Incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1, filed on February 26, 2021 (File No. 333-253599)).</a>
10.7#	<a href="#">First Amendment to Exclusive Patent License Agreement by and between TransCode Therapeutics, Inc. and The General Hospital Corporation, d/b/a Massachusetts General Hospital, dated as of October 30, 2020 (Incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1, filed on February 26, 2021 (File No. 333-253599)).</a>
10.8#	<a href="#">2021 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1, filed on March 24, 2021 (File No. 333-253599)).</a>
10.9#	<a href="#">Employment Agreement, dated as of March 24, 2021, by and Between TransCode Therapeutics, Inc. and Robert Michael Dudley (Incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1, filed on April 8, 2021 (File No. 333-253599)).</a>
10.10#	<a href="#">Letter Agreement, dated as of March 24, 2021, by and Between TransCode Therapeutics, Inc. and Robert Michael Dudley (Incorporated by reference to Exhibit 10.10 to the Registrant's Amendment No. 2 to Registration Statement on Form S-1, filed on April 8, 2021 (File No. 333-253599)).</a>

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<b>Exhibit number</b>	<b>Description</b>
10.11#	<a href="#">Employment Agreement, dated as of March 24, 2021, by and Between TransCode Therapeutics, Inc. and Thomas A. Fitzgerald (Incorporated by reference to Exhibit 10.11 to the Registrant's Amendment No. 2 to Registration Statement on Form S-1, filed on April 8, 2021 (File No. 333-253599)).</a>
10.12#	<a href="#">Letter Agreement, dated as of March 24, 2021, by and Between TransCode Therapeutics, Inc. and Thomas A. Fitzgerald (Incorporated by reference to Exhibit 10.12 to the Registrant's Amendment No. 2 to Registration Statement on Form S-1, filed on April 8, 2021 (File No. 333-253599)).</a>
21.1*	<a href="#">List of Subsidiaries of the Registrant.</a>
23.1*	<a href="#">Consent of Withum Smith+Brown, PC, independent registered public accounting firm.</a>
23.2*	<a href="#">Consent of Goodwin Procter LLP (included in Exhibit 5.1).</a>
24.1*	<a href="#">Power of Attorney (included on signature page to this registration statement).</a>
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Presentation Linkbase Document
107*	<a href="#">Filing Fee Table.</a>

# Indicates a management contract or any compensatory plan, contract or arrangement.

\* Filed herewith.

(b) Financial Statements Schedules:

None.

**Item 17. Undertakings.**

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

- (1) The undersigned Registrant will provide to the underwriter at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.
- (2) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (3) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Boston, Commonwealth of Massachusetts, on the 1st day of February, 2023.

**TRANSCODE THERAPEUTICS, INC.**

By: /s/ Robert Michael Dudley  
Robert Michael Dudley  
*Chief Executive Officer*

**POWER OF ATTORNEY AND SIGNATURES**

Each individual whose signature appears below hereby constitutes and appoints each of Robert Michael Dudley and Thomas A. Fitzgerald, MBA as such person's true and lawful attorney-in-fact and agent with full power of substitution and re-substitution, for such person in such person's name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement (or any Registration Statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933), and to file the same, with all exhibits thereto, and all documents in connection therewith, with the Securities and Exchange Commission granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that any said attorney-in-fact and agent, or any substitute or substitutes of any of them, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement and Power of Attorney has been signed by the following person in the capacities and on the date indicated.

<u>NAME</u>	<u>TITLE</u>	<u>DATE</u>
<u>/s/ Robert Michael Dudley</u> Robert Michael Dudley	<i>Director and Chief Executive Officer</i> <i>(Principal Executive Officer)</i>	February 1, 2023
<u>/s/ Thomas A. Fitzgerald</u> Thomas A. Fitzgerald, MBA	<i>Director and Chief Financial Officer</i> <i>(Principal Financial and Accounting Officer)</i>	February 1, 2023
<u>/s/ Philippe P. Calais</u> Philippe P. Calais, PhD	<i>Director</i>	February 1, 2023
<u>/s/ Erik Manting</u> Erik Manting, PhD	<i>Director</i>	February 1, 2023
<u>/s/ Magda Marquet</u> Magda Marquet, PhD	<i>Director</i>	February 1, 2023

**UNDERWRITING AGREEMENT**

**between**

**TRANSCODE THERAPEUTICS, INC.**

**and**

**EF HUTTON, DIVISION OF BENCHMARK INVESTMENTS, LLC**

**as Representative of the Several Underwriters**

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UNDERWRITING AGREEMENTNew York, New York  
[·], 2023

EF Hutton, division of Benchmark Investments, LLC  
As Representative of the several Underwriters named on Schedule 1 attached hereto  
590 Madison Avenue, 39th Floor  
New York, NY 10022

Ladies and Gentlemen:

The undersigned, TransCode Therapeutics, Inc., a corporation formed under the laws of the State of Delaware (the “**Company**”), hereby confirms its agreement (this “**Agreement**”) with EF Hutton, division of Benchmark Investments, LLC (hereinafter referred to as “**you**” (including its correlatives) or the “**Representative**”) and with the other underwriters named on Schedule 1 hereto for which the Representative is acting as representative (the Representative and such other underwriters being collectively called the “**Underwriters**” or, individually, an “**Underwriter**”) as follows:

1. Purchase and Sale of Shares.

1.1 Firm Shares.

1.1.1. Nature and Purchase of Firm Securities.

(i) On the basis of the representations and warranties herein contained, but subject to the terms and conditions herein set forth, the Company agrees to issue and sell to the several Underwriters, an aggregate of (i) [·] shares (“**Firm Shares**”) of the Company’s common stock, par value \$0.0001 per share (the “**Common Stock**”) and Pre-funded warrants, in substantially the form attached hereto as Exhibit A (“**Pre-funded Warrants**”) to purchase [·] shares of Common Stock (the “**Firm Pre-funded Warrants**”).

(ii) The Underwriters, severally and not jointly, agree to purchase from the Company the number of Firm Shares and Firm Pre-funded Warrants set forth opposite their respective names on Schedule 1 attached hereto and made a part hereof at a purchase price of \$[·] per share (93% of the per Firm Share offering price) and \$[·] per Pre-funded Warrant (93% of the per Firm Share offering price, less \$0.01). The Firm Shares and the Firm Pre-funded Warrants (together, the “**Firm Securities**”) are to be offered initially to the public at the offering prices set forth on the cover page of the Prospectus (as defined in Section 2.1.1).

1.1.2. Shares Payment and Delivery.

(i) Delivery and payment for the Firm Securities shall be made at 10:00 a.m., Eastern time, on the second (2<sup>nd</sup>) Business Day following the effective date (the “**Effective Date**”) of the Registration Statement (as defined in Section 2.1.1) (or the third (3<sup>rd</sup>) Business Day following the Effective Date if the Registration Statement is declared effective after 4:01 p.m., Eastern time) or at such earlier time as shall be agreed upon by the Representative and the Company, at the offices of McGuireWoods LLP, 1251 Avenue of the Americas, 20<sup>th</sup> Floor, New York, New York 10020 (“**Representative Counsel**”), or at such other place (or remotely by e-mail or other electronic transmission) as shall be agreed upon by the

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Representative and the Company. The hour and date of delivery and payment for the Firm Securities is called the “**Closing Date.**”

(ii) Payment for the Firm Securities shall be made on the Closing Date by wire transfer in Federal (same day) funds, payable to the order of the Company upon delivery of the certificates (in form and substance satisfactory to the Underwriters) representing the Firm Securities (or through the facilities of the Depository Trust Company (“**DTC**”)) for the account of the Underwriters. The Firm Securities shall be registered in such name or names and in such authorized denominations as the Representative may request in writing at least two (2) full Business Days prior to the Closing Date. The Company shall not be obligated to sell or deliver the Firm Securities except upon tender of payment by the Representative for all of the Firm Securities. The term “**Business Day**” means any day other than a Saturday, a Sunday or a legal holiday or a day on which banking institutions are authorized or obligated by law to close in New York, New York.

## 1.2 Over-allotment Option.

1.2.1. Option Securities. For the purposes of covering any over-allotments in connection with the distribution and sale of the Firm Shares, the Company hereby grants to the Underwriters an option to purchase up to [·] additional shares of Common Stock or additional Pre-funded Warrants to purchase up to [·] shares of Common Stock, together representing an aggregate of fifteen percent (15%) of the Firm Securities sold in the offering, from the Company (the “**Over-allotment Option**”). Such [·] additional shares of Common Stock, the net proceeds of which will be deposited with the Company’s account, are hereinafter referred to as “**Option Shares.**” Such additional Pre-funded Warrants to purchase [·] shares of Common Stock, the net proceeds of which will be deposited with the Company’s account, are hereinafter referred to as “**Option Pre-funded Warrants.**” The Option Shares and Option Pre-funded Warrants may be referred to herein collectively as the “**Option Securities.**” The purchase price to be paid per Option Share and per Option Pre-funded Warrant shall be equal to the price per Firm Share and per Firm Pre-funded Warrant set forth in Section 1.1.1. The Firm Securities and the Option Securities are hereinafter referred to together as the “**Public Securities.**” The offering and sale of the Public Securities is hereinafter referred to as the “**Offering.**”

1.2.2. Exercise of Option. The Over-allotment Option granted pursuant to Section 1.2.1 may be exercised by the Representative as to all (at any time) or any part (from time to time) of the Option Securities within 45 days after the Effective Date. The Underwriters shall not be under any obligation to purchase any Option Securities prior to the exercise of the Over-allotment Option. The Over-allotment Option granted hereby may be exercised by the giving of oral notice to the Company from the Representative, which must be confirmed in writing by overnight mail or facsimile or other electronic transmission setting forth the number of Option Securities to be purchased and the date and time for delivery of and payment for the Option Securities (the “**Option Closing Date**”), which shall not be later than one (1) full Business Day after the date of the notice or such other time as shall be agreed upon by the Company and the Representative, at the offices of Representative Counsel or at such other place (including remotely by e-mail or other electronic transmission) as shall be agreed upon by the Company and the Representative. If such delivery and payment for the Option Securities does not occur on the Closing Date, the Option Closing Date will be as set forth in the notice. Upon exercise of the Over-allotment Option with respect to all or any portion of the Option Securities, subject to the terms and conditions set forth herein, (i) the Company shall become obligated to sell to the Underwriters the number of Option Securities specified in such notice and (ii) each of the Underwriters, acting severally and not jointly, shall purchase that portion of the total number of Option Securities then being purchased as set forth in Schedule 1 opposite the name of such Underwriter.

1.2.3. Payment and Delivery. Payment for the Option Securities shall be made on the Option Closing Date by wire transfer in Federal (same day) funds, payable to the order of the Company

upon delivery to you of certificates (in form and substance satisfactory to the Underwriters) representing the Option Shares (or through the facilities of DTC) and/or Option Pre-funded Warrants for the account of the Underwriters. The Option Securities shall be registered in such name or names and in such authorized denominations as the Representative may request in writing at least one (1) full Business Day prior to the Option Closing Date. The Company shall not be obligated to sell or deliver the Option Securities except upon tender of payment by the Representative for applicable Option Securities. The Option Closing Date may be simultaneous with, but not earlier than, the Closing Date, and in the event that such time and date are simultaneous with the Closing Date, the term “Closing Date” share refer to the time and date of delivery of the Firm Securities and the Option Securities.

2. Representations and Warranties of the Company. The Company represents and warrants to the Underwriters as of the Applicable Time (as defined below), as of the Closing Date and as of the Option Closing Date, if any, as follows:

2.1 Filing of Registration Statement.

2.1.1. Pursuant to the Securities Act. The Company has filed with the U.S. Securities and Exchange Commission (the “**Commission**”) a registration statement, and an amendment or amendments thereto, on Form S-1 (File No. 333-[·]), including any related prospectus or prospectuses, for the registration of the Public Securities under the Securities Act of 1933, as amended (the “**Securities Act**”), which registration statement and amendment or amendments have been prepared by the Company in all material respects in conformity with the requirements of the Securities Act and the rules and regulations of the Commission under the Securities Act (the “**Securities Act Regulations**”) and will contain all material statements that are required to be stated therein in accordance with the Securities Act and the Securities Act Regulations. Except as the context may otherwise require, such registration statement, as amended, on file with the Commission at the time the registration statement became effective (including the Preliminary Prospectus included in the registration statement, financial statements, schedules, exhibits and all other documents filed as a part thereof or incorporated therein and all information deemed to be a part thereof as of the Effective Date pursuant to paragraph (b) of Rule 430A of the Securities Act Regulations (the “**Rule 430A Information**”), is referred to herein as the “**Registration Statement.**” If the Company files any registration statement pursuant to Rule 462(b) of the Securities Act Regulations, then after such filing, the term “Registration Statement” shall include such registration statement filed pursuant to Rule 462(b). The Registration Statement has been declared effective by the Commission on the date hereof.

Each prospectus used prior to the effectiveness of the Registration Statement, and each prospectus that omitted the Rule 430A Information that was used after such effectiveness and prior to the execution and delivery of this Agreement, is herein called a “**Preliminary Prospectus.**” The Preliminary Prospectus, subject to completion, dated [·], 2023, that was included in the Registration Statement immediately prior to the Applicable Time is hereinafter called the “**Pricing Prospectus.**” The final prospectus in the form first furnished to the Underwriters for use in the Offering is hereinafter called the “**Prospectus.**” Any reference to the “most recent Preliminary Prospectus” shall be deemed to refer to the latest Preliminary Prospectus included in the Registration Statement.

As used herein, the terms “Registration Statement,” “Preliminary Prospectus,” “Pricing Prospectus” and “Prospectus” shall include the documents, if any, incorporated by reference therein. The terms “**supplement,**” “**amendment,**” and “**amend**” as used herein with respect to the Registration Statement, the Pricing Prospectus, the Prospectus, any preliminary prospectus or free writing prospectus shall include all documents subsequently filed by the Company with the Commission pursuant to the Securities Exchange Act of 1934, as amended (the “**Exchange Act**”), that are deemed to be incorporated by reference therein.

“**Applicable Time**” means [TIME] [a.m./p.m.], Eastern time, on the date of this Agreement.



**“Issuer Free Writing Prospectus”** means any “issuer free writing prospectus,” as defined in Rule 433 of the Securities Act Regulations (“**Rule 433**”), including without limitation any “free writing prospectus” (as defined in Rule 405 of the Securities Act Regulations) relating to the Public Securities that is (i) required to be filed with the Commission by the Company, (ii) a “road show that is a written communication” within the meaning of Rule 433(d)(8)(i), whether or not required to be filed with the Commission, or (iii) exempt from filing with the Commission pursuant to Rule 433(d)(5)(i) because it contains a description of the Public Securities or of the Offering that does not reflect the final terms, in each case in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company’s records pursuant to Rule 433(g).

**“Issuer General Use Free Writing Prospectus”** means any Issuer Free Writing Prospectus that is intended for general distribution to prospective investors (other than a “*bona fide* electronic road show,” as defined in Rule 433), as evidenced by its being specified in Schedule 2-B hereto.

**“Issuer Limited Use Free Writing Prospectus”** means any Issuer Free Writing Prospectus that is not an Issuer General Use Free Writing Prospectus.

**“Pricing Disclosure Package”** means any Issuer General Use Free Writing Prospectus issued at or prior to the Applicable Time, the Pricing Prospectus and the information included on Schedule 2-A hereto, all considered together.

2.1.2. Pursuant to the Exchange Act. The Common Stock is registered pursuant to Section 12(b) under the Exchange Act. The Company has taken no action designed to, or likely to have the effect of, terminating the registration of the shares of Common Stock under the Exchange Act, nor has the Company received any notification that the Commission is contemplating terminating such registration.

2.2 Stock Exchange Listing. The shares of Common Stock have been approved for listing on the NASDAQ Capital Market (the “**Exchange**”), and the Company has taken no action designed to, or likely to have the effect of, delisting the shares of Common Stock from the Exchange, nor has the Company received any notification that the Exchange is contemplating terminating such listing except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus.

2.3 No Stop Orders, etc. Neither the Commission nor, to the Company’s knowledge, any state regulatory authority has issued any order preventing or suspending the use of the Registration Statement, any Preliminary Prospectus or the Prospectus or has instituted or, to the Company’s knowledge, threatened to institute, any proceedings with respect to such an order. The Company has complied with each request (if any) from the Commission for additional information.

2.4 Disclosures in Registration Statement.

2.4.1. Compliance with Securities Act and 10b-5 Representation.

(i) Each of the Registration Statement and any post-effective amendment thereto, at the time it became effective complied in all material respects with the requirements of the Securities Act and the Securities Act Regulations. Each Preliminary Prospectus, including the prospectus filed as part of the Registration Statement as originally filed or as part of any amendment or supplement thereto, and the Prospectus, at the time each was filed with the Commission, complied in all material respects with the requirements of the Securities Act and the Securities Act Regulations. Each Preliminary Prospectus delivered to the Underwriters for use in connection with this Offering and the Prospectus was or will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to the Commission’s Electronic Data Gathering, Analysis, and Retrieval (“**EDGAR**”) system, except to the extent permitted by Regulation S-T.

(ii) Neither the Registration Statement nor any amendment thereto, at its effective time, as of the Applicable Time, at the Closing Date or at any Option Closing Date (if any), contained, contains or will contain an untrue statement of a material fact or omitted, omits or will omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading.

(iii) The Pricing Disclosure Package, as of the Applicable Time, at the Closing Date or at any Option Closing Date (if any), did not, does not and will not include an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; and each Issuer Limited Use Free Writing Prospectus hereto does not conflict with the information contained in the Registration Statement, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, and each such Issuer Limited Use Free Writing Prospectus, as supplemented by and taken together with the Pricing Prospectus as of the Applicable Time, did not include an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading; provided, however, that this representation and warranty shall not apply to statements made or statements omitted in reliance upon and in conformity with written information furnished to the Company with respect to the Underwriters by the Representative expressly for use in the Registration Statement, the Pricing Prospectus or the Prospectus or any amendment thereof or supplement thereto. The parties acknowledge and agree that such information provided by or on behalf of any Underwriter consists solely of the following disclosure contained in the “Underwriting” section of the Prospectus: the first paragraph under the subheading “Discounts, Commissions and Reimbursement,” the first sentence of the first paragraph, the last sentence of the second paragraph and the first sentence of the fourth paragraph under the subheading “Price Stabilization, Short Positions and Penalty Bids,” the paragraphs under the subheadings “Other Relationships” and “Electronic Offer, Sale and Distribution of Securities” (the “**Underwriters’ Information**”); and

(iv) Neither the Prospectus nor any amendment or supplement thereto (including any prospectus wrapper), as of its issue date, at the time of any filing with the Commission pursuant to Rule 424(b), at the Closing Date or at any Option Closing Date, included, includes or will include an untrue statement of a material fact or omitted, omits or will omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided, however, that this representation and warranty shall not apply to the Underwriters’ Information.

2.4.2. Disclosure of Agreements. The agreements and documents described in the Registration Statement, the Pricing Disclosure Package and the Prospectus conform in all material respects to the descriptions thereof contained therein and there are no agreements or other documents required by the Securities Act and the Securities Act Regulations to be described in the Registration Statement, the Pricing Disclosure Package and the Prospectus or to be filed with the Commission as exhibits to the Registration Statement, that have not been so described or filed. Each agreement or other instrument (however characterized or described) to which the Company is a party or by which it is or may be bound or affected and (i) that is referred to or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus, or (ii) is material to the Company’s business, has been duly authorized and validly executed by the Company, is in full force and effect in all material respects and is enforceable against the Company and, to the Company’s knowledge, the other parties thereto, in accordance with its terms, except (x) as such enforceability may be limited by bankruptcy, insolvency, reorganization or similar laws affecting creditors’ rights generally, (y) as enforceability of any indemnification or contribution provision may be limited under the federal and state securities laws, and (z) that the remedy of specific performance and injunctive and other forms of equitable relief may be subject to the equitable defenses and to the discretion of the court before which any proceeding therefor may be brought. None of such agreements or instruments has been assigned by the Company, and neither the Company nor, to the Company’s knowledge, any other party is in default thereunder and, to the Company’s knowledge, no event

has occurred that, with the lapse of time or the giving of notice, or both, would constitute a default thereunder. To the Company's knowledge, performance by the Company of the material provisions of such agreements or instruments will not result in a violation of any existing applicable law, rule, regulation, judgment, order or decree of any governmental agency or court, domestic or foreign, having jurisdiction over the Company or any of its assets or businesses (each, a "**Governmental Entity**"), including, without limitation, those relating to environmental laws and regulations.

2.4.3. Prior Securities Transactions. No securities of the Company have been sold by the Company or by or on behalf of, or for the benefit of, any person or persons controlling, controlled by or under common control with the Company, except as disclosed in the Registration Statement, the Pricing Disclosure Package and the Preliminary Prospectus or in reports filed under Section 16 of the Exchange Act.

2.4.4. Regulations. The disclosures in the Registration Statement, the Pricing Disclosure Package and the Prospectus concerning the effects of federal, state, local and all foreign regulation on the Offering and the Company's business as currently contemplated are correct in all material respects and no other such regulations are required to be disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus which are not so disclosed.

2.4.5. No Other Distribution of Offering Materials. The Company has not, directly or indirectly, distributed and will not distribute any offering material in connection with the Offering other than any Preliminary Prospectus, the Pricing Disclosure Package, the Prospectus and other materials, if any, permitted under the Securities Act and consistent with Section 3.2.

## 2.5 Changes After Dates in Registration Statement.

2.5.1. No Material Adverse Change. Since the respective dates as of which information is given in the Registration Statement, the Pricing Disclosure Package and the Prospectus, except as otherwise specifically stated therein: (i) there has been no material adverse change in the financial position or results of operations of the Company, nor any change or development that, singularly or in the aggregate, would involve a material adverse change or a prospective material adverse change, in or affecting the condition (financial or otherwise), results of operations, business, assets or prospects of the Company (a "**Material Adverse Change**"); (ii) there have been no material transactions entered into by the Company, other than as contemplated pursuant to this Agreement; and (iii) no officer or director of the Company has resigned from any position with the Company.

2.5.2. Recent Securities Transactions, etc. Subsequent to the respective dates as of which information is given in the Registration Statement, the Pricing Disclosure Package and the Prospectus, and except as may otherwise be indicated or contemplated herein or disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the Company has not: (i) issued any securities or incurred any liability or obligation, direct or contingent, for borrowed money; or (ii) declared or paid any dividend or made any other distribution on or in respect to its capital stock.

2.6 Disclosures in Commission Filings. Since January 1, 2021, (i) none of the Company's filings with the Commission contained any untrue statement of a material fact or omitted to state any material fact necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading; and (ii) the Company has made all filings with the Commission required under the Exchange Act and the rules and regulations of the Commission promulgated thereunder (the "Exchange Act Regulations").

2.7 Independent Accountants. To the knowledge of the Company, WithumSmith+Brown, PC (the "**Auditor**"), whose report is included or incorporated by reference in the Registration Statement, the

Pricing Disclosure Package and the Prospectus, is an independent registered public accounting firm as required by the Securities Act and the Securities Act Regulations and the Public Company Accounting Oversight Board. The Auditor has not, during the periods covered by the financial statements included or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus, provided to the Company any non-audit services prohibited by Section 10A(g) of the Exchange Act.

2.8 Financial Statements, etc. The financial statements, including the notes thereto and supporting schedules included or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus, fairly present the financial position and the results of operations of the Company at the dates and for the periods to which they apply; and such financial statements have been prepared in conformity with U.S. generally accepted accounting principles (“GAAP”), consistently applied throughout the periods involved (provided that unaudited interim financial statements are subject to year-end audit adjustments that are not expected to be material in the aggregate and do not contain all footnotes required by GAAP); and the supporting schedules included in the Registration Statement present fairly the information required to be stated therein. Except as included therein, no historical or pro forma financial statements are required to be included in the Registration Statement, the Pricing Disclosure Package or the Prospectus under the Securities Act or the Securities Act Regulations. The pro forma and pro forma as adjusted financial information and the related notes, if any, included or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus have been properly compiled and prepared in accordance with the applicable requirements of the Securities Act and the Securities Act Regulations and present fairly the information shown therein, and the assumptions used in the preparation thereof are reasonable and the adjustments used therein are appropriate to give effect to the transactions and circumstances referred to therein. All disclosures contained in the Registration Statement, the Pricing Disclosure Package or the Prospectus regarding “non-GAAP financial measures” (as such term is defined by the rules and regulations of the Commission), if any, comply with Regulation G of the Exchange Act and Item 10 of Regulation S-K of the Securities Act, to the extent applicable. Each of the Registration Statement, the Pricing Disclosure Package and the Prospectus discloses all material off-balance sheet transactions, arrangements, obligations (including contingent obligations), and other relationships of the Company with unconsolidated entities or other persons that may have a material current or future effect on the Company’s financial condition, changes in financial condition, results of operations, liquidity, capital expenditures, capital resources, or significant components of revenues or expenses. Except as disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus, (a) the Company has not incurred any material liabilities or obligations, direct or contingent, or entered into any material transactions other than in the ordinary course of business, (b) the Company has not declared or paid any dividends or made any distribution of any kind with respect to its capital stock, (c) there has not been any change in the capital stock of the Company, or, other than in the course of business, any grants under any stock compensation plan, and (d) there has not been any material adverse change in the Company’s long-term or short-term debt.

2.9 Authorized Capital; Options, etc. The Company had, at the date or dates indicated in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the duly authorized, issued and outstanding capitalization as set forth therein. Based on the assumptions stated in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the Company will have on the Closing Date the adjusted stock capitalization set forth therein. Except as set forth in, or contemplated by, the Registration Statement, the Pricing Disclosure Package and the Prospectus, on the Effective Date, as of the Applicable Time and on the Closing Date and any Option Closing Date, there will be no stock options, warrants, or other rights to purchase or otherwise acquire any authorized, but unissued shares of Common Stock of the Company or any security convertible or exercisable into shares of Common Stock of the Company, or any contracts or commitments to issue or sell shares of Common Stock or any such options, warrants, rights or convertible securities.

## 2.10 Valid Issuance of Securities, etc.

2.10.1. Outstanding Securities. All issued and outstanding securities of the Company issued prior to the transactions contemplated by this Agreement have been duly authorized and validly issued and are fully paid and non-assessable; the holders thereof have no rights of rescission with respect thereto, and are not subject to personal liability by reason of being such holders; and none of such securities were issued in violation of the preemptive rights, rights of first refusal or rights of participation of any holders of any security of the Company or similar contractual rights granted by the Company. The authorized shares of Common Stock conform in all material respects to all statements relating thereto contained in the Registration Statement, the Pricing Disclosure Package and the Prospectus. The offers and sales of the outstanding shares of Common Stock were at all relevant times either registered under the Securities Act and the applicable state securities or “blue sky” laws or, based in part on the representations and warranties of the purchasers of such shares, exempt from such registration requirements. The description of the Company’s stock option, stock bonus and other stock plans or arrangements, and the options or other rights granted thereunder, as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, accurately and fairly present, in all material respects, the information required to be shown with respect to such plans, arrangements, options and rights.

2.10.2. Securities Sold Pursuant to this Agreement. The Public Securities and the shares of Common Stock issuable upon the exercise of the Pre-funded Warrants (the “**Underlying Shares**”) have been duly authorized for issuance and sale and, when issued and paid for, will be validly issued, fully paid and non-assessable; the holders thereof are not and will not be subject to personal liability by reason of being such holders; the Public Securities and the Underlying Shares are not and will not be subject to the preemptive rights of any holders of any security of the Company or similar contractual rights granted by the Company; and all corporate action required to be taken for the authorization, issuance and sale of the Public Securities and the Underlying Shares has been duly and validly taken. The Public Securities and the Pre-funded Warrants conform in all material respects to all statements with respect thereto contained in the Registration Statement, the Pricing Disclosure Package and the Prospectus. All corporate action required to be taken for the authorization, issuance and sale of the Pre-funded Warrants has been duly and validly taken; the Underlying Shares have been duly authorized and reserved for issuance by all necessary corporate action on the part of the Company and when paid for and issued in accordance with the Pre-funded Warrants, such shares of Common Stock will be validly issued, fully paid and non-assessable; the holders thereof are not and will not be subject to personal liability by reason of being such holders; and such shares of Common Stock are not and will not be subject to the preemptive rights of any holders of any security of the Company or similar contractual rights granted by the Company.

2.11 Registration Rights of Third Parties. Except as set forth in the Registration Statement, the Pricing Disclosure Package and the Prospectus, no holders of any securities of the Company or any rights exercisable for or convertible or exchangeable into securities of the Company have the right to require the Company to register any such securities of the Company under the Securities Act or to include any such securities in a registration statement to be filed by the Company, except as have been validly waived.

2.12 Validity and Binding Effect of Agreements. This Agreement and the Pre-funded Warrants have been duly and validly authorized by the Company, and, when executed and delivered, will constitute, the valid and binding agreements of the Company, enforceable against the Company in accordance with their respective terms, except: (i) as such enforceability may be limited by bankruptcy, insolvency, reorganization or similar laws affecting creditors’ rights generally; (ii) as enforceability of any indemnification or contribution provision may be limited under the federal and state securities laws; and (iii) that the remedy of specific performance and injunctive and other forms of equitable relief may be subject to the equitable defenses and to the discretion of the court before which any proceeding therefor may be brought.

2.13 No Conflicts, etc. The execution, delivery and performance by the Company of this Agreement and the Pre-funded Warrants and all ancillary documents, the consummation by the Company of the transactions herein and therein contemplated and the compliance by the Company with the terms hereof and thereof do not and will not, with or without the giving of notice or the lapse of time or both: (i) result in a material breach of, or conflict with any of the terms and provisions of, or constitute a material default under, or result in the creation, modification, termination or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to the terms of any agreement or instrument to which the Company is a party; (ii) result in any violation of the provisions of the Company's Certificate of Incorporation (as the same may be amended or restated from time to time, the "**Charter**") or the by-laws of the Company; or (iii) violate any existing applicable law, rule, regulation, judgment, order or decree of any Governmental Entity as of the date hereof, except in the case of clauses (i) and (iii) for such breach, conflict, default or violation which would not reasonably be expected to cause a Material Adverse Change.

2.14 No Defaults; Violations. No material default exists and no event has occurred that, with the lapse of time or the giving of notice, or both, would constitute a default, in the due performance and observance of any term, covenant or condition of any material license, contract, indenture, mortgage, deed of trust, note, loan or credit agreement, or any other agreement or instrument evidencing an obligation for borrowed money, or any other material agreement or instrument to which the Company is a party or by which the Company may be bound or to which any of the properties or assets of the Company is subject. The Company is not in violation of any term or provision of its Charter or by-laws, or in violation of any franchise, license, permit, applicable law, rule, regulation, judgment or decree of any Governmental Entity.

2.15 Corporate Power; Licenses; Consents.

2.15.1. Conduct of Business. Except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the Company has all requisite corporate power and authority, and has all necessary authorizations, approvals, orders, licenses, certificates and permits of and from all governmental regulatory officials and bodies that it needs as of the date hereof to conduct its business purpose as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus.

2.15.2. Transactions Contemplated Herein. The Company has all corporate power and authority to enter into this Agreement and to carry out the provisions and conditions hereof, and all consents, authorizations, approvals and orders required in connection therewith have been obtained. No consent, authorization or order of, and no filing with, any court, government agency or other body is required for the valid issuance, sale and delivery of the Public Securities and the consummation of the transactions and agreements contemplated by this Agreement and the Pre-funded Warrants and as contemplated by the Registration Statement, the Pricing Disclosure Package and the Prospectus, except with respect to applicable federal and state securities laws and the rules and regulations of the Financial Industry Regulatory Authority, Inc. ("**FINRA**").

2.16 Litigation, Governmental Proceedings. There is no action, suit, proceeding, inquiry, arbitration, investigation, litigation or governmental proceeding pending or, to the Company's knowledge, threatened against, or involving the Company or, to the Company's knowledge, any executive officer or director which has not been disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus.

2.17 Good Standing. The Company has been duly organized and is validly existing as a corporation and is in good standing under the laws of the State of Delaware as of the date hereof, and is duly qualified to do business and is in good standing in each other jurisdiction in which its ownership or lease of property or the conduct of business requires such qualification, except where the failure to qualify, singularly or in the aggregate, would not have or reasonably be expected to result in a Material Adverse Change.

2.18 Insurance. The Company carries or is entitled to the benefits of insurance, with reputable insurers, in such amounts and covering such risks which the Company believes are adequate, including, but not limited to, directors and officers insurance coverage at least equal to \$5,000,000 and all such insurance is in full force and effect. The Company has no reason to believe that it will not be able (i) to renew its existing insurance coverage as and when such policies expire or (ii) to obtain comparable coverage from similar institutions as may be necessary or appropriate to conduct its business as now conducted and at a cost that would not result in a Material Adverse Change.

2.19 Transactions Affecting Disclosure to FINRA.

2.19.1. Finder's Fees. Except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, there are no claims, payments, arrangements, agreements or understandings relating to the payment of a finder's, consulting or origination fee by the Company or any Insider with respect to the sale of the Public Securities hereunder or any other arrangements, agreements or understandings of the Company or, to the Company's knowledge, any of its shareholders that may affect the Underwriters' compensation, as determined by FINRA.

2.19.2. Payments Within Twelve (12) Months. Except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the Company has not made any direct or indirect payments (in cash, securities or otherwise) to: (i) any person, as a finder's fee, consulting fee or otherwise, in consideration of such person raising capital for the Company or introducing to the Company persons who raised or provided capital to the Company; (ii) any FINRA member; or (iii) any person or entity that has any direct or indirect affiliation or association with any FINRA member, within the twelve (12) months prior to the Effective Date, other than the payment to the Underwriters as provided hereunder in connection with the Offering.

2.19.3. Use of Proceeds. None of the net proceeds of the Offering will be paid by the Company to any participating FINRA member or its affiliates, except as specifically authorized herein.

2.19.4. FINRA Affiliation. There is no (i) officer or director of the Company, (ii) beneficial owner of 5% or more of any class of the Company's securities or (iii) beneficial owner of the Company's unregistered equity securities which were acquired during the 180-day period immediately preceding the filing of the Registration Statement that is an affiliate or associated person of a FINRA member participating in the Offering (as determined in accordance with the rules and regulations of FINRA). The Company does not (within the meaning of FINRA's Conduct Rule 5121(f)(i)) directly or indirectly control, is not controlled by or under common control with, or is an associated person (within the meaning of Article 1, Section 1(ee) of the By-Laws of FINRA) of, any member of FINRA.

2.19.5. Information. All information provided by the Company in its FINRA questionnaire to Representative Counsel specifically for use by Representative Counsel in connection with its Public Offering System filings (and related disclosure) with FINRA is true, correct and complete in all material respects.

2.20 Foreign Corrupt Practices Act. Neither the Company nor, to the Company's knowledge, any director, officer, agent, employee or affiliate of the Company or any other person acting on behalf of the Company, has, directly or indirectly, given or agreed to give any money, gift or similar benefit (other than legal price concessions to customers in the ordinary course of business) to any customer, supplier, employee or agent of a customer or supplier, or official or employee of any governmental agency or instrumentality of any government (domestic or foreign) or any political party or candidate for office (domestic or foreign) or other person who was, is, or may be in a position to help or hinder the business of the Company (or assist it in connection with any actual or proposed transaction) that (i) might subject the Company to any damage or penalty in any civil, criminal or governmental litigation or proceeding, (ii) if not given in the past, might have had a Material Adverse Change or (iii) if not continued in the future, might adversely affect the assets, business, operations or prospects of the Company. The Company has taken reasonable steps to ensure that its accounting controls and procedures are sufficient to cause the Company to comply in all material respects with the Foreign Corrupt Practices Act of 1977, as amended.

2.21 Compliance with OFAC. Neither the Company nor, to the Company's knowledge, any director, officer, agent, employee or affiliate of the Company or any other person acting on behalf of the Company, is currently subject to any U.S. sanctions administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury ("**OFAC**"), and the Company will not, directly or indirectly, use the proceeds of the Offering hereunder, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other person or entity, for the purpose of financing the activities of any person currently subject to any U.S. sanctions administered by OFAC.

2.22 Money Laundering Laws. The operations of the Company are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the money laundering statutes of all jurisdictions, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any Governmental Entity (collectively, the "**Money Laundering Laws**"); and no action, suit or proceeding by or before any Governmental Entity involving the Company with respect to the Money Laundering Laws is pending or, to the best knowledge of the Company, threatened.

2.23 Forward-Looking Statements. No forward-looking statement (within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act) contained in either the Registration Statement, the Pricing Disclosure Package or the Prospectus has been made or reaffirmed without a reasonable basis or has been disclosed other than in good faith.

2.24 Officers' Certificate. Any certificate signed by any duly authorized officer of the Company and delivered to you or to Representative Counsel shall be deemed a representation and warranty by the Company to the Underwriters as to the matters covered thereby.

2.25 Lock-Up Agreements. Schedule 3 hereto contains a complete and accurate list of individuals subject to a Lock-Up Agreement (as defined below), including the Company's officers and directors (collectively, the "**Lock-Up Parties**"). The Company has caused each of the Lock-Up Parties to deliver to the Representative an executed Lock-Up Agreement, in the form attached hereto as Exhibit B (the "**Lock-Up Agreement**"), prior to the execution of this Agreement.

2.26 Subsidiaries. The Company has no subsidiaries.



2.27 Related Party Transactions. There are no business relationships or related party transactions involving the Company or any other person required to be described in the Registration Statement, the Pricing Disclosure Package, the Prospectus or a document or incorporated by reference therein that have not been described as required.

2.27.1. No Unconsolidated Entities. There are no transactions, arrangements or other relationships between and/or among the Company or any of the Company's affiliates (as such term is defined in Rule 405 of the Securities Act) and any unconsolidated entity, including, but not limited to, any structured finance, special purpose or limited purpose entity that could reasonably be expected to materially affect the Company's liquidity or the availability of or requirements for its capital resources required to be described in the Registration Statement, the Pricing Disclosure Package and the Prospectus or a document incorporated by reference therein which have not been described as required.

2.28 Board of Directors. The Board of Directors of the Company is comprised of the persons set forth in the Company's filings made under the Exchange Act incorporated by reference into the Registration Statement, the Pricing Disclosure Package and the Prospectus. The qualifications of the persons serving as board members and the overall composition of the board comply with the Exchange Act, the Exchange Act Regulations, the Sarbanes-Oxley Act of 2002 and the rules promulgated thereunder (the "**Sarbanes-Oxley Act**") applicable to the Company and the listing rules of the Exchange. At least one member of the Audit Committee of the Board of Directors of the Company qualifies as an "audit committee financial expert," as such term is defined under Regulation S-K and the listing rules of the Exchange. In addition, at least a majority of the persons serving on the Board of Directors qualify as "independent," as defined under the listing rules of the Exchange.

2.29 Sarbanes-Oxley Compliance.

2.29.1. Disclosure Controls. The Company has developed and currently maintains disclosure controls and procedures that comply with Rule 13a-15 or 15d-15 under the Exchange Act Regulations, and such controls and procedures are effective to ensure that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Commission's rules and forms and includes, without limitation, controls and procedures designed to ensure that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the Company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

2.29.2. Compliance. The Company is in material compliance with the provisions of the Sarbanes-Oxley Act applicable to it, and has implemented or will implement such programs and taken reasonable steps to ensure the Company's future compliance (not later than the relevant statutory and regulatory deadlines therefor) with all of the material provisions of the Sarbanes-Oxley Act.

2.30 Accounting Controls. The Company maintains systems of "internal control over financial reporting" (as defined under Rules 13a-15 and 15d-15 under the Exchange Act Regulations) that comply with the requirements of the Exchange Act and have been designed by, or under the supervision of, their respective principal executive and principal financial officers, or persons performing similar functions, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP, including, but not limited to, internal accounting controls sufficient to provide reasonable assurance that (i) transactions are executed in accordance with management's general or specific authorizations; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain asset accountability; (iii) access to assets is permitted only in accordance with management's general or specific

authorization; and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. Except as disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the Company is not aware of any material weaknesses in its internal controls. The Company's auditors and the Audit Committee of the Board of Directors of the Company have been advised of: (i) all significant deficiencies and material weaknesses in the design or operation of internal controls over financial reporting which are known to the Company's management and that have adversely affected or are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and (ii) any fraud known to the Company's management, whether or not material, that involves management or other employees who have a significant role in the Company's internal controls over financial reporting.

2.31 No Investment Company Status. The Company is not and, after giving effect to the Offering and the application of the proceeds thereof as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, will not be, required to register as an "investment company," as defined in the Investment Company Act of 1940, as amended.

2.32 No Labor Disputes. No labor dispute with the employees of the Company exists or, to the knowledge of the Company, is imminent.

2.33 Intellectual Property Rights. The Company owns or possesses or has valid rights to use all patents, patent applications, trademarks, service marks, trade names, trademark registrations, service mark registrations, copyrights, licenses, inventions, trade secrets and similar rights ("**Intellectual Property Rights**") necessary for the conduct of the business of the Company as currently carried on and as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus. To the knowledge of the Company, no action or use by the Company necessary for the conduct of its business as currently carried on and as described in the Registration Statement and the Prospectus will involve or give rise to any infringement of, or license or similar fees for, any Intellectual Property Rights of others. The Company has not received any notice alleging any such infringement, fee or conflict with asserted Intellectual Property Rights of others. Except as would not reasonably be expected to result, individually or in the aggregate, in a Material Adverse Change (A) to the knowledge of the Company, there is no infringement, misappropriation or violation by third parties of any of the Intellectual Property Rights owned by the Company; (B) there is no pending or, to the knowledge of the Company, threatened action, suit, proceeding or claim by others challenging the rights of the Company in or to any such Intellectual Property Rights, and the Company is unaware of any facts which would form a reasonable basis for any such claim, that would, individually or in the aggregate, together with any other claims in this Section 2.34, reasonably be expected to result in a Material Adverse Change; (C) the Intellectual Property Rights owned by the Company and, to the knowledge of the Company, the Intellectual Property Rights licensed to the Company have not been adjudged by a court of competent jurisdiction invalid or unenforceable, in whole or in part, and there is no pending or, to the Company's knowledge, threatened action, suit, proceeding or claim by others challenging the validity or scope of any such Intellectual Property Rights, and the Company is unaware of any facts which would form a reasonable basis for any such claim that would, individually or in the aggregate, together with any other claims in this Section 2.34, reasonably be expected to result in a Material Adverse Change; (D) there is no pending or, to the Company's knowledge, threatened action, suit, proceeding or claim by others that the Company infringes, misappropriates or otherwise violates any Intellectual Property Rights or other proprietary rights of others, the Company has not received any written notice of such claim and the Company is unaware of any other facts which would form a reasonable basis for any such claim that would, individually or in the aggregate, together with any other claims in this Section 2.34, reasonably be expected to result in a Material Adverse Change; and (E) to the Company's knowledge, no employee of the Company is in or has ever been in violation in any material respect of any term of any employment contract, patent disclosure agreement, invention assignment agreement, non-competition agreement, non-solicitation agreement, nondisclosure agreement or any restrictive covenant to or with a former employer where the basis of such violation relates to such employee's employment with the Company, or actions

undertaken by the employee while employed with the Company and could reasonably be expected to result, individually or in the aggregate, in a Material Adverse Change. To the Company's knowledge, all material technical information developed by and belonging to the Company which has not been patented has been kept confidential. The Company is not a party to or bound by any options, licenses or agreements with respect to the Intellectual Property Rights of any other person or entity that are required to be set forth in the Registration Statement, the Pricing Disclosure Package and the Prospectus and are not described therein. The Registration Statement, the Pricing Disclosure Package and the Prospectus contain in all material respects the same description of the matters set forth in the preceding sentence. None of the technology employed by the Company has been obtained or is being used by the Company in violation of any contractual obligation binding on the Company or, to the Company's knowledge, any of its officers, directors or employees, or otherwise in violation of the rights of any persons.

2.34 Taxes. Except as would not reasonably be expected to have, individually or in the aggregate, a material adverse effect, the Company has filed all returns (as hereinafter defined) required to be filed with taxing authorities prior to the date hereof or has duly obtained extensions of time for the filing thereof. The Company has paid all taxes (as hereinafter defined) shown as due on such returns that were filed and has paid all taxes imposed on or assessed against the Company.

The provisions for taxes payable, if any, shown on the financial statements filed with or as part of the Registration Statement are sufficient for all accrued and unpaid taxes, whether or not disputed, and for all periods to and including the dates of such consolidated financial statements. Except as disclosed in writing to the Underwriters, (i) no issues have been raised (and are currently pending) by any taxing authority in connection with any of the returns or taxes asserted as due from the Company, and (ii) no waivers of statutes of limitation with respect to the returns or collection of taxes have been given by or requested from the Company. The term "taxes" means all federal, state, local, foreign and other net income, gross income, gross receipts, sales, use, ad valorem, transfer, franchise, profits, license, lease, service, service use, withholding, payroll, employment, excise, severance, stamp, occupation, premium, property, windfall profits, customs, duties or other taxes, fees, assessments or charges of any kind whatever, together with any interest and any penalties, additions to tax or additional amounts with respect thereto. The term "returns" means all returns, declarations, reports, statements and other documents required to be filed in respect to taxes.

2.35 ERISA Compliance. The Company and any "employee benefit plan" (as defined under the Employee Retirement Income Security Act of 1974, as amended, and the regulations and published interpretations thereunder (collectively, "ERISA")) established or maintained by the Company or its "ERISA Affiliates" (as defined below) are in compliance in all material respects with ERISA. "ERISA Affiliate" means, with respect to the Company, any member of any group of organizations described in Sections 414(b),(c),(m) or (o) of the Internal Revenue Code of 1986, as amended, and the regulations and published interpretations thereunder (the "Code") of which the Company is a member. No "reportable event" (as defined under ERISA) has occurred or is reasonably expected to occur with respect to any "employee benefit plan" established or maintained by the Company or any of its ERISA Affiliates. No "employee benefit plan" established or maintained by the Company or any of its ERISA Affiliates, if such "employee benefit plan" were terminated, would have any "amount of unfunded benefit liabilities" (as defined under ERISA). Neither the Company nor any of its ERISA Affiliates has incurred or reasonably expects to incur any material liability under (i) Title IV of ERISA with respect to termination of, or withdrawal from, any "employee benefit plan" or (ii) Sections 412, 4971, 4975 or 4980B of the Code. Each "employee benefit plan" established or maintained by the Company or any of its ERISA Affiliates that is intended to be qualified under Section 401(a) of the Code is so qualified and, to the knowledge of the Company, nothing has occurred, whether by action or failure to act, which would cause the loss of such qualification.

2.36 Compliance with Laws. The Company: (A) is and at all times has been in compliance with all statutes, rules, or regulations applicable to the ownership, testing, development, manufacture, packaging, processing, use, distribution, marketing, labeling, promotion, sale, offer for sale, storage, import, export or

disposal of any product manufactured or distributed by the Company (“**Applicable Laws**”), except as could not, individually or in the aggregate, reasonably be expected to have a Material Adverse Change; (B) has not received any warning letter, untitled letter or other correspondence or notice from any other governmental authority alleging or asserting noncompliance with any Applicable Laws or any licenses, certificates, approvals, clearances, authorizations, permits and supplements or amendments thereto required by any such Applicable Laws (“**Authorizations**”);(C) possesses all material Authorizations and such Authorizations are valid and in full force and effect and are not in material violation of any term of any such Authorizations; (D) has not received notice of any claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from any governmental authority or third party alleging that any product operation or activity is in violation of any Applicable Laws or Authorizations and has no knowledge that any such governmental authority or third party is considering any such claim, litigation, arbitration, action, suit, investigation or proceeding; (E) has not received notice that any governmental authority has taken, is taking or intends to take action to limit, suspend, modify or revoke any Authorizations and has no knowledge that any such governmental authority is considering such action; (F) has filed, obtained, maintained or submitted all material reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any Applicable Laws or Authorizations and that all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were complete and correct on the date filed (or were corrected or supplemented by a subsequent submission); and (G) has not, either voluntarily or involuntarily, initiated, conducted, or issued or caused to be initiated, conducted or issued, any recall, market withdrawal or replacement, safety alert, post-sale warning, “dear doctor” letter, or other notice or action relating to the alleged lack of safety or efficacy of any product or any alleged product defect or violation and, to the Company’s knowledge, no third party has initiated, conducted or intends to initiate any such notice or action.

2.37 Real Property. Except as set forth in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the Company has good and marketable title in fee simple to, or has valid rights to lease or otherwise use, all items of real or personal property which are material to the business of the Company, in each case free and clear of all liens, encumbrances, security interests, claims and defects that do not, singly or in the aggregate, materially affect the value of such property and do not interfere with the use made and proposed to be made of such property by the Company; and all of the leases and subleases material to the business of the Company and under which the Company holds properties described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, are in full force and effect, and the Company has not received any notice of any material claim of any sort that has been asserted by anyone adverse to the rights of the Company under any of the leases or subleases mentioned above, or affecting or questioning the rights of the Company to the continued possession of the leased or subleased premises under any such lease or sublease.

2.38 Contracts Affecting Capital. There are no transactions, arrangements or other relationships between and/or among the Company, any of its affiliates (as such term is defined in Rule 405 of the Securities Act Regulations) and any unconsolidated entity, including, but not limited to, any structured finance, special purpose or limited purpose entity that could reasonably be expected to materially affect the Company’s liquidity or the availability of or requirements for their capital resources required to be described or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus which have not been described or incorporated by reference as required.

2.39 Loans to Directors or Officers. There are no outstanding loans, advances (except normal advances for business expenses in the ordinary course of business) or guarantees or indebtedness by the Company to or for the benefit of any of the officers or directors of the Company or any of their respective family members, except as disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus. All transactions by the Company with its officers or directors or control persons of the Company have been duly approved by the board of directors of the Company or the audit committee thereof.

2.40 Smaller Reporting Company. As of the time of filing of the Registration Statement, the Company was a “smaller reporting company,” as defined in Rule 12b-2 of the Exchange Act Regulations.

2.41 Industry Data. The statistical and market-related data included in each of the Registration Statement, the Pricing Disclosure Package and the Prospectus are based on or derived from sources that the Company reasonably and in good faith believes are reliable and accurate or represent the Company’s good faith estimates that are made on the basis of data derived from such sources.

2.42 Emerging Growth Company. The Company is an “emerging growth company,” as defined in Section 2(a) of the Securities Act (an “**Emerging Growth Company**”). “Testing-the-Waters Communication” means any oral or written communication with potential investors undertaken in reliance on Section 5(d) of the Securities Act.

2.43 Testing-the-Waters Communications. The Company has not (i) alone engaged in any Testing-the-Waters Communications, other than Testing-the-Waters Communications with the written consent of the Representative and with entities that are qualified institutional buyers within the meaning of Rule 144A under the Securities Act or institutions that are accredited investors within the meaning of Rule 501 under the Securities Act and (ii) authorized anyone other than the Representative to engage in Testing-the-Waters Communications. The Company has not distributed any Written Testing-the-Waters Communications other than those listed on Schedule 2-C hereto. “**Written Testing-the-Waters Communication**” means any Testing-the-Waters Communication that is a written communication within the meaning of Rule 405 under the Securities Act.

2.44 Margin Securities. The Company owns no “margin securities” as that term is defined in Regulation U of the Board of Governors of the Federal Reserve System (the “**Federal Reserve Board**”), and none of the proceeds of Offering will be used, directly or indirectly, for the purpose of purchasing or carrying any margin security, for the purpose of reducing or retiring any indebtedness which was originally incurred to purchase or carry any margin security or for any other purpose which might cause any of the shares of Common Stock to be considered a “purpose credit” within the meanings of Regulation T, U or X of the Federal Reserve Board.

2.45 The Exchange Rules. The Company is and, after giving effect to the Offering will be, in compliance in all material respects with all applicable corporate governance requirements set forth in the rules of the Exchange.

3. Covenants of the Company. The Company covenants and agrees as follows:

3.1 Amendments to Registration Statement. The Company shall deliver to the Representative, prior to filing, any amendment or supplement to the Registration Statement or Prospectus proposed to be filed after the Effective Date and not file any such amendment or supplement to which the Representative shall reasonably object in writing.

3.2 Federal Securities Laws.

3.2.1. Compliance. The Company, subject to Section 3.2.2, shall comply with the requirements of Rule 430A of the Securities Act Regulations, and will during the period required to permit the completion of the distribution of the Public Securities as contemplated in this Agreement and in the Registration Statement, the Pricing Disclosure Package and the Prospectus, notify the Representative

promptly, and confirm the notice in writing, (i) when any post-effective amendment to the Registration Statement shall become effective or any amendment or supplement to the Prospectus shall have been filed; (ii) of the receipt of any comments from the Commission; (iii) of any request by the Commission for any amendment to the Registration Statement or any amendment or supplement to the Prospectus or for additional information; (iv) of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement or any post-effective amendment or of any order preventing or suspending the use of any Preliminary Prospectus or the Prospectus, or of the suspension of the qualification of the Public Securities for offering or sale in any jurisdiction, or of the initiation or threatening of any proceedings for any of such purposes or of any examination pursuant to Section 8(d) or 8(e) of the Securities Act concerning the Registration Statement and (v) if the Company becomes the subject of a proceeding under Section 8A of the Securities Act in connection with the Offering of the Public Securities. The Company shall effect all filings required under Rule 424(b) of the Securities Act Regulations, in the manner and within the time period required by Rule 424(b) (without reliance on Rule 424(b)(8)), and shall take such steps as it deems necessary to ascertain promptly whether the form of prospectus transmitted for filing under Rule 424(b) was received for filing by the Commission and, in the event that it was not, it will promptly file such prospectus. The Company shall use its commercially reasonable efforts to prevent the issuance of any stop order, prevention or suspension and, if any such order is issued, to obtain the lifting thereof at the earliest possible moment.

3.2.2. Continued Compliance. The Company shall comply with the Securities Act, the Securities Act Regulations, the Exchange Act and the Exchange Act Regulations so as to permit the completion of the distribution of the Public Securities as contemplated in this Agreement and in the Registration Statement, the Pricing Disclosure Package and the Prospectus. If at any time when a prospectus relating to the Public Securities is (or, but for the exception afforded by Rule 172 of the Securities Act Regulations (“**Rule 172**”), would be) required by the Securities Act to be delivered in connection with sales of the Public Securities, any event shall occur or condition shall exist as a result of which it is necessary, in the opinion of counsel for the Underwriters or for the Company, to (i) amend the Registration Statement in order that the Registration Statement will not include an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading; (ii) amend or supplement the Pricing Disclosure Package or the Prospectus in order that the Pricing Disclosure Package or the Prospectus, as the case may be, will not include any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein not misleading in the light of the circumstances existing at the time it is delivered to a purchaser or (iii) amend the Registration Statement or amend or supplement the Pricing Disclosure Package or the Prospectus, as the case may be, in order to comply with the requirements of the Securities Act or the Securities Act Regulations, the Company will promptly (A) give the Representative notice of such event; (B) prepare any amendment or supplement as may be necessary to correct such statement or omission or to make the Registration Statement, the Pricing Disclosure Package or the Prospectus comply with such requirements and, a reasonable amount of time prior to any proposed filing or use, furnish the Representative with copies of any such amendment or supplement and (C) file with the Commission any such amendment or supplement; provided that the Company shall not file or use any such amendment or supplement to which the Representative or counsel for the Underwriters shall reasonably object. The Company will furnish to the Underwriters such number of copies of such amendment or supplement as the Underwriters may reasonably request. The Company has given the Representative notice of any filings made pursuant to the Exchange Act or the Exchange Act Regulations within 48 hours prior to the Applicable Time. The Company shall give the Representative notice of its intention to make any such filing from the Applicable Time until the later of the Closing Date and the exercise in full or expiration of the Over-allotment Option specified in Section 1.2 and will furnish the Representative with copies of the related document(s) a reasonable amount of time prior to such proposed filing, as the case may be, and will not file or use any such document to which the Representative or counsel for the Underwriters shall reasonably object.

3.2.3. Exchange Act Registration. For a period of three (3) years after the date of this Agreement, the Company shall use its best efforts to maintain the registration of the shares of Common Stock under the Exchange Act. The Company shall not deregister the shares of Common Stock under the Exchange Act during this period without the prior written consent of the Representative.

3.2.4. Free Writing Prospectuses. The Company agrees that, unless it obtains the prior written consent of the Representative, it shall not make any offer relating to the Public Securities that would constitute an Issuer Free Writing Prospectus or that would otherwise constitute a “free writing prospectus,” or a portion thereof, required to be filed by the Company with the Commission or retained by the Company under Rule 433; provided that the Representative shall be deemed to have consented to each Issuer General Use Free Writing Prospectus hereto and any “road show that is a written communication” within the meaning of Rule 433(d)(8)(i) that has been reviewed by the Representative. The Company represents that it has treated or agrees that it will treat each such free writing prospectus consented to, or deemed consented to, by the Underwriters as an “issuer free writing prospectus,” as defined in Rule 433, and that it has complied and will comply with the applicable requirements of Rule 433 with respect thereto, including timely filing with the Commission where required, legending and record keeping. If at any time following issuance of an Issuer Free Writing Prospectus there occurred or occurs an event or development as a result of which such Issuer Free Writing Prospectus conflicted or would conflict with the information contained in the Registration Statement or included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances existing at that subsequent time, not misleading, the Company will promptly notify the Underwriters and will promptly amend or supplement, at its own expense, such Issuer Free Writing Prospectus to eliminate or correct such conflict, untrue statement or omission.

3.2.5. Testing-the-Waters Communications. If at any time following the distribution of any Written Testing-the-Waters Communication there occurred or occurs an event or development as a result of which such Written Testing-the-Waters Communication included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances existing at that subsequent time, not misleading, the Company shall promptly notify the Representative and shall promptly amend or supplement, at its own expense, such Written Testing-the-Waters Communication to eliminate or correct such untrue statement or omission.

3.3 Delivery to the Underwriters of Registration Statements. The Company has delivered or made available or shall deliver or make available to the Representative and counsel for the Representative, without charge, signed copies of the Registration Statement as originally filed and each amendment thereto (including exhibits filed therewith) and signed copies of all consents and certificates of experts, and will also deliver to the Underwriters, without charge, a conformed copy of the Registration Statement as originally filed and each amendment thereto (without exhibits) for each of the Underwriters. The copies of the Registration Statement and each amendment thereto furnished to the Underwriters will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

3.4 Delivery to the Underwriters of Prospectuses. The Company has delivered or made available or will deliver or make available to each Underwriter, without charge, as many copies of each Preliminary Prospectus as such Underwriter reasonably requested, and the Company hereby consents to the use of such copies for purposes permitted by the Securities Act. The Company will furnish to each Underwriter, without charge, during the period when a prospectus relating to the Public Securities is (or, but for the exception afforded by Rule 172, would be) required to be delivered under the Securities Act, such number of copies of the Prospectus (as amended or supplemented) as such Underwriter may reasonably request. The Prospectus and any amendments or supplements thereto furnished to the

Underwriters will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

3.5 Effectiveness and Events Requiring Notice to the Representative. The Company shall notify the Representative promptly and confirm the notice in writing: (i) of the effectiveness of the Registration Statement and any amendment thereto; (ii) of the issuance by the Commission of any stop order or of the initiation, or the threatening, of any proceeding for that purpose; (iii) of the issuance by any state securities commission of any proceedings for the suspension of the qualification of the Public Securities for offering or sale in any jurisdiction or of the initiation, or the threatening, of any proceeding for that purpose; (iv) of the mailing and delivery to the Commission for filing of any amendment or supplement to the Registration Statement or Prospectus; (v) of the receipt of any comments or request for any additional information from the Commission; and (vi) of the happening of any event during the Prospectus Delivery Period (defined below) that, in the judgment of the Company, makes any statement of a material fact made in the Registration Statement, the Pricing Disclosure Package or the Prospectus untrue or that requires the making of any changes in (a) the Registration Statement in order to make the statements therein not misleading, or (b) in the Pricing Disclosure Package or the Prospectus in order to make the statements therein, in light of the circumstances under which they were made, not misleading. If the Commission or any state securities commission shall enter a stop order or suspend such qualification at any time, the Company shall make every reasonable effort to obtain promptly the lifting of such order. As used herein, the term "Prospectus Delivery Period" means such period of time after the first date of the public offering of the Public Securities is required by law to be delivered (or required to be delivered but for Rule 172 under the Securities Act) in connection with sales of the Public Securities by any underwriter or dealer. If during the Prospectus Delivery Period (i) any event or development shall occur or condition statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances existing when the Prospectus is delivered to a purchaser, not misleading or (ii) it is necessary to amend or supplement the Prospectus to comply with applicable law, the Company will promptly notify the Underwriters thereof and forthwith prepare and file with the Commission and furnish to the Underwriters and to such dealers as the Representative may designate such amendments or supplements to the Prospectus as may be necessary so that the statements in the Prospectus as so amended or supplemented will not, in the light of the circumstances existing when the Prospectus is delivered to a purchaser, be misleading or so that the Prospectus will comply with applicable law.

3.6 Review of Financial Statements. For a period of three (3) years after the date of this Agreement, the Company, at its expense, shall cause its regularly engaged independent registered public accounting firm to review (but not audit) the Company's financial statements for each of the three fiscal quarters immediately preceding the announcement of any quarterly financial information.

3.7 Listing. The Company shall use its best efforts to maintain the listing of the shares of Common Stock (including the Public Securities) on the Exchange for at least three years from the date of this Agreement.

3.8 Financial Public Relations Firm. As of the Effective Date or as soon thereafter as practical, the Company shall have retained a financial public relations firm reasonably acceptable to the Representative and the Company, which firm shall be experienced in assisting issuers in public offerings of securities and in their relations with their security holders, and shall retain such firm or another firm reasonably acceptable to the Representative for a period of not less than two (2) years after the Effective Date.

3.9 Reports to the Representative.

3.9.1. Periodic Reports, etc. For a period of three (3) years after the date of this Agreement, the Company shall furnish or make available to the Representative copies of such financial



statements and other periodic and special reports as the Company from time to time furnishes generally to holders of any class of its securities and also promptly furnish to the Representative: (i) a copy of each periodic report the Company shall be required to file with the Commission under the Exchange Act and the Exchange Act Regulations; (ii) a copy of every press release and every news item and article with respect to the Company or its affairs which was released by the Company; (iii) a copy of each Form 8-K prepared and filed by the Company; (iv) five copies of each registration statement filed by the Company under the Securities Act; and (v) such additional documents and information with respect to the Company and the affairs of any future subsidiaries of the Company as the Representative may from time to time reasonably request; provided the Representative shall sign, if requested by the Company, a Regulation FD compliant confidentiality agreement which is reasonably acceptable to the Representative and Representative Counsel in connection with the Representative's receipt of such information. Documents filed with the Commission pursuant to its EDGAR system shall be deemed to have been delivered to the Representative pursuant to this Section 3.9.1.

3.9.2. Transfer Agent; Transfer Sheets. For a period of three (3) years after the date of this Agreement, the Company shall retain a transfer agent and registrar acceptable to the Representative (the "**Transfer Agent**") and shall furnish to the Representative at the Company's sole cost and expense such transfer sheets of the Company's securities as the Representative may reasonably request, including the daily and monthly consolidated transfer sheets of the Transfer Agent and DTC. Vstock Transfer, LLC is acceptable to the Representative to act as Transfer Agent for the shares of Common Stock.

3.9.3. Trading Reports. During such time as the Public Securities are listed on the Exchange, the Company shall provide to the Representative, at the Company's expense, such reports published by Exchange relating to price trading of the Public Securities, as the Representative shall reasonably request.

### 3.10 Payment of Expenses

3.10.1. General Expenses Related to the Offering. The Company hereby agrees to pay on each of the Closing Date and the Option Closing Date, if any, to the extent not paid at the Closing Date, all expenses incident to the performance of the obligations of the Company under this Agreement, including, but not limited to: (a) all filing fees and communication expenses relating to the registration of the shares of Common Stock to be sold in the Offering (including the Option Securities) with the Commission; (b) all Public Filing System filing fees associated with the review of the Offering by FINRA; (c) all fees and expenses relating to the listing of such Public Securities on the Exchange and such other stock exchanges as the Company and the Representative together determine, including any fees charged by The Depository Trust Company (DTC) for new securities; (d) all fees, expenses and disbursements relating to background checks of the Company's officers and directors; (e) all fees, expenses and disbursements relating to the registration or qualification of the Public Securities under the "blue sky" securities laws of such states and other jurisdictions as the Representative may reasonably designate; (f) all fees, expenses and disbursements relating to the registration, qualification or exemption of the Public Securities under the securities laws of such foreign jurisdictions as the Representative may reasonably designate; (g) the costs of all mailing and printing of the underwriting documents (including, without limitation, this Agreement, any Blue Sky Surveys and, if appropriate, any Agreement Among Underwriters, Selected Dealers' Agreement, Underwriters' Questionnaire and Power of Attorney), Registration Statements, Prospectuses and all amendments, supplements and exhibits thereto and as many preliminary and final Prospectuses as the Representative may reasonably deem necessary; (h) the costs of preparing, printing and delivering certificates representing the Public Securities; (i) fees and expenses of the transfer agent for the shares of Common Stock; (j) stock transfer and/or stamp taxes, if any, payable upon the transfer of securities from the Company to the Underwriters; (k) the costs associated with bound volumes of the public offering materials as well as commemorative mementos and lucite tombstones, each of which the Company or its designee shall provide within a reasonable time after the Closing Date in such

quantities as the Representative may reasonably request; (l) the fees and expenses of the Company's accountants; (m) the fees and expenses of the Company's legal counsel and other agents and representatives; (n) all reasonable and documented out-of-pocket costs and expenses incident to the performance of the obligations of the Underwriters under this Agreement (including, without limitation, the fees and expenses of the Underwriter's outside attorneys, such fees and expenses not to exceed \$100,000); provided, however, that the expenses to be reimbursed by the Company to the Underwriters under this Section 3.10.1 shall not exceed \$125,000 in the aggregate. The Representative may deduct from the net proceeds of the Offering payable to the Company on the Closing Date, or the Option Closing Date, if any, the expenses set forth herein to be paid by the Company to the Underwriters.

3.10.2. [Reserved]

3.11 Application of Net Proceeds. The Company shall apply the net proceeds from the Offering received by it in a manner consistent with the application thereof described under the caption "Use of Proceeds" in the Registration Statement, the Pricing Disclosure Package and the Prospectus.

3.12 Delivery of Earnings Statements to Security Holders. The Company shall make generally available to its security holders as soon as practicable, but not later than the first day of the fifteenth (15<sup>th</sup>) full calendar month following the date of this Agreement, an earnings statement (which need not be certified by independent registered public accounting firm unless required by the Securities Act or the Securities Act Regulations, but which shall satisfy the provisions of Rule 158(a) under Section 11(a) of the Securities Act) covering a period of at least twelve (12) consecutive months beginning after the date of this Agreement. If such earnings statement is available on EDGAR it shall be deemed to have been delivered to the Representative pursuant to this Section 3.12.

3.13 Stabilization. Neither the Company nor, to its knowledge, any of its employees or directors has taken or shall take, directly or indirectly, any action designed to or that has constituted or that might reasonably be expected to cause or result in, under Regulation M of the Exchange Act, or otherwise, stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Public Securities.

3.14 Internal Controls. The Company shall maintain a system of internal accounting controls sufficient to provide reasonable assurances that: (i) transactions are executed in accordance with management's general or specific authorization; (ii) transactions are recorded as necessary in order to permit preparation of financial statements in accordance with GAAP and to maintain accountability for assets; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with existing assets at reasonable intervals and appropriate action is taken with respect to any differences.

3.15 Accountants. As of the date of this Agreement, the Company shall retain an independent registered public accounting firm reasonably acceptable to the Representative, and the Company shall continue to retain a nationally recognized independent registered public accounting firm for a period of at least three (3) years after the date of this Agreement. The Representative acknowledges that the Auditor is acceptable to the Representative.

3.16 FINRA. The Company shall advise the Representative (who shall make an appropriate filing with FINRA) if it is or becomes aware that (i) any officer or director of the Company, (ii) any beneficial owner of 5% or more of any class of the Company's securities or (iii) any beneficial owner of the Company's unregistered equity securities which were acquired during the 180 days immediately preceding the filing of the Registration Statement is or becomes an affiliate or associated person of a FINRA member participating in the Offering (as determined in accordance with the rules and regulations of FINRA).

3.17 No Fiduciary Duties. The Company acknowledges and agrees that the Underwriters' responsibility to the Company is solely contractual in nature and that none of the Underwriters or their affiliates or any selling agent shall be deemed to be acting in a fiduciary capacity, or otherwise owes any fiduciary duty to the Company or any of its affiliates in connection with the Offering and the other transactions contemplated by this Agreement.

3.18 Company Lock-Up Agreements.

3.18.1. Restriction on Sales of Capital Stock. The Company, on behalf of itself and any successor entity, agrees that, without the prior written consent of the Representative, it will not, for a period of 90 days after the date of this Agreement (the "**Lock-Up Period**"), (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of capital stock of the Company or any securities convertible into or exercisable or exchangeable for shares of capital stock of the Company; (ii) file or caused to be filed any registration statement with the Commission relating to the offering of any shares of capital stock of the Company or any securities convertible into or exercisable or exchangeable for shares of capital stock of the Company; (iii) complete any offering of debt securities of the Company, other than entering into a line of credit with a traditional bank or (iv) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of capital stock of the Company, whether any such transaction described in clause (i), (ii), (iii) or (iv) above is to be settled by delivery of shares of capital stock of the Company or such other securities, in cash or otherwise.

The restrictions contained in this Section 3.18.1 shall not apply to (i) the shares of Common Stock to be sold hereunder; (ii) the issuance by the Company of shares of Common Stock upon the exercise of a stock option or warrant or the conversion of a security outstanding on the date hereof, which is disclosed in the Registration Statement, Pricing Disclosure Package and Prospectus, provided that such options, warrants, and securities have not been amended since the date of this Agreement to increase the number of such securities or to decrease the exercise price, exchange price or conversion price of such securities or to extend the term of such securities; (iii) the issuance by the Company of stock options or shares of capital stock of the Company under any equity compensation plan of the Company; (iv) the filing of any registration statement on Form S-8 or a successor form thereto relating to the shares of Common Stock granted pursuant to or reserved for issuance under the equity compensation plans of the Company referred to in clause (iii); (v) the issuance up to 10% of the Company's outstanding shares of Common Stock in the aggregate in connection with one or more acquisitions or other similar strategic transactions or Collaboration Agreements (as defined below); or (vi) the filing of a new shelf registration statement on Form S-3, provided that (a) in each of clauses (ii) and (iii) above, the underlying shares shall be restricted from sale during the entire Lock-Up Period and (b) in case of clause (v) above, the shares of Common Stock are issued as "restricted securities" (as defined in Rule 144) and carry no registration rights that require or permit the filing of any registration statement in connection therewith during the Lock-Up Period, and provided further that any such issuance shall only be to a Person (or to equityholders of a Person) which is, itself or through its subsidiaries, an operating company or an owner of an asset in a business synergistic with the business of the Company and shall provide to the Company additional benefits in addition to the investment of funds, but shall not include a transaction in which the Company is issuing securities primarily for the purpose of raising capital or to an entity whose primary business is investing in securities. For the purposes of this Agreement, a "Collaboration Agreement" shall mean a licensing or collaboration agreement with one or more third parties involving the Company.

3.18.2. Restriction on Continuous Offerings. Notwithstanding the restrictions contained in Section 3.18.1, the Company, on behalf of itself and any successor entity, agrees that, without the prior written consent of the Representative, such consent not to be unreasonably withheld, it will not, for a period of 12 months after the date of this Agreement, directly or indirectly in any "at-the-market" or continuous equity transaction, offer to sell, sell, contract to

sell, grant any option to sell or otherwise dispose of shares of capital stock of the Company or any securities convertible into or exercisable or exchangeable for shares of capital stock of the Company.

3.19 [Reserved]

3.20 Blue Sky Qualifications. The Company shall use its commercially reasonable efforts, in cooperation with the Underwriters, if necessary, to qualify the Public Securities for offering and sale under the applicable securities laws of such states and other jurisdictions (domestic or foreign) as the Representative may designate and to maintain such qualifications in effect so long as required to complete the distribution of the Public Securities; provided, however, that the Company shall not be obligated to file any general consent to service of process or to qualify as a foreign corporation or as a dealer in securities in any jurisdiction in which it is not so qualified or to subject itself to taxation in respect of doing business in any jurisdiction in which it is not otherwise so subject.

3.21 Reporting Requirements. The Company, during the period when a prospectus relating to the Public Securities is (or, but for the exception afforded by Rule 172, would be) required to be delivered under the Securities Act, will file all documents required to be filed with the Commission pursuant to the Exchange Act within the time periods required by the Exchange Act and Exchange Act Regulations.

3.22 Emerging Growth Company Status. The Company shall promptly notify the Representative if the Company ceases to be an Emerging Growth Company at any time prior to the later of (i) completion of the distribution of the Public Securities within the meaning of the Securities Act and (ii) fifteen (15) days following the completion of the Lock-Up Period.

4. Conditions of Underwriters' Obligations. The obligations of the Underwriters to purchase and pay for the Public Securities, as provided herein, shall be subject to (i) the continuing accuracy of the representations and warranties of the Company as of the date hereof and as of each of the Closing Date and the Option Closing Date, if any; (ii) the accuracy of the statements of officers of the Company made pursuant to the provisions hereof; (iii) the performance by the Company of its obligations hereunder; and (iv) the following conditions:

4.1 Regulatory Matters.

4.1.1. Effectiveness of Registration Statement; Rule 430A Information. The Registration Statement has become effective not later than 5:00 p.m., Eastern time, on the date of this Agreement or such later date and time as shall be consented to in writing by you, and, at each of the Closing Date and any Option Closing Date, no stop order suspending the effectiveness of the Registration Statement or any post-effective amendment thereto has been issued under the Securities Act, no order preventing or suspending the use of any Preliminary Prospectus or the Prospectus has been issued and no proceedings for any of those purposes have been instituted or are pending or, to the Company's knowledge, contemplated by the Commission. The Company has complied with each request (if any) from the Commission for additional information. The Prospectus containing the Rule 430A Information shall have been filed with the Commission in the manner and within the time frame required by Rule 424(b) (without reliance on Rule 424(b)(8)) or a post-effective amendment providing such information shall have been filed with, and declared effective by, the Commission in accordance with the requirements of Rule 430A.

4.1.2. FINRA Clearance. On or before the date of this Agreement, the Representative shall have received clearance from FINRA as to the amount of compensation allowable or payable to the Underwriters as described in the Registration Statement.

4.1.3. Exchange Stock Market Clearance. The Company shall have submitted the Listing of Additional Shares Notification Form to the Nasdaq with respect to the Offering of the Public Securities

and the Exchange shall not have raised any objection to the submission prior the Closing Date or each Option Closing Date, as applicable.

#### 4.2 Company Counsel Matters.

4.2.1. Closing Date Opinion of Counsel. On the Closing Date, the Representative shall have received the favorable opinion of Goodwin Procter LLP, counsel to the Company, dated the Closing Date and addressed to the Representative, substantially in form and substance reasonably satisfactory to the Representative.

4.2.2. Option Closing Date Opinions of Counsel. On the Option Closing Date, if any, the Representative shall have received the favorable opinion of the counsel listed in Section 4.2, dated the Option Closing Date, addressed to the Representative and in form and substance reasonably satisfactory to the Representative, confirming as of the Option Closing Date, the statements made by such counsels in their respective opinions delivered on the Closing Date.

4.2.3. Reliance. In rendering such opinions, such counsel may rely: (i) as to matters involving the application of laws other than the laws of the United States and jurisdictions in which they are admitted, to the extent such counsel deems proper and to the extent specified in such opinion, if at all, upon an opinion or opinions (in form and substance reasonably satisfactory to the Representative) of other counsel reasonably acceptable to the Representative, familiar with the applicable laws; and (ii) as to matters of fact, to the extent they deem proper, on certificates or other written statements of officers of the Company and officers of departments of various jurisdictions having custody of documents respecting the corporate existence or good standing of the Company, provided that copies of any such statements or certificates shall be delivered to Representative Counsel if requested. The opinion of Goodwin Procter LLP and any opinion relied upon by Goodwin Procter LLP shall include a statement to the effect that it may be relied upon by Representative Counsel in its opinion delivered to the Underwriters.

#### 4.3 Comfort Letters.

4.3.1. Cold Comfort Letter. At the time this Agreement is executed you shall have received a cold comfort letter containing statements and information of the type customarily included in accountants' comfort letters with respect to the financial statements and certain financial information contained in the Registration Statement, the Pricing Disclosure Package and the Prospectus, addressed to the Representative and in form and substance satisfactory in all respects to you and to the Auditor, dated as of the date of this Agreement.

4.3.2. Bring-down Comfort Letter. At each of the Closing Date and the Option Closing Date, if any, the Representative shall have received from the Auditor a letter, dated as of the Closing Date or the Option Closing Date, as applicable, to the effect that the Auditor reaffirms the statements made in the letter furnished pursuant to Section 4.3.1, except that the specified date referred to shall be a date not more than three (3) business days prior to the Closing Date or the Option Closing Date, as applicable.

#### 4.4 Officers' Certificates.

4.4.1. Officers' Certificate. The Company shall have furnished to the Representative a certificate, dated the Closing Date and any Option Closing Date (if such date is other than the Closing Date), of its Chief Executive Officer, its President and its Chief Financial Officer stating that (i) such officers have carefully examined the Registration Statement, the Pricing Disclosure Package, any Issuer Free Writing Prospectus and the Prospectus and, in their opinion, the Registration Statement and each amendment thereto, as of the Applicable Time and as of the Closing Date (or any Option Closing Date if such date is other than the Closing Date) did not include any untrue statement of a material fact and did not

omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading, and the Pricing Disclosure Package, as of the Applicable Time and as of the Closing Date (or any Option Closing Date if such date is other than the Closing Date), any Issuer Free Writing Prospectus as of its date and as of the Closing Date (or any Option Closing Date if such date is other than the Closing Date), the Prospectus and each amendment or supplement thereto, as of the respective date thereof and as of the Closing Date, did not include any untrue statement of a material fact and did not omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances in which they were made, not misleading, (ii) since the effective date of the Registration Statement, no event has occurred which should have been set forth in a supplement or amendment to the Registration Statement, the Pricing Disclosure Package or the Prospectus, (iii) to the their knowledge, as of the Closing Date (or any Option Closing Date if such date is other than the Closing Date), the representations and warranties of the Company in this Agreement are true and correct and the Company has complied with all agreements and satisfied all conditions on its part to be performed or satisfied hereunder at or prior to the Closing Date (or any Option Closing Date if such date is other than the Closing Date), and (iv) there has not been, subsequent to the date of the most recent audited financial statements included or incorporated by reference in the Pricing Disclosure Package, any material adverse change in the financial position or results of operations of the Company, or any change or development that, singularly or in the aggregate, would involve a material adverse change or a prospective material adverse change, in or affecting the condition (financial or otherwise), results of operations, business, assets or prospects of the Company, except as set forth in the Prospectus.

4.4.2. Secretary's Certificate. At each of the Closing Date and the Option Closing Date, if any, the Representative shall have received a certificate of the Company signed by the Secretary of the Company, dated the Closing Date or the Option Closing Date, as the case may be, respectively, certifying: (i) that each of the Charter and Bylaws is true and complete, has not been modified and is in full force and effect; (ii) that the resolutions of the Company's Board of Directors relating to the Offering are in full force and effect and have not been modified; and (iii) as to the incumbency of the officers of the Company. The documents referred to in such certificate shall be attached to such certificate.

4.5 No Material Changes. Prior to and on each of the Closing Date and each Option Closing Date, if any: (i) there shall have been no material adverse change or development involving a prospective material adverse change in the condition or prospects or the business activities, financial or otherwise, of the Company from the latest dates as of which such condition is set forth in the Registration Statement, the Pricing Disclosure Package and the Prospectus; (ii) no action, suit or proceeding, at law or in equity, shall have been pending or threatened against the Company or any Insider before or by any court or federal or state commission, board or other administrative agency wherein an unfavorable decision, ruling or finding may materially adversely affect the business, operations, prospects or financial condition or income of the Company, except as set forth in the Registration Statement, the Pricing Disclosure Package and the Prospectus; (iii) no stop order shall have been issued under the Securities Act and no proceedings therefor shall have been initiated or threatened by the Commission; and (iv) the Registration Statement, the Pricing Disclosure Package and the Prospectus and any amendments or supplements thereto shall contain all material statements which are required to be stated therein in accordance with the Securities Act and the Securities Act Regulations and shall conform in all material respects to the requirements of the Securities Act and the Securities Act Regulations, and neither the Registration Statement, the Pricing Disclosure Package nor the Prospectus nor any amendment or supplement thereto shall contain any untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein, in light of the circumstances under which they were made, not misleading.

#### 4.6 Delivery of Agreements.

4.6.1. Lock-Up Agreements. On or before the date of this Agreement, the Company shall have delivered to the Representative executed copies of the Lock-Up Agreements from each of the persons

listed in Schedule 3 hereto.

4.7 Additional Documents. At the Closing Date and at each Option Closing Date (if any) Representative Counsel shall have been furnished with such documents and opinions as they may require for the purpose of enabling Representative Counsel to deliver an opinion to the Underwriters, or in order to evidence the accuracy of any of the representations or warranties, or the fulfillment of any of the conditions, herein contained; and all proceedings taken by the Company in connection with the issuance and sale of the Public Securities as herein contemplated shall be satisfactory in form and substance to the Representative and Representative Counsel.

5. Indemnification.

5.1 Indemnification of the Underwriters.

5.1.1. General. Subject to the conditions set forth below, the Company agrees to indemnify and hold harmless each Underwriter, its affiliates and each of its and their respective directors, officers, members, employees, representatives, partners, shareholders, affiliates, counsel, and agents and each person, if any, who controls any such Underwriter within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act (collectively the **“Underwriter Indemnified Parties,”** and each an **“Underwriter Indemnified Party”**), against any and all loss, liability, claim, damage and expense whatsoever (including but not limited to any and all legal or other expenses reasonably incurred in investigating, preparing or defending against any litigation, commenced or threatened, or any claim whatsoever, whether arising out of any action between any of the Underwriter Indemnified Parties and the Company or between any of the Underwriter Indemnified Parties and any third party, or otherwise) to which they or any of them may become subject under the Securities Act, the Exchange Act or any other statute or at common law or otherwise or under the laws of foreign countries (a **“Claim”**), (i) arising out of or based upon any untrue statement or alleged untrue statement of a material fact contained in (A) the Registration Statement, the Pricing Disclosure Package, any Preliminary Prospectus, the Prospectus, or in any Issuer Free Writing Prospectus or in any Written Testing-the-Waters Communication or any document incorporated by reference therein (as from time to time each may be amended and supplemented); (B) any materials or information provided to investors by, or with the approval of, the Company in connection with the marketing of the Offering, including any “road show” or investor presentations made to investors by the Company (whether in person or electronically); or (C) any application or other document or written communication (in this Section 5, collectively called **“application”**) executed by the Company or based upon written information furnished by the Company in any jurisdiction in order to qualify the Public Securities under the securities laws thereof or filed with the Commission, any state securities commission or agency, the Exchange or any other national securities exchange; or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading, unless such statement or omission was made in reliance upon, and in conformity with, the Underwriters’ Information or (ii) otherwise arising in connection with the Offering. The Company also agrees that it will reimburse each Underwriter Indemnified Party for all fees and expenses (including but not limited to any and all legal or other expenses reasonably incurred in investigating, preparing or defending against any litigation, commenced or threatened, or any claim whatsoever, whether arising out of any action between any of the Underwriter Indemnified Parties and the Company or between any of the Underwriter Indemnified Parties and any third party, or otherwise) (collectively, the **“Expenses”**), and further agrees wherever and whenever possible to advance payment of Expenses as they are incurred by an Underwriter Indemnified Party in investigating, preparing, pursuing or defending any Claim.

5.1.2. Procedure. If any action is brought against an Underwriter Indemnified Party in respect of which indemnity may be sought against the Company pursuant to Section 5.1.1, such Underwriter Indemnified Party shall promptly notify the Company in writing of the institution of such action and the

Company shall assume the defense of such action, including the employment and fees of counsel (subject to the approval of such Underwriter Indemnified Party) and payment of actual expenses if an Underwriter Indemnified Party requests that the Company do so. Such Underwriter Indemnified Party shall have the right to employ its or their own counsel in any such case, but the fees and expenses of such counsel shall be at the expense of the Company, and shall be advanced by the Company. The Company shall not be liable for any settlement of any action effected without its consent (which shall not be unreasonably withheld). In addition, the Company shall not, without the prior written consent of the Underwriters, settle, compromise or consent to the entry of any judgment in or otherwise seek to terminate any pending or threatened action in respect of which advancement, reimbursement, indemnification or contribution may be sought hereunder (whether or not such Underwriter Indemnified Party is a party thereto) unless such settlement, compromise, consent or termination (i) includes an unconditional release of each Underwriter Indemnified Party, acceptable to such Underwriter Indemnified Party, from all liabilities, expenses and claims arising out of such action for which indemnification or contribution may be sought and (ii) does not include a statement as to or an admission of fault, culpability or a failure to act, by or on behalf of any Underwriter Indemnified Party.

5.2 Indemnification of the Company. Each Underwriter, severally and not jointly, agrees to indemnify and hold harmless the Company, its directors, its officers who signed the Registration Statement and persons who control the Company within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act against any and all loss, liability, claim, damage and expense described in the foregoing indemnity from the Company to the several Underwriters, as incurred, but only with respect to untrue statements or omissions, or alleged untrue statements or omissions made in the Registration Statement, any Preliminary Prospectus, the Pricing Disclosure Package or Prospectus or any amendment or supplement thereto or in any application, in reliance upon, and in strict conformity with, the Underwriters' Information. In case any action shall be brought against the Company or any other person so indemnified based on any Preliminary Prospectus, the Registration Statement, the Pricing Disclosure Package or Prospectus or any amendment or supplement thereto or any application, and in respect of which indemnity may be sought against any Underwriter, such Underwriter shall have the rights and duties given to the Company, and the Company and each other person so indemnified shall have the rights and duties given to the several Underwriters by the provisions of Section 5.1. The Company agrees promptly to notify the Representative of the commencement of any litigation or proceedings against the Company or any of its officers, directors or any person, if any, who controls the Company within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act, in connection with the issuance and sale of the Public Securities or in connection with the Registration Statement, the Pricing Disclosure Package, the Prospectus, or any Issuer Free Writing Prospectus or any Written Testing-the-Waters Communication.

5.3 Contribution.

5.3.1. Contribution Rights. If the indemnification provided for in this Section 5 shall for any reason be unavailable to or insufficient to hold harmless an indemnified party under Section 5.1 or 5.2 in respect of any loss, claim, damage or liability, or any action in respect thereof, referred to therein, then each indemnifying party shall, in lieu of indemnifying such indemnified party, contribute to the amount paid or payable by such indemnified party as a result of such loss, claim, damage or liability, or action in respect thereof, (i) in such proportion as shall be appropriate to reflect the relative benefits received by the Company, on the one hand, and the Underwriters, on the other, from the Offering of the Public Securities, or (ii) if the allocation provided by clause (i) above is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) above but also the relative fault of the Company, on the one hand, and the Underwriters, on the other, with respect to the statements or omissions that resulted in such loss, claim, damage or liability, or action in respect thereof, as well as any other relevant equitable considerations. The relative benefits received by the Company, on the one hand, and the Underwriters, on the other, with respect to such Offering shall be deemed to be in the same proportion as the total net proceeds from the Offering of the Public Securities purchased under this



Agreement (before deducting expenses) received by the Company, as set forth in the table on the cover page of the Prospectus, on the one hand, and the total underwriting discounts and commissions received by the Underwriters with respect to the shares of the Common Stock purchased under this Agreement, as set forth in the table on the cover page of the Prospectus, on the other hand. The relative fault shall be determined by reference to whether the untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company or the Underwriters, the intent of the parties and their relative knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and the Underwriters agree that it would not be just and equitable if contributions pursuant to this Section 5.3.1 were to be determined by pro rata allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation that does not take into account the equitable considerations referred to herein. The amount paid or payable by an indemnified party as a result of the loss, claim, damage or liability, or action in respect thereof, referred to above in this Section 5.3.1 shall be deemed to include, for purposes of this Section 5.3.1, any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim. Notwithstanding the provisions of this Section 5.3.1 in no event shall an Underwriter be required to contribute any amount in excess of the amount by which the total underwriting discounts and commissions received by such Underwriter with respect to the Offering of the Public Securities exceeds the amount of any damages that such Underwriter has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation.

5.3.2. Contribution Procedure. Within fifteen (15) days after receipt by any party to this Agreement (or its representative) of notice of the commencement of any action, suit or proceeding, such party will, if a claim for contribution in respect thereof is to be made against another party (“**contributing party**”), notify the contributing party of the commencement thereof, but the failure to so notify the contributing party will not relieve it from any liability which it may have to any other party other than for contribution hereunder. In case any such action, suit or proceeding is brought against any party, and such party notifies a contributing party or its representative of the commencement thereof within the aforesaid 15 days, the contributing party will be entitled to participate therein with the notifying party and any other contributing party similarly notified. Any such contributing party shall not be liable to any party seeking contribution on account of any settlement of any claim, action or proceeding affected by such party seeking contribution on account of any settlement of any claim, action or proceeding affected by such party seeking contribution without the written consent of such contributing party. The contribution provisions contained in this Section 5.3.2 are intended to supersede, to the extent permitted by law, any right to contribution under the Securities Act, the Exchange Act or otherwise available. Each Underwriter’s obligations to contribute pursuant to this Section 5.3 are several and not joint.

6. Default by an Underwriter.

6.1 Default Not Exceeding 10% of Firm Securities or Option Securities. If any Underwriter or Underwriters shall default in its or their obligations to purchase the Firm Securities or the Option Securities, if the Over-allotment Option is exercised hereunder, and if the number of the Firm Securities or Option Securities with respect to which such default relates does not exceed in the aggregate 10% of the number of Firm Securities or Option Securities that all Underwriters have agreed to purchase hereunder, then such Firm Securities or Option Securities to which the default relates shall be purchased by the non-defaulting Underwriters in proportion to their respective commitments hereunder.

6.2 Default Exceeding 10% of Firm Securities or Option Securities. In the event that the default addressed in Section 6.1 relates to more than 10% of the Firm Securities or Option Securities, you may in your discretion arrange for yourself or for another party or parties to purchase such Firm Securities or Option Securities to which such default relates on the terms contained herein. If, within one (1) Business

Day after such default relating to more than 10% of the Firm Securities or Option Securities, you do not arrange for the purchase of such Firm Securities or Option Securities, then the Company shall be entitled to a further period of one (1) Business Day within which to procure another party or parties satisfactory to you to purchase said Firm Securities or Option Securities on such terms. In the event that neither you nor the Company arrange for the purchase of the Firm Securities or Option Securities to which a default relates as provided in this Section 6, this Agreement will automatically be terminated by you or the Company without liability on the part of the Company (except as provided in Sections 3.8 and 5) or the several Underwriters (except as provided in Section 5); provided, however, that if such default occurs with respect to the Option Securities, this Agreement will not terminate as to the Firm Securities; and provided, further, that nothing herein shall relieve a defaulting Underwriter of its liability, if any, to the other Underwriters and to the Company for damages occasioned by its default hereunder.

6.3 Postponement of Closing Date. In the event that the Firm Securities or Option Securities to which the default relates are to be purchased by the non-defaulting Underwriters, or are to be purchased by another party or parties as aforesaid, you or the Company shall have the right to postpone the Closing Date or Option Closing Date for a reasonable period, but not in any event exceeding five (5) Business Days, in order to effect whatever changes may thereby be made necessary in the Registration Statement, the Pricing Disclosure Package or the Prospectus or in any other documents and arrangements, and the Company agrees to file promptly any amendment to the Registration Statement, the Pricing Disclosure Package or the Prospectus that in the opinion of counsel for the Underwriter may thereby be made necessary. The term “Underwriter” as used in this Agreement shall include any party substituted under this Section 6 with like effect as if it had originally been a party to this Agreement with respect to such shares of Common Stock.

7. Additional Covenants.

7.1 Board Composition and Board Designations. The Company shall ensure that: (i) the qualifications of the persons serving as members of the Company’s Board of Directors and the overall composition of its Board of Directors comply with the Sarbanes-Oxley Act, with the Exchange Act and with the listing rules of the Exchange or any other national securities exchange, as the case may be, in the event the Company seeks to have its Public Securities listed on another exchange or quoted on an automated quotation system, and (ii) if applicable, at least one member of the Audit Committee of the Board of Directors qualifies as an “audit committee financial expert,” as such term is defined under Regulation S-K and the listing rules of the Exchange.

7.2 Prohibition on Press Releases and Public Announcements. The Company shall not issue press releases or engage in any other publicity, without the Representative’s prior written consent, for a period ending at 5:00 p.m., Eastern time, on the first (1<sup>st</sup>) Business Day following the forty-fifth (45<sup>th</sup>) day after the Closing Date, other than normal and customary releases issued in the ordinary course of the Company’s business.

7.3 [Reserved]

8. Effective Date of this Agreement and Termination Thereof.

8.1 Effective Date. This Agreement shall become effective when both the Company and the Representative have executed the same and delivered counterparts of such signatures to the other party.

8.2 Termination. The Representative shall have the right to terminate this Agreement at any time prior to any Closing Date, (i) if any domestic or international event or act or occurrence has materially disrupted, or in your opinion will in the immediate future materially disrupt, general securities markets in the United States; or (ii) if trading on the New York Stock Exchange or the Nasdaq Stock Market LLC shall

have been suspended or materially limited, or minimum or maximum prices for trading shall have been fixed, or maximum ranges for prices for securities shall have been required by FINRA or by order of the Commission or any other government authority having jurisdiction; or (iii) if the United States shall have become involved in a new war or an increase in major hostilities; or (iv) if a banking moratorium has been declared by a New York State or federal authority; or (v) if a moratorium on foreign exchange trading has been declared which materially adversely impacts the United States securities markets; or (vi) if the Company shall have sustained a material loss by fire, flood, accident, hurricane, earthquake, theft, sabotage or other calamity or malicious act which, whether or not such loss shall have been insured, will, in your opinion, make it inadvisable to proceed with the delivery of the Firm Securities or Option Securities; or (vii) if the Company is in material breach of any of its representations, warranties or covenants hereunder; or (viii) if the Representative shall have become aware after the date hereof of such a material adverse change in the conditions or prospects of the Company, or such adverse material change in general market conditions as in the Representative's judgment would make it impracticable to proceed with the offering, sale and/or delivery of the Public Securities or to enforce contracts made by the Underwriters for the sale of the Public Securities.

8.3 Expenses. Notwithstanding anything to the contrary in this Agreement, except in the case of a default by the Underwriters, pursuant to Section 6.2, in the event that this Agreement shall not be carried out for any reason whatsoever, within the time specified herein or any extensions thereof pursuant to the terms herein, the Company shall be obligated to pay to the Underwriters their actual and accountable out-of-pocket expenses (as referenced in Section 3.10.1) related to the transactions contemplated herein then due and payable (including the fees and disbursements of Representative Counsel) up to \$125,000, and upon demand the Company shall pay the full amount thereof to the Representative on behalf of the Underwriters; provided, however, that such expense cap in no way limits or impairs the indemnification and contribution provisions of this Agreement. Notwithstanding the foregoing, any advance received by the Representative will be reimbursed to the Company to the extent not actually incurred in compliance with FINRA Rule 5110(g)(4)(A).

8.4 Indemnification. Notwithstanding any contrary provision contained in this Agreement, any election hereunder or any termination of this Agreement, and whether or not this Agreement is otherwise carried out, the provisions of Section 5 shall remain in full force and effect and shall not be in any way affected by, such election or termination or failure to carry out the terms of this Agreement or any part hereof.

8.5 Representations, Warranties, Agreements to Survive. All representations, warranties and agreements contained in this Agreement or in certificates of officers of the Company submitted pursuant hereto, shall remain operative and in full force and effect regardless of (i) any investigation made by or on behalf of any Underwriter or its affiliates or selling agents, any person controlling any Underwriter, its officers or directors or any person controlling the Company or (ii) delivery of and payment for the Public Securities.

9. Miscellaneous.

9.1 Notices. All communications hereunder, except as herein otherwise specifically provided, shall be in writing and shall be mailed (registered or certified mail, return receipt requested), personally delivered or sent by facsimile transmission and confirmed and shall be deemed given when so delivered or faxed and confirmed or if mailed, two (2) days after such mailing.

If to the Representative:

EF Hutton, division of Benchmark Investments, LLC  
590 Madison Avenue, 39th Floor

New York, NY 10022  
Attn: Jack Terranova, Managing Director, Co-Head of Healthcare, Head of Healthcare Investment Banking  
Email: jtterranova@efhuttongroup.com

with a copy (which shall not constitute notice) to:

McGuireWoods LLP  
1251 Avenue of the Americas, 20th Floor  
New York, New York 10020  
Attn: Stephen Older, Esq.  
Rakesh Gopalan, Esq.  
Email: solder@mcguirewoods.com  
rgopalan@mcguirewoods.com

If to the Company:

TransCode Therapeutics, Inc.  
6 Liberty Square, #2382  
Boston, MA  
Attn: R. Michael Dudley, Chief Executive Officer

with a copy (which shall not constitute notice) to:

Goodwin Procter LLP  
100 Northern Avenue  
Boston, MA 02210  
Attn: Michael Bison, Esq.

9.2 Headings. The headings contained herein are for the sole purpose of convenience of reference, and shall not in any way limit or affect the meaning or interpretation of any of the terms or provisions of this Agreement.

9.3 Amendment. This Agreement may only be amended by a written instrument executed by each of the parties hereto.

9.4 Entire Agreement. This Agreement (together with the other agreements and documents being delivered pursuant to or in connection with this Agreement) constitutes the entire agreement of the parties hereto with respect to the subject matter hereof and thereof, and supersedes all prior agreements and understandings of the parties, oral and written, with respect to the subject matter hereof. Notwithstanding anything to the contrary set forth herein, it is understood and agreed by the parties hereto that all other terms and conditions of that certain engagement letter between the Company and EF Hutton, division of Benchmark Investments, LLC dated [-], 2023, shall remain in full force and effect.

9.5 Binding Effect. This Agreement shall inure solely to the benefit of and shall be binding upon the Representative, the Underwriters, the Company and the controlling persons, directors and officers referred to in Section 5, and their respective successors, legal representatives, heirs and assigns, and no other person shall have or be construed to have any legal or equitable right, remedy or claim under or in respect of or by virtue of this Agreement or any provisions herein contained. The term "successors and assigns" shall not include a purchaser, in its capacity as such, of securities from any of the Underwriters.

9.6 Governing Law; Consent to Jurisdiction; Trial by Jury. This Agreement shall be governed by and construed and enforced in accordance with the laws of the State of New York, without giving effect to conflict of laws principles thereof. The Company hereby agrees that any action, proceeding or claim against it arising out of, or relating in any way to this Agreement shall be brought and enforced in the New York Supreme Court, County of New York, or in the United States District Court for the Southern District of New York, and irrevocably submits to such jurisdiction, which jurisdiction shall be exclusive. The Company hereby waives any objection to such exclusive jurisdiction and that such courts represent an inconvenient forum. Any such process or summons to be served upon the Company may be served by transmitting a copy thereof by registered or certified mail, return receipt requested, postage prepaid, addressed to it at the address set forth in Section 9.1. Such mailing shall be deemed personal service and shall be legal and binding upon the Company in any action, proceeding or claim. The Company agrees that the prevailing party(ies) in any such action shall be entitled to recover from the other party(ies) all of its reasonable attorneys' fees and expenses relating to such action or proceeding and/or incurred in connection with the preparation therefor. The Company (on its behalf and, to the extent permitted by applicable law, on behalf of its stockholders and affiliates) and each of the Underwriters hereby irrevocably waives, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to this Agreement or the transactions contemplated hereby.

9.7 Execution in Counterparts. This Agreement may be executed in one or more counterparts, and by the different parties hereto in separate counterparts, each of which shall be deemed to be an original, but all of which taken together shall constitute one and the same agreement, and shall become effective when one or more counterparts has been signed by each of the parties hereto and delivered to each of the other parties hereto. Delivery of a signed counterpart of this Agreement by facsimile or email/pdf transmission shall constitute valid and sufficient delivery thereof.

9.8 Waiver, etc. The failure of any of the parties hereto to at any time enforce any of the provisions of this Agreement shall not be deemed or construed to be a waiver of any such provision, nor to in any way effect the validity of this Agreement or any provision hereof or the right of any of the parties hereto to thereafter enforce each and every provision of this Agreement. No waiver of any breach, non-compliance or non-fulfillment of any of the provisions of this Agreement shall be effective unless set forth in a written instrument executed by the party or parties against whom or which enforcement of such waiver is sought; and no waiver of any such breach, non-compliance or non-fulfillment shall be construed or deemed to be a waiver of any other or subsequent breach, non-compliance or non-fulfillment.

[Signature Page Follows]

If the foregoing correctly sets forth the understanding between the Underwriters and the Company, please so indicate in the space provided below for that purpose, whereupon this letter shall constitute a binding agreement between us.

Very truly yours,

TRANSCODE THERAPEUTICS, INC.

By: \_\_\_\_\_  
Name:  
Title:

Confirmed as of the date first written above mentioned, on behalf of itself and as Representative of the several Underwriters named on Schedule 1 hereto:

EF HUTTON, DIVISION OF BENCHMARK INVESTMENTS, LLC

By: \_\_\_\_\_  
Name:  
Title:

[SIGNATURE PAGE]  
TRANSCODE THERAPEUTICS, INC. – UNDERWRITING AGREEMENT

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**SCHEDULE 1**

	<b>Total Number of Firm Shares to be Purchased</b>	<b>Total Number of Firm Pre- funded Warrants to be Purchased</b>	<b>Number of Option Shares to be Purchased if the Over- Allotment Option is Fully Exercised</b>	<b>Number of Option Pre- funded Warrants to be Purchased if the Over- Allotment Option is Fully Exercised</b>
<b>Underwriter</b> EF Hutton, division of Benchmark Investments, LLC				
<b>TOTAL</b>	_____	_____	_____	_____
	=====	=====	=====	=====

**SCHEDULE 2-A**

**Pricing Information**

Number of Firm Shares: [·]

Number of Firm Pre-funded Warrants: [·]

Number of Option Shares: [·]

Number of Option Pre-funded Warrants: [·]

Public Offering Price per Share: \$[·]

Public Offering Price per Pre-funded Warrant: \$[·]

Underwriting Discount per Share: \$[·]

Underwriting Discount per Pre-funded Warrant: \$[·]

Proceeds to Company per Share (before expenses): \$[·]

Proceeds to Company per Pre-funded Warrant (before expenses): \$[·]



**SCHEDULE 2-B**

**Issuer General Use Free Writing Prospectuses**

None.

Sch. 2-1

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**SCHEDULE 2-C**

**Written Testing-the-Waters Communications**

None.

Sch. 2-1

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**SCHEDULE 3**

**List of Lock-Up Parties**

1. R. Michael Dudley
2. Thomas A. Fitzgerald
3. Philippe P. Calais
4. Erik Manting
5. Magda Marquet
6. Zdravka Medarova
7. Anna Moore

Sch. 3-1

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**EXHIBIT A**

**Form of Pre-funded Warrant**

Ex. A-1

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**Lock-Up Agreement**

[·], 2023

EF Hutton, division of Benchmark Investments, LLC  
590 Madison Avenue, 39<sup>th</sup> Floor  
New York, NY 10022

As Representative of the several Underwriters named on Schedule 1 to the Underwriting Agreement referenced below

Ladies and Gentlemen:

The undersigned understands that EF Hutton, division of Benchmark Investments, LLC (the “**Representative**”), proposes to enter into an Underwriting Agreement (the “**Underwriting Agreement**”) with TransCode Therapeutics, Inc., a Delaware corporation (the “**Company**”), providing for the public offering (the “**Public Offering**”) of shares of common stock, par value \$0.0001 per share, of the Company (the “**Common Shares**”).

To induce the Representative to continue its efforts in connection with the Public Offering, the undersigned hereby agrees that, without the prior written consent of the Representative, the undersigned will not, during the period commencing on the date hereof and ending 180 days after the date of the Underwriting Agreement relating to the Public Offering (the “**Lock-Up Period**”), (1) offer, pledge, sell, contract to sell, grant, lend, or otherwise transfer or dispose of, directly or indirectly, any Common Shares or any securities convertible into or exercisable or exchangeable for Common Shares, whether now owned or hereafter acquired by the undersigned or with respect to which the undersigned has or hereafter acquires the power of disposition (collectively, the “**Lock-Up Securities**”); (2) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the Lock-Up Securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of Lock-Up Securities, in cash or otherwise; (3) make any demand for or exercise any right with respect to the registration of any Lock-Up Securities; or (4) publicly disclose the intention to make any offer, sale, pledge or disposition, or to enter into any transaction, swap, hedge or other arrangement relating to any Lock-Up Securities. Notwithstanding the foregoing, and subject to the conditions below, the undersigned may transfer Lock-Up Securities without the prior written consent of the Representative in connection with (a) transactions relating to Lock-Up Securities acquired in open market transactions after the completion of the Public Offering; provided that no filing under Section 13 or Section 16(a) of the Securities Exchange Act of 1934, as amended (the “**Exchange Act**”), or other public announcement shall be required or shall be voluntarily made in connection with subsequent sales of Lock-Up Securities acquired in such open market transactions; (b) transfers of Lock-Up Securities as a *bona fide* gift, by will or intestacy or to a family member or trust for the benefit of the undersigned or a family member (for purposes of this lock-up agreement, “family member” means any relationship by blood, marriage or adoption, not more remote than first cousin); (c) transfers of Lock-Up Securities to a charity or educational institution; (d) if the undersigned is a corporation, partnership, limited liability company or other business entity, (i) any transfers of Lock-Up Securities to another corporation, partnership or other business entity that controls, is controlled by or is under common control with the undersigned or (ii) distributions of Lock-Up Securities to members, partners, stockholders, subsidiaries or affiliates (as defined in Rule 405 promulgated under the Securities Act of 1933, as amended) of the undersigned; (e) if the undersigned is a trust, to a trustee or beneficiary of the trust; provided that in the case of any transfer pursuant to the foregoing clauses (b), (c)

(d) or (e), (i) any such transfer shall not involve a disposition for value, (ii) each transferee shall sign and deliver to the Representative a lock-up agreement substantially in the form of this lock-up agreement and (iii) no filing under Section 13 or Section 16(a) of the Exchange Act or other public announcement shall be required or shall be voluntarily made; (f) the receipt by the undersigned from the Company of Common Shares upon the vesting of restricted stock awards or stock units or upon the exercise of options to purchase the Company's Common Shares issued under an equity incentive plan of the Company or an employment arrangement described in the Pricing Prospectus (as defined in the Underwriting Agreement) (the "**Plan Shares**") or the transfer of Common Shares or any securities convertible into Common Shares to the Company upon a vesting event of the Company's securities or upon the exercise of options to purchase the Company's securities, in each case on a "cashless" or "net exercise" basis or to cover tax obligations of the undersigned in connection with such vesting or exercise, but only to the extent such right expires during the Lock-up Period, provided that no filing under Section 13 or Section 16(a) of the Exchange Act or other public announcement shall be required or shall be voluntarily made within 90 days after the date of the Underwriting Agreement, and after such 90<sup>th</sup> day, if the undersigned is required to file a report under Section 13 or Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of Common Shares during the Lock-Up Period, the undersigned shall include a statement in such schedule or report to the effect that the purpose of such transfer was to cover tax withholding obligations of the undersigned in connection with such vesting or exercise and, provided further, that the Plan Shares shall be subject to the terms of this lock-up agreement; (g) the transfer of Lock-Up Securities pursuant to agreements described in the Pricing Prospectus under which the Company has the option to repurchase such securities or a right of first refusal with respect to the transfer of such securities, provided that if the undersigned is required to file a report under Section 13 or Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of Common Shares during the Lock-Up Period, the undersigned shall include a statement in such schedule or report describing the purpose of the transaction; (h) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of Lock-Up Securities, provided that (i) such plan does not provide for the transfer of Lock-Up Securities during the Lock-Up Period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made by or on behalf of the undersigned or the Company regarding the establishment of such plan, such public announcement or filing shall include a statement to the effect that no transfer of Lock-Up Securities may be made under such plan during the Lock-Up Period; (i) the transfer of Lock-Up Securities that occurs by operation of law, such as pursuant to a qualified domestic order or in connection with a divorce settlement, provided that the transferee agrees to sign and deliver a lock-up agreement substantially in the form of this lock-up agreement for the balance of the Lock-Up Period, and provided further, that any filing under Section 13 or Section 16(a) of the Exchange Act that is required to be made during the Lock-Up Period as a result of such transfer shall include a statement that such transfer has occurred by operation of law; and (j) the transfer of Lock-Up Securities pursuant to a bona fide third party tender offer, merger, consolidation or other similar transaction made to all holders of the Common Shares involving a change of control (as defined below) of the Company after the closing of the Public Offering and approved by the Company's board of directors; provided that in the event that the tender offer, merger, consolidation or other such transaction is not completed, the Lock-Up Securities owned by the undersigned shall remain subject to the restrictions contained in this lock-up agreement. For purposes of clause (j) above, "change of control" shall mean the consummation of any bona fide third party tender offer, merger, amalgamation, consolidation or other similar transaction the result of which is that any "person" (as defined in Section 13(d)(3) of the Exchange Act), or group of persons, becomes the beneficial owner (as defined in Rules 13d-3 and 13d-5 of the Exchange Act) of a majority of total voting power of the voting stock of the Company. The undersigned also agrees and consents to the entry of stop transfer instructions with the Company's transfer agent and registrar against the transfer of the undersigned's Lock-Up Securities except in compliance with this lock-up agreement.

The undersigned understands that the Company and the Representative are relying upon this lock-up agreement in proceeding toward consummation of the Public Offering. The undersigned further understands that this lock-up agreement is irrevocable and shall be binding upon the undersigned's heirs, legal representatives, successors and assigns.

The undersigned understands that, if the Underwriting Agreement is not executed by February 15, 2023, or if the Underwriting Agreement (other than the provisions thereof which survive termination) shall terminate or be terminated prior to payment for and delivery of the Common Shares to be sold thereunder, then this lock-up agreement shall be void and of no further force or effect.

Ex. B-3

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Whether or not the Public Offering actually occurs depends on a number of factors, including market conditions. Any Public Offering will only be made pursuant to an Underwriting Agreement, the terms of which are subject to negotiation between the Company and the Representative.

Very truly yours,

\_\_\_\_\_  
(Name - Please Print)

\_\_\_\_\_  
(Signature)

\_\_\_\_\_  
(Name of Signatory, in the case of entities - Please Print)

\_\_\_\_\_  
(Title of Signatory, in the case of entities - Please Print)

Address: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Ex. B-4

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## PRE-FUNDED COMMON STOCK PURCHASE WARRANT

## TRANSCODE THERAPEUTICS, INC.

Warrant Shares: \_\_\_\_\_

Issue Date: \_\_\_\_\_, 2023

Initial Exercise Date: \_\_\_\_\_, 2023

THIS PRE-FUNDED COMMON STOCK PURCHASE WARRANT (the "Warrant") certifies that, for value received, \_\_\_\_\_ or its assigns (the "Holder") is entitled, upon the terms and subject to the limitations on exercise and the conditions hereinafter set forth, at any time on or after the Issue Date and until this Warrant is exercised in full (the "Termination Date") but not thereafter, to subscribe for and purchase from TransCode Therapeutics, Inc., a Delaware corporation (the "Company"), up to \_\_\_\_\_ shares of Common Stock (as subject to adjustment hereunder, the "Warrant Shares"). The purchase price of one share of Common Stock under this Warrant shall be equal to the Exercise Price, as defined in Section 2(b).

Section 1. Definitions. In addition to the terms defined elsewhere in this Warrant, the following terms have the meanings indicated in this Section 1:

"Affiliate" means any Person that, directly or indirectly through one or more intermediaries, controls or is controlled by or is under common control with a Person, as such terms are used in and construed under Rule 405 under the Securities Act.

"Commission" means the United States Securities and Exchange Commission.

"Common Stock" means the common stock of the Company, par value \$.0001 per share, and any other class of securities into which such securities may hereafter be reclassified or changed.

"Common Stock Equivalents" means any securities of the Company or the Subsidiaries which would entitle the holder thereof to acquire at any time Common Stock, including, without limitation, any debt, preferred stock, right, option, warrant or other instrument that is at any time convertible into or exercisable or exchangeable for, or otherwise entitles the holder thereof to receive, Common Stock.

"Exchange Act" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

"Person" means an individual or corporation, partnership, trust, incorporated or unincorporated association, joint venture, limited liability company, joint stock company, government (or an agency or subdivision thereof) or other entity of any kind.

"Proceeding" means an action, claim, suit, investigation or proceeding (including, without limitation, an informal investigation or partial proceeding, such as a deposition), whether commenced or threatened.

"Registration Statement" means the Company's registration statement on Form S-1 (File No. 333-\_\_\_\_\_).

"Rule 144" means Rule 144 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended or interpreted from time to time, or any similar rule or regulation hereafter adopted by the Commission having substantially the same purpose and effect as such Rule.

"Securities Act" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"Trading Day" means a day on which the Common Stock is traded on a Trading Market.

“Trading Market” means any of the following markets or exchanges on which the Common Stock is listed or quoted for trading on the date in question: the OTCQB, OTCQX or Pink Open Market operated by OTC Markets Group, the NYSE American, the Nasdaq Capital Market, the Nasdaq Global Market, the Nasdaq Global Select Market, or the New York Stock Exchange (or any successors to any of the foregoing).

“Transfer Agent” means VStock Transfer, LLC, 18 Lafayette Place, Woodmere, NY 11598, and any successor transfer agent of the Company.

“Warrants” means this Warrant and other Pre-Funded Common Stock Purchase Warrants issued by the Company pursuant to the Registration Statement.

Section 2.        Exercise.

a)        Exercise of the purchase rights represented by this Warrant may be made, in whole or in part, at any time or times on or after the Issue Date and on or before the Termination Date by delivery to the Company of a duly executed facsimile copy (or e-mail attachment) of the Notice of Exercise in the form annexed hereto (the “Notice of Exercise”). Within the earlier of (i) two (2) Trading Days and (ii) the number of Trading Days comprising the Standard Settlement Period (as defined in Section 2(d)(i)) following the date of exercise as aforesaid, the Holder shall deliver to the Company the aggregate Exercise Price for the Warrant Shares specified in the applicable Notice of Exercise by wire transfer or cashier’s check drawn on a United States bank unless the cashless exercise procedure specified in Section 2(c) below is specified in the applicable Notice of Exercise. No ink-original Notice of Exercise shall be required, nor shall any medallion guarantee (or other type of guarantee or notarization) of any Notice of Exercise form be required. Notwithstanding anything herein to the contrary, the Holder shall not be required to physically surrender this Warrant to the Company until the Holder has purchased all of the Warrant Shares available hereunder and the Warrant has been exercised in full, in which case, the Holder shall surrender this Warrant to the Company for cancellation within three (3) Trading Days of the date on which the final Notice of Exercise is delivered to the Company. Partial exercises of this Warrant resulting in purchases of a portion of the total number of Warrant Shares available hereunder shall have the effect of lowering the outstanding number of Warrant Shares purchasable hereunder in an amount equal to the applicable number of Warrant Shares purchased. The Holder and the Company shall maintain records showing the number of Warrant Shares purchased and the date of such purchases. The Company shall deliver any objection to any Notice of Exercise within one (1) Trading Day of receipt of such notice. **The Holder and any assignee, by acceptance of this Warrant, acknowledge and agree that, by reason of the provisions of this paragraph, following the purchase of a portion of the Warrant Shares hereunder, the number of Warrant Shares available for purchase hereunder at any given time may be less than the amount stated on the face hereof.**

b)        Exercise Price. The aggregate exercise price of this Warrant, except for a nominal exercise price of \$0.01 per Warrant Share, was pre-funded to the Company on or prior to the Issue Date and, consequently, no additional consideration (other than the nominal exercise price of \$0.01 per Warrant Share) shall be required to be paid by the Holder to any Person to effect any exercise of this Warrant. The Holder shall not be entitled to the return or refund of all, or any portion, of such pre-paid aggregate exercise price under any circumstance or for any reason whatsoever, including in the event this Warrant shall not have been exercised prior to the Termination Date. The remaining unpaid exercise price per share of Common Stock under this Warrant shall be \$0.01, subject to adjustment hereunder (the “Exercise Price”).

c)        Cashless Exercise. This Warrant may also be exercised, in whole or in part, at any time by means of a “cashless exercise” in which the Holder shall be entitled to receive a number of Warrant Shares for the deemed surrender of the Warrant in whole or in part equal to the quotient obtained by dividing [(A-B) (X)] by (A), where:

(A) = as applicable: (i) the Closing Sale Price of the Common Stock on the Trading Day immediately preceding the date of the applicable Notice of Exercise if such Notice of Exercise is (1) both executed and delivered pursuant to Section 2(a) on a day that is not a Trading Day or (2) both executed and delivered pursuant to Section 2(a) on a Trading Day prior to the opening of “regular trading hours” (as defined in Rule 600(b)(68) of Regulation NMS

promulgated under the federal securities laws) on such Trading Day; (ii) at the option of the Holder, either (x) the VWAP on the Trading Day immediately preceding the date of the applicable Notice of Exercise or (y) the Bid Price of the Common Stock as of the time of the Holder's execution of the applicable Notice of Exercise if such Notice of Exercise is executed during "regular trading hours" on a Trading Day and is delivered within two (2) hours thereafter pursuant to Section 2(a) (including until two (2) hours after the close of "regular trading hours" on a Trading Day); or (iii) the Closing Sale Price of the Common Stock on the date of the applicable Notice of Exercise if the date of such Notice of Exercise is a Trading Day and such Notice of Exercise is both executed and delivered pursuant to Section 2(a) after the close of "regular trading hours" on such Trading Day;

(B) = the Exercise Price of this Warrant, as adjusted hereunder; and

(X) = the number of Warrant Shares that would be issuable upon exercise of this Warrant in accordance with the terms of this Warrant if such exercise were by means of a cash exercise rather than a cashless exercise.

The issue price for each such Warrant Share to be issued pursuant to the cashless exercise of a Warrant will be equal to (B), as defined above, and the total issue price for the aggregate number of Warrant Shares issued pursuant to the cashless exercise of a Warrant will be deemed paid and satisfied in full by the deemed surrender to the Company of the portion of such Warrant being exercised in accordance with this Section 1(c). Notwithstanding anything herein to the contrary, the Company shall not be required to make any cash payments or net cash settlement to the Holder in lieu of delivery of the Warrant Shares. If Warrant Shares are issued in such a cashless exercise, the parties acknowledge and agree that in accordance with Section 3(a)(9) of the Securities Act, the Warrant Shares shall take on the registered characteristics of the Warrants being exercised. The Company agrees not to take any position contrary to this Section 2(c).

"Bid Price" means, for any security as of the particular time of determination, the bid price for such security on the Trading Market as reported by Bloomberg as of such time of determination, or, if the Trading Market is not the principal securities exchange or trading market for such security, the bid price of such security on the principal securities exchange or trading market where such security is listed or traded as reported by Bloomberg as of such time of determination, or if the foregoing does not apply, the bid price of such security in the over-the-counter market on the electronic bulletin board for such security as reported by Bloomberg as of such time of determination, or, if no bid price is reported for such security by Bloomberg as of such time of determination, the average of the bid prices of any market makers for such security as reported on the Pink Open Market as of such time of determination. If the Bid Price cannot be calculated for a security as of the particular time of determination on any of the foregoing bases, the Bid Price of such security as of such time of determination shall be the fair market value as mutually determined by the Company and the Holder. If the Company and the Holder are unable to agree upon the fair market value of such security, then such fair market value shall be determined pursuant to the provisions set forth in clause (d) of the definition of VWAP. All such determinations to be appropriately adjusted for any stock dividend, share split, share consolidation, reclassification or other similar transaction during the applicable calculation period.

"Closing Sale Price" means, for any security as of any date, the last closing trade price for such security on the Trading Market, as reported by Bloomberg, or, if the Trading Market begins to operate on an extended hours basis and does not designate the closing trade price, then the last trade price of such security prior to 4:00:00 p.m., New York time, as reported by Bloomberg, or, if the Trading Market is not the principal securities exchange or trading market for such security, the last trade price of such security on the principal securities exchange or trading market where such security is listed or traded as reported by Bloomberg, or if the foregoing do not apply, the last trade price of such security in the over-the-counter market on the electronic bulletin board for such security as reported by Bloomberg, or, if no last trade price is reported for such security by Bloomberg, the average of the ask prices of any market makers for such security as reported on the in the OTC Link or on the Pink Open Market. If the Closing Sale Price cannot be calculated for a security on a particular date on any of the foregoing bases, the Closing Sale Price of such security on such date shall be the fair market value as mutually determined by the Company and the Holder. If the Company

and the Holder are unable to agree upon the fair market value of such security, then such fair market value shall be determined pursuant to the provisions set forth in clause (d) of the definition of VWAP. All such determinations to be appropriately adjusted for any stock dividend, share split, share consolidation, reclassification or other similar transaction during the applicable calculation period.

“VWAP” means, for any date, the price determined by the first of the following clauses that applies: (a) if the Common Stock is then listed or quoted for trading on a Trading Market other than the OTCQB, OTCQX or Pink Open Market operated by OTC Markets Group, the daily volume weighted average price of the Common Stock for such date (or the nearest preceding date) on the Trading Market on which the Common Stock is then listed or quoted as reported by Bloomberg L.P. (based on a Trading Day from 9:30 a.m. (New York City time) to 4:02 p.m. (New York City time)), (b) if the Common Stock is then quoted for trading on the OTCQB or OTCQX operated by OTC Markets Group, the volume weighted average price of the Common Stock for such date (or the nearest preceding date) on OTCQB or OTCQX as applicable, (c) if the Common Stock is then quoted for trading on the Pink Open Market operated by OTC Markets Group (or a similar organization or agency succeeding to its functions of reporting prices), the most recent bid price per share of Common Stock reported on the Pink Open Market, or (d) in all other cases, the fair market value of a share of Common Stock as determined by an independent appraiser selected in good faith by the holders of a majority in interest of the Warrants then outstanding and reasonably acceptable to the Company, the fees and expenses of which shall be paid by the Company.

d) Mechanics of Exercise.

i. Delivery of Warrant Shares Upon Exercise. The Company shall cause the Warrant Shares purchased hereunder to be transmitted by the Transfer Agent to the Holder by crediting the account of the Holder’s or its designee’s balance account with The Depository Trust Company through its Deposit or Withdrawal at Custodian system (the “DWAC”) if the Company is then a participant in such system and either (A) there is an effective registration statement permitting the issuance of the Warrant Shares to or resale of the Warrant Shares by the Holder or (B) this Warrant is being exercised via cashless exercise, and otherwise by physical delivery of a certificate, registered in the Company’s share register in the name of the Holder or its designee, for the number of Warrant Shares to which the Holder is entitled pursuant to such exercise to the address specified by the Holder in the Notice of Exercise by the date that is the earlier of (i) two (2) Trading Days and (ii) the number of Trading Days comprising the Standard Settlement Period after the delivery to the Company of the Notice of Exercise (such date, the “Warrant Share Delivery Date”). Upon delivery of the Notice of Exercise, the Holder shall be deemed for all corporate purposes to have become the Holder of record of the Warrant Shares with respect to which this Warrant has been exercised, irrespective of the date of delivery of the Warrant Shares, provided that payment of the aggregate Exercise Price (other than in the case of a cashless exercise) is received within the earlier of (i) two (2) Trading Days and (ii) the number of Trading Days comprising the Standard Settlement Period following delivery of the Notice of Exercise. If the Company fails for any reason to deliver to the Holder the Warrant Shares subject to a Notice of Exercise by the Warrant Share Delivery Date, the Company shall pay to the Holder, in cash, as liquidated damages and not as a penalty, for each \$1,000 of Warrant Shares subject to such exercise (based on the VWAP of the Common Stock on the date of the applicable Notice of Exercise), \$10 per Trading Day (increasing to \$20 per Trading Day on the fifth Trading Day after such liquidated damages begin to accrue) for each Trading Day after such Warrant Share Delivery Date until such Warrant Shares are delivered to said Holder or the Holder rescinds such exercise. The Company agrees to maintain a transfer agent that is a participant in the Fast Automated Securities Transfer or FAST program so long as this Warrant remains outstanding and exercisable. As used herein, “Standard Settlement Period” means the standard settlement period, expressed in a number of Trading Days, on the Company’s primary Trading Market with respect to the Common Stock as in effect on the date of delivery of the Notice of Exercise. Notwithstanding the foregoing, with respect to any Notice(s) of Exercise delivered on or prior to 12:00 p.m. (New York City time) on the Issue Date, which may be

delivered at any time after the time of execution of the Underwriting Agreement, dated February [·], 2023 between the Company and EF Hutton, division of Benchmark Investments, LLC, the Company agrees to deliver the Warrant Shares subject to such notice(s) by 4:00 p.m. (New York City time) on the Issue Date.

ii. Delivery of New Warrants Upon Exercise. If this Warrant shall have been exercised in part, the Company shall, at the request of a Holder and upon surrender of this Warrant certificate, at the time of delivery of the Warrant Shares, deliver to the Holder a new Warrant evidencing the rights of the Holder to purchase the unpurchased Warrant Shares called for by this Warrant, which new Warrant shall in all other respects be identical with this Warrant.

iii. Rescission Rights. If the Company fails to cause the Transfer Agent to transmit to the Holder the Warrant Shares pursuant to Section 2(d)(i) by the Warrant Share Delivery Date, then the Holder will have the right to rescind such exercise.

iv. Compensation for Buy-In on Failure to Timely Deliver Warrant Shares Upon Exercise. In addition to any other rights available to the Holder, if the Company fails to cause the Transfer Agent to transmit to the Holder the Warrant Shares in accordance with the provisions of Section 2(d)(i) pursuant to an exercise on or before the Warrant Share Delivery Date, and if after such date the Holder is required by its broker to purchase (in an open market transaction or otherwise) or the Holder's brokerage firm otherwise purchases, share of Common Stock to deliver in satisfaction of a sale by the Holder of the Warrant Shares which the Holder anticipated receiving upon such exercise (a "Buy-In"), then the Company shall (A) pay in cash to the Holder the amount, if any, by which (x) the Holder's total purchase price (including brokerage commissions, if any) for the shares of Common Stock so purchased exceeds (y) the amount obtained by multiplying (1) the number of Warrant Shares that the Company was required to deliver to the Holder in connection with the exercise at issue by (2) the price at which the sell order giving rise to such purchase obligation was executed, and (B) at the option of the Holder, either reinstate the portion of the Warrant and equivalent number of Warrant Shares for which such exercise was not honored (in which case such exercise shall be deemed rescinded) or deliver to the Holder the number of Common Stock that would have been issued had the Company timely complied with its exercise and delivery obligations hereunder. For example, if the Holder purchases Common Stock having a total purchase price of \$11,000 to cover a Buy-In with respect to an attempted exercise of this Warrant to purchase Common Stock with an aggregate sale price giving rise to such purchase obligation of \$10,000, under clause (A) of the immediately preceding sentence the Company shall be required to pay the Holder \$1,000. The Holder shall provide the Company written notice indicating the amounts payable to the Holder in respect of the Buy-In and, upon request of the Company, evidence of the amount of such loss. Nothing herein shall limit a Holder's right to pursue any other remedies available to it hereunder, at law or in equity including, without limitation, a decree of specific performance and/or injunctive relief with respect to the Company's failure to timely deliver Common Stock upon exercise of the Warrant as required pursuant to the terms hereof.

v. No Fractional Shares or Scrip. No fractional shares or scrip representing fractional shares shall be issued upon the exercise of this Warrant. As to any fraction of a share which the Holder would otherwise be entitled to purchase upon such exercise, the Company shall, at its election, either pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the Exercise Price or round up to the next whole share.

vi. Charges, Taxes and Expenses. Issuance of Warrant Shares shall be made without charge to the Holder for any issue or transfer tax or other incidental expense in respect of the issuance of such Warrant Shares, all of which taxes and expenses shall be

paid by the Company, and such Warrant Shares shall be issued in the name of the Holder or in such name or names as may be directed by the Holder; provided, however, that in the event that Warrant Shares are to be issued in a name other than the name of the Holder, this Warrant when surrendered for exercise shall be accompanied by the Assignment Form attached hereto duly executed by the Holder and the Company may require, as a condition thereto, the payment of a sum sufficient to reimburse it for any transfer tax incidental thereto. The Company shall pay all Transfer Agent fees required for same-day processing of any Notice of Exercise and all fees to the Depository Trust Company (or another established clearing corporation performing similar functions) required for same-day electronic delivery of the Warrant Shares.

vii. Closing of Books. The Company shall not close its stockholder books or records in any manner which prevents the timely exercise of this Warrant, pursuant to the terms hereof.

e) Holder's Exercise Limitations. The Company shall not effect any exercise of this Warrant, and a Holder shall not have the right to exercise any portion of this Warrant, pursuant to Section 2 or otherwise, to the extent that after giving effect to such issuance after exercise as set forth on the applicable Notice of Exercise, the Holder (together with the Holder's Affiliates, and any other Persons acting as a group together with the Holder or any of the Holder's Affiliates (such Persons, "Attribution Parties")), would beneficially own in excess of the Beneficial Ownership Limitation (as defined below). For purposes of the foregoing sentence, the number of shares of Common Stock beneficially owned by the Holder and its Affiliates and Attribution Parties shall include the number of shares of Common Stock issuable upon exercise of this Warrant with respect to which such determination is being made, but shall exclude the number of shares of Common Stock which would be issuable upon (i) exercise of the remaining, non-exercised portion of this Warrant beneficially owned by the Holder or any of its Affiliates or Attribution Parties and (ii) exercise or conversion of the unexercised or non-converted portion of any other securities of the Company (including, without limitation, any other Common Stock Equivalents) that exceed any limitation on conversion or exercise in such securities that is analogous to the limitation contained herein beneficially owned by the Holder or any of its Affiliates or Attribution Parties. Except as set forth in the preceding sentence, for purposes of this Section 2(e), beneficial ownership shall be calculated in accordance with Section 13(d) of the Exchange Act and the rules and regulations promulgated thereunder, it being acknowledged by the Holder that the Company is not representing to the Holder that such calculation is in compliance with Section 13(d) of the Exchange Act and the Holder is solely responsible for any schedules required to be filed in accordance therewith. To the extent that the limitation contained in this Section 2(e) applies, the determination of whether this Warrant is exercisable (in relation to other securities owned by the Holder together with any Affiliates and Attribution Parties) and of which portion of this Warrant is exercisable shall be in the sole discretion of the Holder, and the submission of a Notice of Exercise shall be deemed to be the Holder's determination of whether this Warrant is exercisable (in relation to other securities owned by the Holder together with any Affiliates and Attribution Parties) and of which portion of this Warrant is exercisable, in each case subject to the Beneficial Ownership Limitation, and the Company shall have no obligation to verify or confirm the accuracy of such determination. In addition, a determination as to any group status as contemplated above shall be determined in accordance with Section 13(d) of the Exchange Act and the rules and regulations promulgated thereunder. For purposes of this Section 2(e), in determining the number of outstanding shares of Common Stock, a Holder may rely on the number of outstanding shares of Common Stock as reflected in (A) the Company's most recent periodic or annual report filed with the Commission, as the case may be, (B) a more recent public announcement by the Company or (C) a more recent written notice by the Company or the Transfer Agent setting forth the number of shares of Common Stock outstanding. Upon the written or oral request of a Holder, the Company shall within two Trading Days confirm orally and in writing to the Holder the number of shares of Common Stock then outstanding. In any case, the number of outstanding shares of Common Stock shall be determined after giving effect to the conversion or exercise of securities of the Company, including this Warrant, by the Holder or its Affiliates or Attribution Parties since the date as of which such number of outstanding shares of Common Stock was reported. The "Beneficial Ownership Limitation" shall be 4.99% (or, upon election by a Holder prior to the issuance of any Warrants, 9.99%) of the number of shares of Common Stock outstanding immediately after giving effect to the issuance of Common Stock issuable upon exercise of this Warrant. The Holder, upon notice to the Company, may

increase or decrease the Beneficial Ownership Limitation provisions of this Section 2(e), provided that the Beneficial Ownership Limitation in no event exceeds 9.99% of the number of shares of Common Stock outstanding immediately after giving effect to the issuance of Common Stock upon exercise of this Warrant held by the Holder and the provisions of this Section 2(e) shall continue to apply. Any increase in the Beneficial Ownership Limitation will not be effective until the 61<sup>st</sup> day after such notice is delivered to the Company. The provisions of this paragraph shall be construed and implemented in a manner otherwise than in strict conformity with the terms of this Section 2(e) to correct this paragraph (or any portion hereof) which may be defective or inconsistent with the intended Beneficial Ownership Limitation herein contained or to make changes or supplements necessary or desirable to properly give effect to such limitation. The limitations contained in this paragraph shall apply to a successor holder of this Warrant.

Section 3. Certain Adjustments.

a) Stock Dividends and Splits. If the Company, at any time while this Warrant is outstanding: (i) pays a stock dividend or otherwise makes a distribution or distributions on its Common Stock or any other equity or equity equivalent securities payable in Common Stock (which, for avoidance of doubt, shall not include any Common Stock issued by the Company upon exercise of this Warrant), (ii) subdivides outstanding Common Stock into a larger number of shares, (iii) combines (including by way of reverse share split or consolidation) outstanding Common Stock into a smaller number of shares, or (iv) issues by reclassification of Common Stock any shares of capital stock of the Company, then in each case the Exercise Price shall be multiplied by a fraction of which the numerator shall be the number of Common Stock (excluding treasury shares, if any) outstanding immediately before such event and of which the denominator shall be the number of shares of Common Stock outstanding immediately after such event, and the number of shares issuable upon exercise of this Warrant shall be proportionately adjusted such that the aggregate Exercise Price of this Warrant shall remain unchanged. Any adjustment made pursuant to this Section 3(a) shall become effective immediately after the record date for the determination of stockholders entitled to receive such dividend or distribution and shall become effective immediately after the effective date in the case of a subdivision, combination or re-classification.

b) Subsequent Rights Offerings. In addition to any adjustments pursuant to Section 3(a), if at any time the Company grants, issues or sells any Common Stock Equivalents or rights to purchase stock, warrants, securities or other property pro rata to all or substantially all of the record holders of shares of Common Stock (the "Purchase Rights"), then the Holder will be entitled to acquire, upon the terms applicable to such Purchase Rights, the aggregate Purchase Rights which the Holder could have acquired if the Holder had held the number of shares of Common Stock acquirable upon complete exercise of this Warrant (without regard to any limitations on exercise hereof, including without limitation, the Beneficial Ownership Limitation) immediately before the date on which a record is taken for the grant, issuance or sale of such Purchase Rights, or, if no such record is taken, the date as of which the record holders of shares of Common Stock are to be determined for the grant, issue or sale of such Purchase Rights; provided, however, to the extent that the Holder's right to participate in any such Purchase Right would result in the Holder exceeding the Beneficial Ownership Limitation, then the Holder shall not be entitled to participate in such Purchase Right to such extent (or beneficial ownership of such shares of Common Stock as a result of such Purchase Right to such extent) and such Purchase Right to such extent shall be held in abeyance for the Holder until such time, if ever, as its right thereto would not result in the Holder exceeding the Beneficial Ownership Limitation.

c) Pro Rata Distributions. During such time as this Warrant is outstanding, if the Company shall declare or make any dividend or other distribution of its assets (or rights to acquire its assets) to all or substantially all holders of shares of Common Stock, by way of return of capital or otherwise (including, without limitation, any distribution of cash, stock or other securities, property or options by way of a dividend, spin off, reclassification, corporate rearrangement, scheme of arrangement or other similar transaction) (a "Distribution"), at any time after the issuance of this Warrant, then, in each such case, except to the extent an adjustment was already made pursuant to Section 3(a), the Holder shall be entitled to participate in such Distribution to the same extent that the Holder would have participated therein if the Holder had held the number of shares of Common Stock acquirable upon complete exercise of this Warrant (without regard to any limitations on exercise hereof, including without limitation, the Beneficial Ownership Limitation)

immediately before the date of which a record is taken for such Distribution, or, if no such record is taken, the date as of which the record holders of shares of Common Stock are to be determined for the participation in such Distribution; provided, however, to the extent that the Holder's right to participate in any such Distribution would result in the Holder exceeding the Beneficial Ownership Limitation, then the Holder shall not be entitled to participate in such Distribution to such extent (or in the beneficial ownership of any shares of Common Stock as a result of such Distribution to such extent) and the portion of such Distribution shall be held in abeyance for the benefit of the Holder until such time, if ever, as its right thereto would not result in the Holder exceeding the Beneficial Ownership Limitation.

d) Fundamental Transaction. If, at any time while this Warrant is outstanding, (i) the Company, directly or indirectly, in one or more related transactions effects any merger or amalgamation or consolidation of the Company with or into another Person, (ii) the Company, directly or indirectly, effects any sale, lease, license, assignment, transfer, conveyance or other disposition of all or substantially all of its assets in one or a series of related transactions, (iii) any, direct or indirect, purchase offer, tender offer or exchange offer (whether by the Company or another Person) is completed pursuant to which holders of Common Stock are permitted to sell, tender or exchange their shares for other securities, cash or property and has been accepted by the holders of 50% or more of the outstanding Common Stock or 50% or more of the voting power of the common equity of the Company, (iv) the Company, directly or indirectly, in one or more related transactions effects any reclassification, reorganization or recapitalization of the Common Stock or any compulsory share exchange pursuant to which the Common Stock is effectively converted into or exchanged for other securities, cash or property, or (v) the Company, directly or indirectly, in one or more related transactions consummates a share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) with another Person or group of Persons whereby such other Person or group acquires more than 50% of the outstanding shares of Common Stock (not including any shares of Common Stock held by the other Person or other Persons making or party to, or associated or affiliated with the other Persons making or party to, such share purchase agreement or other business combination) (each a "Fundamental Transaction"), then, upon any subsequent exercise of this Warrant, the Holder shall have the right to receive, for each Warrant Share that would have been issuable upon such exercise immediately prior to the occurrence of such Fundamental Transaction, at the option of the Holder (without regard to any limitation in Section 2(e) on the exercise of this Warrant), the number of shares of Common Stock of the successor or acquiring corporation or of the Company, if it is the surviving corporation or is otherwise the continuing corporation, and any additional consideration (together, the "Alternate Consideration") receivable as a result of such Fundamental Transaction by a holder of the number of shares of Common Stock for which this Warrant is exercisable immediately prior to such Fundamental Transaction (without regard to any limitation in Section 2(e) on the exercise of this Warrant). For purposes of any such exercise, the determination of the Exercise Price shall be appropriately adjusted to apply to such Alternate Consideration based on the amount of Alternate Consideration issuable in respect of one shares of Common Stock in such Fundamental Transaction, and the Company shall apportion the Exercise Price among the Alternate Consideration in a reasonable manner reflecting the relative value of any different components of the Alternate Consideration. If holders of Common Stock are given any choice as to the securities, cash or property to be received in a Fundamental Transaction, then the Holder shall be given the same choice as to the Alternate Consideration it receives upon any exercise of this Warrant following such Fundamental Transaction.

The Company shall cause any successor entity in a Fundamental Transaction in which the Company is not the survivor (the "Successor Entity") to assume in writing all of the obligations of the Company under this Warrant in accordance with the provisions of this Section 3(d) pursuant to written agreements prior to such Fundamental Transaction and shall, at the option of the Holder, deliver to the Holder in exchange for this Warrant a security of the Successor Entity evidenced by a written instrument substantially similar in form and substance to this Warrant which is exercisable for a corresponding number of shares or other securities of such Successor Entity (or its parent entity) equivalent to the shares of Common Stock acquirable and receivable upon exercise of this Warrant (without regard to any limitations on the exercise of this Warrant) prior to such Fundamental Transaction, and with an exercise price which applies the exercise price hereunder to such shares of or other securities (but taking into account the relative value of the shares of Common Stock pursuant to such Fundamental Transaction and the value of such shares or securities, such number of shares or securities and such exercise price being for the purpose of protecting the economic value



of this Warrant immediately prior to the consummation of such Fundamental Transaction). Upon the occurrence of any such Fundamental Transaction, the Successor Entity shall succeed to, and be substituted for (so that from and after the date of such Fundamental Transaction, the provisions of this Warrant referring to the "Company" shall refer instead to the Successor Entity), and may exercise every right and power of the Company and shall assume all of the obligations of the Company under this Warrant with the same effect as if such Successor Entity had been named as the Company herein. For the avoidance of doubt, the Holder shall be entitled to the benefits of the provisions of this Section 3(d) regardless of (i) whether the Company has sufficient authorized shares of Common Stock for the issuance of Warrant Shares and/or (ii) whether a Fundamental Transaction occurs prior to the date of exercise.

e) Calculations. All calculations under this Section 3 shall be made to the nearest cent or the nearest 1/100th of a share, as the case may be. For purposes of this Section 3, the number of shares of Common Stock deemed to be issued and outstanding as of a given date shall be the sum of the number of shares of Common Stock (excluding treasury shares, if any) issued and outstanding.

f) Notice to Holder.

i. Adjustment to Exercise Price. Whenever the Exercise Price is adjusted pursuant to any provision of this Section 3, the Company shall promptly deliver to the Holder by facsimile or email a notice setting forth the Exercise Price after such adjustment and any resulting adjustment to the number of Warrant Shares and setting forth a brief statement of the facts requiring such adjustment.

ii. Notice to Allow Exercise by Holder. If (A) the Company shall declare a dividend (or any other distribution in whatever form) on the Common Stock, (B) the Company shall declare a special nonrecurring cash dividend on or a redemption of the Common Stock, (C) the Company shall authorize the granting to all holders of the Common Stock rights or warrants to subscribe for or purchase any shares of the Company or of any rights, (D) the approval of any stockholders of the Company shall be required in connection with any reclassification of the Common Stock, any consolidation or merger, amalgamation or arrangement to which the Company is a party, any sale or transfer of all or substantially all of the assets of the Company, or any compulsory share exchange whereby the Common Stock is converted into other securities, cash or property, or (E) the Company shall authorize the voluntary or involuntary dissolution, liquidation or winding up of the affairs of the Company, then, in each case, the Company shall cause to be delivered by facsimile or email to the Holder at its last facsimile number or email address as it shall appear upon the Warrant Register of the Company, at least 20 calendar days prior to the applicable record or effective date hereinafter specified, a notice stating (x) the date on which a record is to be taken for the purpose of such dividend, distribution, redemption, rights or warrants, or if a record is not to be taken, the date as of which the holders of the Common Stock of record to be entitled to such dividend, distributions, redemption, rights or warrants are to be determined or (y) the date on which such reclassification, consolidation, merger, amalgamation, arrangement, sale, transfer or share exchange is expected to become effective or close, and the date as of which it is expected that holders of the Common Stock of record shall be entitled to exchange their shares of Common Stock for securities, cash or other property deliverable upon such reclassification, consolidation, merger, amalgamation, arrangement sale, transfer or share exchange; provided that the failure to deliver such notice or any defect therein or in the delivery thereof shall not affect the validity of the corporate action required to be specified in such notice. To the extent that any notice provided in this Warrant constitutes, or contains, material, non-public information regarding the Company or any of its subsidiaries (the "Subsidiaries"), the Company shall simultaneously file such notice with the Commission pursuant to a Current Report on Form 8-K. The Holder shall remain entitled to exercise this Warrant during the period commencing on the date of such notice to the effective date of the event triggering such notice except as may otherwise be expressly set forth herein.

Section 4.        Transfer of Warrant.

a)        Transferability. This Warrant and all rights hereunder are transferable, in whole or in part, upon surrender of this Warrant at the principal office of the Company or its designated agent, together with a written assignment of this Warrant substantially in the form attached hereto duly executed by the Holder or its agent or attorney and funds sufficient to pay any transfer taxes payable upon the making of such transfer. Upon such surrender and, if required, such payment, the Company shall execute and deliver a new Warrant or Warrants in the name of the assignee or assignees, as applicable, and in the denomination or denominations specified in such instrument of assignment, and shall issue to the assignor a new Warrant evidencing the portion of this Warrant not so assigned, and this Warrant shall promptly be cancelled. Notwithstanding anything herein to the contrary, the Holder shall not be required to physically surrender this Warrant to the Company unless the Holder has assigned this Warrant in full, in which case, the Holder shall surrender this Warrant to the Company within three (3) Trading Days of the date on which the Holder delivers an assignment form to the Company assigning this Warrant in full. This Warrant, if properly assigned in accordance herewith, may be exercised by a new holder for the purchase of Warrant Shares without having a new Warrant issued.

b)        New Warrants. This Warrant may be divided or combined with other Warrants upon presentation hereof at the aforesaid office of the Company, together with a written notice specifying the names and denominations in which new Warrants are to be issued, signed by the Holder or its agent or attorney. Subject to compliance with Section 4(a), as to any transfer which may be involved in such division or combination, the Company shall execute and deliver a new Warrant or Warrants in exchange for the Warrant or Warrants to be divided or combined in accordance with such notice. All Warrants issued on transfers or exchanges shall be dated the original Issue Date of this Warrant and shall be identical with this Warrant except as to the number of Warrant Shares issuable pursuant thereto.

c)        Warrant Register. The Company shall register this Warrant, upon records to be maintained by the Company for that purpose (the "Warrant Register"), in the name of the record Holder hereof from time to time. The Company may deem and treat the registered Holder of this Warrant as the absolute owner hereof for the purpose of any exercise hereof or any distribution to the Holder, and for all other purposes, absent actual notice to the contrary.

Section 5.        Miscellaneous.

a)        No Rights as Stockholder Until Exercise. This Warrant does not entitle the Holder to any voting rights, dividends or other rights as a stockholder of the Company prior to the exercise hereof as set forth in Section 2(d)(i), except as expressly set forth in Section 3. Without limiting any rights of a Holder to receive Warrant Shares on a "cashless exercise" pursuant to Section 2(c) or to receive cash payments pursuant to Section 2(d)(i) and Section 2(d)(iv), in no event, including if the Company is for any reason unable to issue and deliver Warrant Shares upon exercise of this Warrant as required pursuant to the terms thereof, shall the Company be required to net cash settle an exercise of this Warrant.

b)        Loss, Theft, Destruction or Mutilation of Warrant. The Company covenants that upon receipt by the Company of evidence reasonably satisfactory to it of the loss, theft, destruction or mutilation of this Warrant or any stock certificate relating to the Warrant Shares, and in case of loss, theft or destruction, of indemnity or security reasonably satisfactory to it (which shall in no event include the posting of any bond), and upon surrender and cancellation of such Warrant or stock certificate, if mutilated, the Company shall make and deliver a new Warrant or stock certificate of like tenor and dated as of such cancellation, in lieu of such Warrant or stock certificate.

c)        Saturdays, Sundays, Holidays, etc. If the last or appointed day for the taking of any action or the expiration of any right required or granted herein shall not be a Trading Day, then, such action may be taken or such right may be exercised on the next succeeding Trading Day.

d)        Authorized Shares.

The Company covenants that, during the period the Warrant is outstanding, it will reserve from its authorized and unissued Common Stock a sufficient number of shares to provide for the issuance of the Warrant Shares upon the exercise of any purchase rights under this Warrant. The Company further covenants that its issuance of this Warrant shall constitute full authority to its officers who are charged with the duty of issuing the necessary Warrant Shares upon the exercise of the purchase rights under this Warrant. The Company shall take all such reasonable action as may be necessary to assure that such Warrant Shares may be issued as provided herein without violation of any applicable law or regulation, or of any requirements of the Trading Market upon which the Common Stock may be listed or quoted for trading. The Company covenants that all Warrant Shares which may be issued upon the exercise of the purchase rights represented by this Warrant will, upon exercise of the purchase rights represented by this Warrant and payment for such Warrant Shares in accordance herewith, be duly authorized, validly issued, fully paid and non-assessable and free from all taxes, liens and charges created by the Company in respect of the issue thereof (other than taxes in respect of any transfer occurring contemporaneously with such issue).

Except and to the extent as waived or consented to by the Holder, the Company shall not by any action, including, without limitation, amending its certificate of incorporation or through any reorganization, transfer of assets, consolidation, merger, amalgamation, arrangement dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such actions as may be necessary or appropriate to protect the rights of Holder as set forth in this Warrant against impairment. Without limiting the generality of the foregoing, the Company shall (i) not increase the par value of any Warrant Shares above the amount payable therefor upon such exercise immediately prior to such increase in par value, (ii) take all such action as may be necessary or appropriate in order that the Company may validly and legally issue fully paid and non-assessable Warrant Shares upon the exercise of this Warrant and (iii) use commercially reasonable efforts to obtain all such authorizations, exemptions or consents from any public regulatory body having jurisdiction thereof, as may be, necessary to enable the Company to perform its obligations under this Warrant.

Before taking any action which would result in an adjustment in the number of Warrant Shares for which this Warrant is exercisable or in the Exercise Price, the Company shall obtain all such authorizations or exemptions thereof, or consents thereto, as may be necessary from any public regulatory body or bodies having jurisdiction thereof.

e) Governing Law. All questions concerning the construction, validity, enforcement and interpretation of this Warrant shall be governed by and construed and enforced in accordance with the internal laws of the State of New York, without regard to the principles of conflict of laws thereof. Each party agrees that all legal Proceedings concerning the interpretation, enforcement and defense of this Warrant shall be commenced in the state and federal courts sitting in the City of New York, Borough of Manhattan (the "New York Courts"). Each party hereto hereby irrevocably submits to the exclusive jurisdiction of the New York Courts for the adjudication of any dispute hereunder or in connection herewith or with any transaction contemplated hereby or discussed herein (including with respect to the enforcement of any provision hereunder), and hereby irrevocably waives, and agrees not to assert in any suit, action or Proceeding, any claim that it is not personally subject to the jurisdiction of such New York Courts, or such New York Courts are improper or inconvenient venue for such Proceeding. If any party shall commence an action or Proceeding to enforce any provisions of this Warrant, then the prevailing party in such action or Proceeding shall be reimbursed by the other party for its attorneys' fees and other costs and expenses incurred in the investigation, preparation and prosecution of such action or Proceeding. Notwithstanding the foregoing, nothing in this paragraph shall limit or restrict the federal district court in which a Holder may bring a claim under the federal securities laws.

f) Restrictions. The Holder acknowledges that the Warrant Shares acquired upon the exercise of this Warrant, if such issuance is not registered, and the Holder does not utilize cashless exercise, will have restrictions upon resale imposed by state and federal securities laws.

g) Nonwaiver and Expenses. No course of dealing or any delay or failure to exercise any right hereunder on the part of Holder shall operate as a waiver of such right or otherwise prejudice the Holder's rights, powers or remedies. No provision of this Warrant shall be construed as a waiver by the Holder of any rights which the Holder may have under the federal securities laws and the rules and regulations of the Commission thereunder. Without limiting any other provision of this Warrant, if the Company willfully and knowingly fails to comply with any provision of this Warrant, which results in any material damages to the Holder, the Company shall pay to the Holder such amounts as shall be sufficient to cover any costs and expenses including, but not limited to, reasonable attorneys' fees, including those of appellate Proceedings, incurred by the Holder in collecting any amounts due pursuant hereto or in otherwise enforcing any of its rights, powers or remedies hereunder.

h) Notices. Any and all notices or other communications or deliveries to be provided by the Holders hereunder including, without limitation, any Notice of Exercise, shall be in writing and delivered personally, by facsimile or by e-mail, or sent by a nationally recognized overnight courier service, addressed to the Company, at 6 Liberty Square, #2382, Boston, Massachusetts, Attention: Chief Financial Officer, facsimile number: [ ], email address: tom.fitzgerald@transcodetherapeutics.com, or such other facsimile number, email address or address as the Company may specify for such purposes by notice to the Holders. Any and all notices or other communications or deliveries to be provided by the Company hereunder shall be in writing and delivered personally, by facsimile, email or sent by a nationally recognized overnight courier service addressed to each Holder at the facsimile number, email address or address of such Holder appearing on the books of the Company. Any notice or other communication or deliveries hereunder shall be deemed given and effective on the earliest of (i) the time of transmission, if such notice or communication is delivered via facsimile at the facsimile number or e-mail at the e-mail address set forth in this Section prior to 5:30 p.m. (New York City time) on any date, (ii) the next Trading Day after the date of transmission, if such notice or communication is delivered via facsimile at the facsimile number or e-mail at the e-mail address set forth in this Section on a day that is not a Trading Day or later than 5:30 p.m. (New York City time) on any Trading Day, (iii) the second Trading Day following the date of mailing, if sent by U.S. nationally recognized overnight courier service, or (iv) upon actual receipt by the party to whom such notice is required to be given.

i) Limitation of Liability. No provision hereof, in the absence of any affirmative action by the Holder to exercise this Warrant to purchase Warrant Shares, and no enumeration herein of the rights or privileges of the Holder, shall give rise to any liability of the Holder for the purchase price of any Common Stock or as a stockholder of the Company, whether such liability is asserted by the Company or by creditors of the Company.

j) Remedies. The Holder, in addition to being entitled to exercise all rights granted by law, including recovery of damages, will be entitled to specific performance of its rights under this Warrant. The Company agrees that monetary damages would not be adequate compensation for any loss incurred by reason of a breach by it of the provisions of this Warrant and hereby agrees to waive and not to assert the defense in any action for specific performance that a remedy at law would be adequate.

k) Successors and Assigns. Subject to applicable securities laws, this Warrant and the rights and obligations evidenced hereby shall inure to the benefit of and be binding upon the successors and permitted assigns of the Company and the successors and permitted assigns of Holder. The provisions of this Warrant are intended to be for the benefit of any Holder from time to time of this Warrant and shall be enforceable by the Holder or holder of Warrant Shares.

l) Amendment. This Warrant may be modified or amended or the provisions hereof waived with the written consent of the Company, on the one hand, and the Holder on the other hand.

m) Severability. Wherever possible, each provision of this Warrant shall be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Warrant shall be prohibited by or invalid under applicable law, such provision shall be ineffective to the extent of such prohibition or invalidity, without invalidating the remainder of such provisions or the remaining provisions of this Warrant.

n) No Expense Reimbursement. The Holder shall no way be required the pay, or to reimburse the Company for, any fees or expenses of the Company's transfer agent in connection with the issuance or holding or sale of the Common Stock, Warrant and/or Warrant Shares. The Company shall solely be responsible for any and all such fees and expenses.

o) Headings. The headings used in this Warrant are for the convenience of reference only and shall not, for any purpose, be deemed a part of this Warrant.

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*(Signature Page Follows)*

IN WITNESS WHEREOF, the Company has caused this Warrant to be executed by its officer thereunto duly authorized as of the date first above indicated.

**TRANSCODE THERAPEUTICS, INC.**

By: \_\_\_\_\_  
Name:  
Title:

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**NOTICE OF EXERCISE**

TO: TRANSCODE THERAPEUTICS, INC.

(1) The undersigned hereby elects to purchase \_\_\_\_\_ Warrant Shares of the Company pursuant to the terms of the attached Warrant (only if exercised in full), and tenders herewith payment of the exercise price in full, together with all applicable transfer taxes, if any.

(2) Payment shall take the form of (check applicable box):

in lawful money of the United States; or

the cancellation of such number of Warrant Shares as is necessary, in accordance with the formula set forth in subsection 2(c), to exercise this Warrant with respect to the maximum number of Warrant Shares purchasable pursuant to the cashless exercise procedure set forth in subsection 2(c).

(3) Please issue said Warrant Shares in the name of the undersigned or in such other name as is specified below:

\_\_\_\_\_

The Warrant Shares shall be delivered to the following DWAC Account Number:

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

[SIGNATURE OF HOLDER]

Name of Investing Entity: \_\_\_\_\_

*Signature of Authorized Signatory of Investing Entity:* \_\_\_\_\_

Name of Authorized Signatory: \_\_\_\_\_

Title of Authorized Signatory: \_\_\_\_\_

Date: \_\_\_\_\_



**ASSIGNMENT FORM**

*(To assign the foregoing Warrant, execute this form and supply required information. Do not use this form to purchase shares.)*

FOR VALUE RECEIVED, the foregoing Warrant and all rights evidenced thereby are hereby assigned to

Name: \_\_\_\_\_  
(Please Print)

Address: \_\_\_\_\_  
(Please Print)

Phone Number: \_\_\_\_\_

Email Address: \_\_\_\_\_

Dated: \_\_\_\_\_, \_\_\_\_\_

Holder's Signature: \_\_\_\_\_

Holder's Address: \_\_\_\_\_





February 1, 2023

TransCode Therapeutics, Inc.  
6 Liberty Square, #2382  
Boston, MA 02109

Re: Securities Registered under Registration Statement on Form S-1

We have acted as counsel to you in connection with your filing of a Registration Statement on Form S-1 (as amended or supplemented, the "Registration Statement") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), relating to the registration of the offering by TransCode Therapeutics, Inc., a Delaware corporation (the "Company"), of (i) up to 13,875,000 shares (the "Common Shares") of the Company's Common Stock, \$0.0001 par value per share (the "Common Stock"), including Common Shares purchasable by the underwriters upon their exercise of an over-allotment option granted to the underwriters by the Company or (ii) up to 13,875,000 pre-funded warrants (the "Warrants" and each share of Common Stock underlying a Pre-Funded Warrant, a "Warrant Share") to purchase 13,875,000 shares of Common Stock. The Common Shares and the Pre-Funded Warrant Shares are being sold to the several underwriters named in, and pursuant to, an underwriting agreement among the Company and such underwriters (the "Underwriting Agreement").

We have reviewed such documents and made such examination of law as we have deemed appropriate to give the opinions set forth below. We have relied, without independent verification, on certificates of public officials and, as to matters of fact material to the opinions set forth below, on certificates of officers of the Company. For purposes of the opinion set forth in numbered paragraph (iii), we have assumed that before the Warrant Shares are issued, the Company does not issue shares of Common Stock or reduce the total number of shares of Common Stock that the Company is authorized to issue under its certificate of incorporation such that the number of unissued shares of Common Stock authorized under the Company's certificate of incorporation is less than the number of Warrant Shares.

The opinions in numbered paragraphs (i) and (iii) set forth below are limited to the Delaware General Corporation Law and the opinion in numbered paragraph (ii), as to the Warrants constituting valid and binding obligations of the Company, are limited to the law of New York.

Based on the foregoing, we are of the opinion that (i) the Common Shares have been duly authorized and, when delivered and paid for in accordance with the terms of the Underwriting Agreement, will be validly issued, fully paid and non-assessable, (ii) when the Warrants are delivered and paid for in accordance with the Underwriting Agreement, assuming the due authorization, execution and delivery of such Warrants, the Warrants will constitute valid and binding obligations of the Company, and (iii) the Warrant Shares, when issued, sold and

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TransCode Therapeutics, Inc.

February 1, 2023

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paid for in accordance with the terms of the Warrants, will be validly issued, fully paid and non-assessable.

This opinion letter and the opinion it contains shall be interpreted in accordance with the Core Opinion Principles as published in 74 *Business Lawyer* 815 (Summer 2019).

We hereby consent to the inclusion of this opinion as Exhibit 5.1 to the Registration Statement and to the references to our firm under the caption "Legal Matters" in the Registration Statement. In giving our consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.

Very truly yours,  
/s/ GOODWIN PROCTER LLP  
GOODWIN PROCTER LLP

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List of Subsidiaries

None

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**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the use in the Prospectus constituting a part of this Registration Statement on Form S-1, of our report dated March 31, 2022, which includes an explanatory paragraph relating to Transcode Therapeutics, Inc.'s ability to continue as a going concern, relating to the financial statements of Transcode Therapeutics, Inc., which is contained in that Prospectus. We also consent to the reference to us under the caption "Experts" in the Prospectus.

/s/ WithumSmith+Brown, PC

East Brunswick, New Jersey  
February 1, 2023

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**Calculation of Filing Fee Tables**

**Form S-1**

(Form Type)

**TransCode Therapeutics, Inc.**

(Exact Name of Registrant as Specified in its Charter)

**Table 1: Newly Registered Securities**

	Security Type	Security Class	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price <sup>(1)(2)(5)</sup>	Fee Rate	Amount of Registration Fee
Fees to be Paid	Equity	Common Stock, \$0.0001 par value per share <sup>(5)</sup>	457(o)			\$11,500,000	0.0001102	\$1,267.30
Fees to be Paid	Equity	Pre-funded warrants to purchase Common Stock, \$0.0001 par value per share <sup>(3)</sup> <sup>(5)(6)</sup>	457(g)					
Fees to be Paid	Equity	Common Stock, \$0.0001 par value per share underlying the Pre-funded warrants <sup>(4)</sup> <sup>(5)(6)</sup>	Other					
Total Offering Amounts						\$11,500,000		\$1,267.30
Total Fees Previously Paid								\$0
Net Fee Due								\$1,267.30

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended (the "Securities Act").

(2) Includes the aggregate offering price of additional shares that the underwriter has the option to purchase pursuant to its over-allotment option.

(3) No registration fee is required pursuant to Rule 457(g) under the Securities Act.

(4) In addition to the common stock set forth in this table, pursuant to Rule 416 under the Securities Act, this registration statement also registers such indeterminate number of common stock as may become issuable upon exercise of the Pre-Funded Warrants.

(5) The proposed maximum aggregate offering price of the common stock proposed to be sold in the offering will be reduced on a dollar-for-dollar basis based on the offering price of any pre-funded warrants offered and sold in the offering, and as such the proposed maximum offering price of the common stock and pre-funded warrants (including the common stock issuable upon exercise of the pre-funded warrants) if any, is \$11,500,000.

(6) The registrant may issue pre-funded warrants to purchase common stock in the offering. The purchase price of each pre-funded warrant will equal the price per share at which shares of common stock are being sold to the public in this offering, minus \$0.01, which constitutes the pre-funded portion of the exercise price, and the remaining unpaid exercise price of the pre-funded warrant will equal \$0.01 per share (subject to adjustment as provided for therein).