

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2022

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO

Commission File Number 001-39485

TANGO THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

Delaware

(State or other jurisdiction of incorporation or organization)

201 Brookline Ave., Suite 901

Boston, MA

(Address of principal executive offices)

85-1195036

(I.R.S. Employer Identification No.)

02215

(Zip Code)

Registrant's telephone number, including area code: (857) 320-4900

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value \$0.001 per share	TNGX	Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES NO

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES NO

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES NO

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES NO

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

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 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES NO

As of June 30, 2022, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the shares of common stock on The Nasdaq Stock Market LLC on June 30, 2022, was approximately \$302.3 million.

As of March 20, 2023, the registrant had 88,203,478 shares of common stock, \$0.001 par value per share, outstanding.

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Summary of Material Risks Associated with Our Business

Our business is subject to numerous material and other risks that you should be aware of before making an investment decision. These risks are described more fully in Item 1A of this Annual Report on Form 10-K entitled “Risk Factors.” These risks include, among others, the following:

- We are a precision oncology company with a limited operating history. We have no products approved for commercial sale, have not generated any revenue from product sales and may never become profitable.
 - We have incurred significant net losses since our inception and anticipate that we will continue to incur losses for the foreseeable future. We expect our operating results to fluctuate significantly in the future as our business advances.
 - We will need to raise substantial additional funding. If we are unable to raise capital when needed or on terms acceptable to us, we would be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts.
 - We have never successfully completed any clinical trials and we may be unable to do so for any product candidates we develop. Certain of our programs are still in preclinical development and may never advance to clinical development.
 - Our programs are focused on the development of oncology therapeutics for patients with genetically defined or biomarker-driven cancers, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs is novel and may never lead to approved or marketable products.
 - If we are unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these product candidates. We will also rely on third-parties for screening for biomarkers that enable patient selection for trials.
 - Clinical product development involves a lengthy and expensive process, with an uncertain outcome. Further, our current and potential future collaborations may not realize the anticipated benefits.
 - Interim, top-line, and initial data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to confirmation, audit and verification procedures that could result in material changes in the final data.
 - Results from early preclinical studies of our programs and product candidates are not necessarily predictive of the results of later preclinical studies and clinical trials of our programs and product candidates. If we cannot replicate the results from our earlier preclinical studies of our programs and product candidates in our later preclinical studies and clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.
 - If we experience delays or difficulties in the initiation, enrollment or dosing of patients in clinical trials, the announcement of clinical trial results and our receipt of necessary regulatory approvals (if any) could be delayed or prevented.
 - Our clinical trials or those of our current or future collaborators may reveal significant adverse events not seen in our preclinical or nonclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.
 - Some of our product candidates modulate pathways for which there are currently no approved or effective therapies, and utilize novel binding locations, which may result in greater research and development expenses, regulatory issues that could delay or prevent approval, or discovery of unknown or unanticipated adverse effects.
 - If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.
-

- The COVID-19 pandemic, or a similar pandemic, epidemic, or outbreak of an infectious disease, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates and the initiation and completion of clinical trials.
- We expect to rely on third parties to conduct our clinical trials, as well as investigator-sponsored clinical trials of our product candidates (if any). If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.
- We contract with third parties for the manufacture of our product candidates for preclinical development and clinical trials and expect to continue to do so for future clinical testing and commercialization (if approved). This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- The third parties upon whom we rely for the supply of the active pharmaceutical ingredients and drug product to be used in our product candidates are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.
- If we cannot obtain new patents, maintain our existing patents and protect the confidentiality and proprietary nature of our trade secrets and other intellectual property, our business and competitive position may be harmed.
- If we are found to be infringing third party patents, we may be forced to pay damages to the patent owner and/or obtain a license to continue the manufacture, sale or development of our products. If we cannot obtain a license, we may be prevented from the manufacture, sale or development of our products or product candidates, which may adversely affect our business.

Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains express or implied forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Words such as "anticipates," "continue," "could," "may," "forecasts," "expects," "intends," "plans," "potentially," "believes," "seeks," "estimates," "predict," "target," and variations of such words and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements are not guarantees of future performance and are subject to certain risks, uncertainties, and assumptions that are difficult to predict; therefore, actual results may differ materially from those expressed or forecasted in any such statements. Such forward-looking statements are based on current expectations, estimates and projections about our industry and business, management's beliefs, and certain assumptions made by our management, and may include, but are not limited to, statements regarding:

- the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of IND filings, active enrollment in clinical trials, and initiation and completion of studies or clinical trials and related preparatory work, and the period during which the results of the clinical trials (including initial and final trial results) will become available;
- our ability to discover and develop product candidates efficiently (including the advancement of development candidates on the timelines identified and the ability to identify clinical trial investigators to use our product candidates in trials);
- our ability and the potential to manufacture our drug substances and product candidates successfully for preclinical use, for clinical trials and on a larger scale for commercial use, if approved;
- the ability and willingness of our third-party strategic collaborators to license and to continue research and development activities relating to our development candidates and product candidates;
- our ability to obtain funding for our operations necessary to complete further research, development and commercialization of our product candidates (and that existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements at least into 2025);
- our ability to obtain and, if approved, maintain regulatory approval of our product candidates;
- our ability to commercialize our products, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, and strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- estimates of our future expenses, capital requirements, and our need for additional financing;
- the potential benefits of strategic collaboration agreements, our ability to enter into strategic collaborations or arrangements, and our ability to attract collaborators with development, regulatory and commercialization expertise;
- future agreements with third parties in connection with the commercialization of product candidates (if approved) and any other approved products;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our financial performance, including the expectation that we will continue to incur operating losses and negative cash flow;
- the rate and degree of market acceptance of our product candidates, if approved;

- regulatory developments in the United States and foreign countries, including pricing regulations by U.S. (such as CMS) and foreign regulatory authorities;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our ability to produce our products or product candidates with advantages in turnaround times or manufacturing cost;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the impact of laws and regulations;
- developments relating to our competitors and industry;
- the effect of the on-going COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and clinical trials and any future studies or trials; and
- other risks and uncertainties, including those listed in this Annual Report on Form 10-K under the section titled “Risk Factors.”

The forward-looking statements contained in this Annual Report on Form 10-K are based on current expectations and beliefs concerning future developments and their potential effects on us. There can be no assurance that future developments affecting us will be those that we have anticipated. These forward-looking statements involve a number of risks, uncertainties (some of which are beyond our control) or other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements. These risks and uncertainties include, but are not limited to, those factors described under the heading “Risk Factors” in Item 1A of this Annual Report on Form 10-K. Should one or more of these risks or uncertainties materialize, or should any of our assumptions prove incorrect, actual results may vary in material respects from those projected in these forward-looking statements. Some of these risks and uncertainties may in the future be amplified by the COVID-19 outbreak and there may be additional risks that we consider immaterial or which are unknown. It is not possible to predict or identify all such risks. We do not undertake any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required under applicable securities laws.

Corporate Information

We were formerly known as BCTG Acquisition Corp. (“BCTG”) and were incorporated in Delaware May 2020 as a special purpose acquisition company, formed for the purpose of effecting a merger, capital stock exchange, asset acquisition, stock purchase, reorganization or other similar business. On August 10, 2021, we consummated the merger pursuant to the Agreement and Plan of Merger, dated as of April 13, 2021, by and among BCTG, BCTG Merger Sub Inc. and Tango Therapeutics Sub, Inc. Upon the consummation of the merger, we changed our name to “Tango Therapeutics, Inc.

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available through the “Investors” portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission (“SEC”). We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. Accordingly, investors should monitor such portions of the company’s website, in addition to following the company’s press releases, SEC filings and public conference calls and webcasts (if any). Information on our website is not to be deemed to be incorporated by reference in, and is not part of, this Annual Report on Form 10-K or any of our other securities filings, unless specifically incorporated herein by reference, and should not be relied upon in making a decision as to whether or not to purchase our common stock. Our filings with the SEC may be accessed through the SEC’s Interactive Data Electronic Applications system at <http://www.sec.gov>. All statements made in any of our securities filings, including all

forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Further, the company intends to use its website <http://www.tangotx.com> as a means of disclosing material non-public information and for complying with its disclosure obligations under the SEC Regulation FD. Such disclosures will be included on the company's website under the heading "Investors." Accordingly, investors should monitor such portions of the company's website, in addition to following the company's press releases, SEC filings and public conference calls and webcasts (if any). The information contained on, or that may be accessed through, the website is not part of, and is not incorporated into, this Annual Report on Form 10-K.

Our principal executive office is located at 201 Brookline Avenue, Suite 901, Boston, Massachusetts.

USE OF DEFINED TERMS IN THIS ANNUAL REPORT ON FORM 10-K

Unless the context otherwise requires in this Annual Report on Form 10-K for the year ended December 31, 2022 we use the following defined terms:

- i. "2022 Annual Report" means this Annual Report on Form 10-K for the year ended December 31, 2022;
- ii. "the Company", "we", "our" and "us" mean Tango Therapeutics, Inc. and its wholly-owned subsidiaries;
- iii. "CoREST" means Co-repressor of Repressor Element-1 Silencing Transcription;
- iv. "CSF" means cerebrospinal fluid
- v. "Gilead" means Gilead Sciences, Inc.;
- vi. "GBM" means glioblastoma;
- vii. "HRD+" means homologous recombination deficient;
- viii. "MPNST" means malignant peripheral nerve sheath tumors;
- ix. "MTA" means methylthioadenosine;
- x. "MTAP" means methylthioadenosine phosphorylase;
- xi. "NSCLC" means non-small cell lung cancer;
- xii. "PDX" means patient-derived xenograft
- xiii. "PRMT5" means protein arginine methyltransferase 5;
- xiv. "SAM" means S-adenosyl-L-methionine;
- xv. "SDMA" means symmetric di-methylation of specific arginine
- xvi. "STK11" means serine-threonine kinase 11; and
- xvii. "USP1" means ubiquitin-specific protease 1.

PART I

Item 1. Business.

Overview

Tango Therapeutics was founded with a clear mission: discover the next generation of precision medicines to help patients with cancer through addressing the specific genetic alterations that fuel the cancer. We leverage our state-of-the-art target discovery platform to identify novel targets and develop new drugs directed at tumor suppressor gene loss in defined patient populations with high unmet medical need. Tumor suppressor gene loss remains a largely unaddressed target space specifically because these genetic events cannot be directly targeted. Our novel small molecules are designed to be selectively active in cancer cells with specific tumor suppressor gene loss, killing those cancer cells while sparing normal cells. We also are extending this target space beyond the classic, cell-autonomous effects of tumor suppressor gene loss to include the discovery of novel targets that reverse the effects of tumor suppressor gene loss that prevent the immune system from recognizing and killing cancer cells (immune evasion). We believe our approach will provide the ability to deliver the deep, sustained target inhibition necessary to optimize tumor response and clinical benefit as a result of the unique ability of synthetic lethal targeting to spare normal cells.

Our lead program, TNG908, is an MTA-cooperative inhibitor of PRMT5 designed to work selectively in cancer cells with an MTAP deletion. MTAP-deletion occurs in approximately 10% to 15% of all human tumors including NSCLC, mesothelioma, pancreatic cancer, cholangiocarcinoma and GBM. In preclinical studies, TNG908 demonstrated 15-fold greater potency in MTAP-deleted cancer cells versus normal cells and robust efficacy in vitro and in vivo. Patients are actively being enrolled in the Phase 1/2 clinical trial and we expect to provide an update on the ongoing dose escalation portion of the trial, focusing on proof-of-mechanism, in the second quarter of 2023.

Given the large number of patients with MTAP-deleted cancers who may benefit from a PRMT5 inhibitor, and the resulting business opportunity, we also developed a next-generation PRMT5 inhibitor, TNG462, with increased potency, MTAP-deletion selectivity, as well as longer target coverage. TNG462 is 45 times more potent in cells with an MTAP deletion than those without and induces deep tumor regressions in preclinical models of multiple cancer types which is expected to significantly increase the therapeutic index. The clinical development path for TNG462 is expected to be similar to TNG908, evaluating safety and efficacy in multiple tumor types in a Phase 1/2 clinical trial. GBM will be excluded from the clinical trial as TNG462 is not expected to cross the blood-brain barrier. We expect to initiate the Phase 1/2 clinical trial for TNG462 in mid-2023.

Discovered as part of our immune evasion target discovery platform, TNG260 is a first-in-class, CoREST inhibitor, which has shown to reverse the immune evasion effect of STK11 loss-of-function mutations. STK11 loss-of-function mutations are present in approximately 15% of NSCLC, 15% of cervical, 10% of carcinoma of unknown primary, 5% of breast and 3% of pancreatic cancers. In syngeneic models with an STK11 mutation and an intact immune system, the combination of TNG260 with an anti-PD-1 antibody resulted in sustained complete tumor regressions and the induction of immune memory against re-implantation of tumors. We plan to file an IND for TNG260 in the first half of 2023. We expect that TNG260 will be among the first oncology molecules to leverage the benefits of genetically-based patient selection (STK11-mutation) with checkpoint inhibitor therapy.

We are developing TNG348, a novel allosteric inhibitor of USP1 for treatment of BRCA1 and BRCA2-mutant and other HRD+ cancers. BRCA1 or BRCA 2 mutations are present in approximately 15% of ovarian cancers, 10% of breast cancers, 10% of prostate cancers, 5% of endometrial cancers and 5% of pancreatic cancers and additionally, BRCA wild-type HRD+ mutations are present in approximately 40% of ovarian, 15% of breast, 3% of prostate and 2% of pancreatic cancers. In vivo preclinical studies for TNG348 have shown single agent efficacy and combination benefit with PARP inhibitors in BRCA1, BRCA2-mutant and other HRD+ cell-line and patient derived xenografts, including those that are intrinsically resistant to PARP inhibition. These preclinical data further demonstrate that TNG348 is synergistic with PARP inhibition across a panel of human ovarian and breast cancer cell lines, including both PARP inhibitor sensitive and resistant models. Clinically, we expect TNG348 to have single agent activity in PARP inhibitor -naïve and PARP inhibitor-resistant BRCA1/2 mutant and other HRD+ cancers, and to synergize with PARP inhibitors. We expect to file an IND for this program in mid-2023.

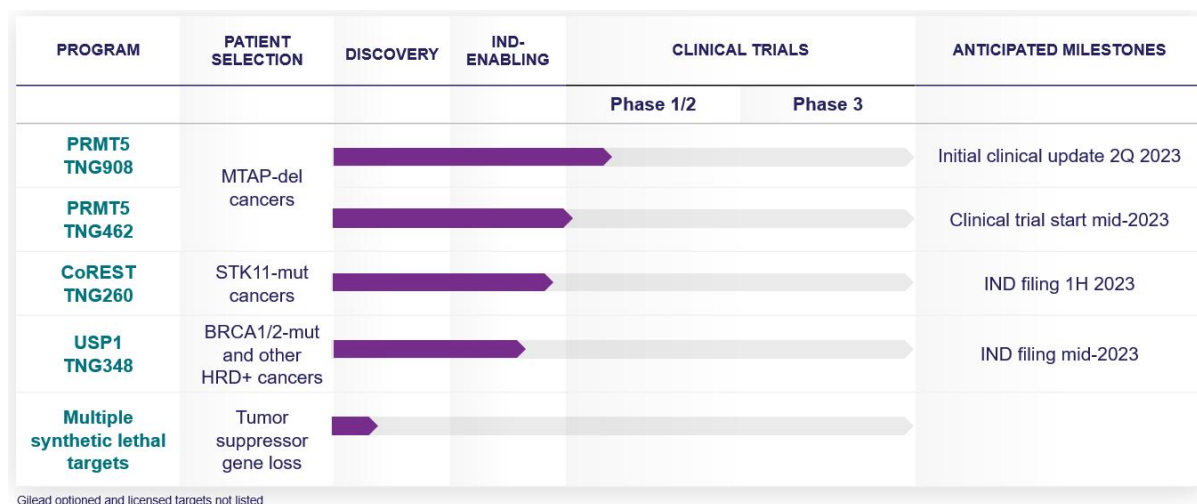
In October 2018, we entered into a collaboration agreement with Gilead (Gilead Agreement), which was expanded in August 2020. Our immune evasion platform is the foundation for this collaboration. Under the Gilead Agreement, we work together to identify and develop novel immune evasion targets by leveraging our proprietary functional genomics-based

discovery platform. To date, Gilead has licensed two programs and has extended their option on two programs. Our collaboration with Gilead excludes PRMT5, CoREST and USP1 programs as well as a growing pipeline of novel targets identified in our non-immune based target discovery screens. We retain the right to identify and validate targets outside the scope of our collaboration with Gilead, which includes all cell autonomous targets except those discovered in immune evasion contexts, and to develop and commercialize products directed to such targets on our own or in collaboration with third parties. See “— Collaboration and License Agreements — Collaboration and License Agreement with Gilead Sciences” for additional information.

Our Pipeline

We are leveraging the power and productivity of our discovery engine to discover and validate multiple novel targets each year. Our growing pipeline consists of discovery programs for multiple cancer types with limited treatment options as summarized in Figure 1.

Figure 1. Tango Therapeutics' product pipeline



Our Strategy

We are pioneering novel approaches to the discovery and development of innovative precision oncology therapies. We leverage the following core strategic components, enabling bold thinking in pursuit of transformative therapies for patients with cancer:

- Advance TNG908, our MTA-cooperative PRMT5 inhibitor that is synthetic lethal with MTAP deletion, into the clinic in multiple indications with high unmet need
- Maximize the opportunity to help patients with MTAP-deleted cancers and increase our strategic optionality with our next-generation PRMT5 inhibitor, TNG462, that has improved potency and selectivity compared to TNG908 in preclinical models
- Bring one of the first immunotherapy programs within genetically-defined patients into the clinic in STK11-mutant cancers with TNG260
- Advance our USP1 inhibitor, TNG348, into clinical development in multiple BRCA1/2-mutant and other HRD+ cancers
- Discover and drug the next generation of synthetic lethal precision oncology targets to continue to grow our pipeline
- Opportunistically evaluate and maximize the value of strategic collaborations to bring more medicines to patients, accelerate development timelines and explore combination therapy approaches for our product candidates

BACKGROUND

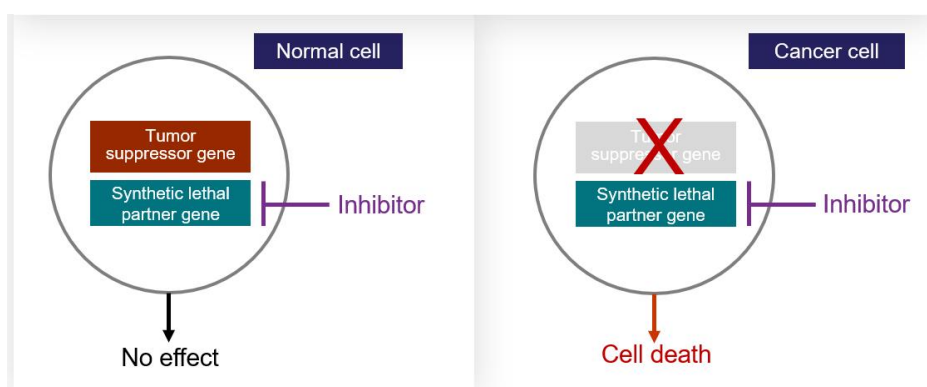
Unmet need of cancers caused by tumor suppressor gene loss

Many genetic drivers of cancer have been well-characterized but have not been directly targeted due to their molecular structure (undruggable oncogenes) or functional loss (tumor suppressor genes). Tumor suppressor gene loss represents a significant portion of the many genetic alterations that drive the formation of cancers but it remains a largely unaddressed target space. Targeting tumor suppressor gene loss directly is not possible because they are deleted or inactivated, and the immune evasion effects of tumor suppressor gene loss has only recently been described. We are using the concept of synthetic lethality to address the unmet medical need of these large groups of patients characterized by tumor suppressor gene loss and activation of immune evasion genes.

Synthetic lethality to address tumor suppressor gene loss

Synthetic lethal therapies for cancer refers to pairs of genes where one is inactivated by a genetic alteration and the other is inhibited pharmacologically. While genetic alterations give rise to the development of cancer, they also create a unique vulnerability that can be exploited therapeutically. Biologically, such vulnerability can be the inability of cancer cells to respond to a specific signal, such as DNA damage or cell cycle arrest, or the inability to remodel chromatin or to maintain cellular homeostasis. The unique advantage of a synthetic lethal approach to cancer therapy is that normal cells are not vulnerable to the synthetic lethal drug target and are largely unaffected at drug doses where the mutant cancer cells are selectively killed, noted in Figure 2 below. The recent success of PARP inhibitors in BRCA-mutant breast, ovarian and prostate cancers is the first clinical example of using synthetic lethality to target tumor suppressor gene loss.

Figure 2. In cancer cells, when a tumor suppressor gene is lost, it creates a genetic vulnerability that allows an inhibitor to target a synthetic lethal partner gene causing cell death. This selective killing only occurs in cancer cells with tumor suppressor loss, therefore largely sparing the normal cells. Therefore, these synthetic lethality targets inherently can offer a wide therapeutic index.



Moreover, we plan to use the tumor suppressor gene loss as a patient selection marker for clinical trial enrollment to ensure we are enrolling the patients most likely to benefit from each new drug candidate. We believe this approach should enable efficient clinical development and increase the probability of success with maximum clinical benefit for the patient.

Our immune evasion platform

Our synthetic lethal target discovery approach can be adapted to identify druggable targets that do not kill cancer cells directly, but rather attract immune cells to destroy them. Our immune evasion target discovery platform was designed to incorporate immuno-oncology therapies with genetically-defined patient populations to maximize clinical benefit. We are addressing the unmet medical need of this large group of patients by identifying novel immune evasion genes that (i) are activated by tumor suppressor gene loss and (ii) the effects of which can be reversed through inhibition with a small molecule. In the first step, we perform an *in vivo* CRISPR-based screen using immune cell-mediated cell killing as the readout. This first step allows us to identify tumor suppressor genes linked to immune evasion. For the second step, we repeat

the in vivo CRISPR screen in animals with an intact immune system looking for potential drug targets that reverse the immune evasion effects of the tumor suppressor gene deletion.

OUR PROGRAMS

PRMT5 inhibitors

Overview

We are currently developing TNG908 and TNG462, potent and selective oral small molecule MTA-cooperative inhibitors of PRMT5, which are designed to be synthetic lethal with MTAP deletion. Current preclinical data suggest the PRMT5-MTAP synthetic lethal interaction is one of the strongest and most prevalent synthetic lethal interactions in human cancers and represents a subset of synthetic lethality termed collateral lethality. This synthetic lethal interaction occurs when MTAP is co-deleted as a “passenger” with the frequently deleted tumor suppressor gene, CDKN2A (p16). The synthetic lethality occurs because MTAP-deleted cells accumulate the PRMT5 inhibitory factor MTA. As a result, PRMT5 is partially inhibited in MTAP-deleted cells, making those cells more sensitive than normal cells to further inhibition of PRMT5 activity.

Taking advantage of this unique interaction between PRMT5 inhibition and MTAP deletion requires that the inhibitors have a specific binding mechanism called MTA cooperativity. TNG908 and TNG462 bind cooperatively with MTA to inhibit PRMT5 function by blocking access to the PRMT5 active site for both protein substrates and the activating PRMT5 co-factor SAM. This MTA-cooperative binding mechanism allows selective inhibition of PRMT5 in tumor cells that have lost MTAP (MTAP-null) while being relatively inert in normal cells without MTAP deletion (MTAP WT). We believe TNG908 and TNG462 are differentiated from non-MTA-cooperative PRMT5 inhibitors as a result of this mechanism of action. This approach is expected to result in a large therapeutic window in patients with MTAP-deleted tumors, potentially limiting toxicity and leading to meaningful clinical responses.

We are developing TNG908 for the treatment of patients with solid tumors with homozygous MTAP deletion (10- 15% of all human tumors) including NSCLC, mesothelioma, pancreatic cancer, cholangiocarcinoma and GBM. In preclinical studies, TNG908 has 15-fold greater selectivity for MTAP-null cancer cells over MTAP WT cells, strong anti-tumor effects in vivo, and pharmacokinetics that support its potential to be a leading PRMT5 inhibitor if approved. The FDA granted TNG908 Fast Track designation to TNG908 and additionally, the granted Orphan Drug Designations to TNG908 for the treatment of MPNST and malignant glioma, including GBM. We are actively dosing patients in the Phase 1/2 clinical trial and we expect to provide an update on the ongoing dose escalation portion of the trial, focusing on proof-of-mechanism, in the second quarter of 2023.

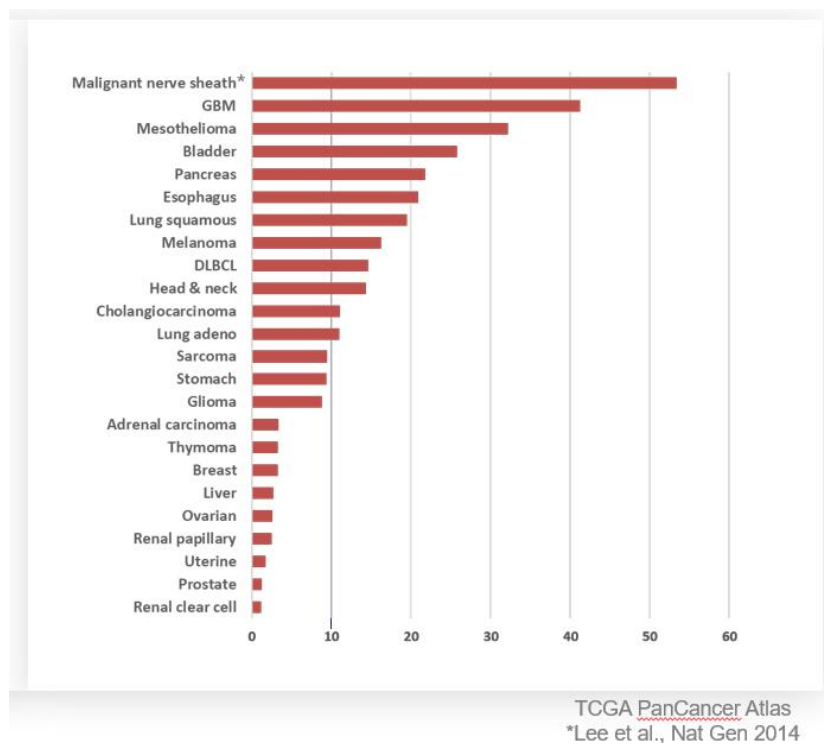
We also are developing TNG462, a more potent and selective PRMT5 inhibitor with improved pharmacokinetic properties as compared to TNG908. We believe additional potency may allow stronger target inhibition and thus clinical efficacy, and additional selectivity for MTAP-deleted cells may provide a wider therapeutic index. In the first quarter of 2023, the FDA cleared the IND for the Phase 1/2 trial and granted Fast Track designation to TNG462. We expect to initiate a Phase 1/2 clinical trial in mid-2023. The trial, which will require all patients to have a homozygous MTAP deletion, will evaluate cancers including NSCLC, mesothelioma and cholangiocarcinoma. Unlike TNG908, GBM will be excluded from the clinical trial as TNG462 is not expected to cross the blood-brain barrier.

By advancing both TNG908 and TNG462 into the clinic, we not only maximize the opportunity to help patients with MTAP-deleted cancers but also increase our strategic optionality to develop and potentially commercialize a PRMT5 inhibitor. We look forward to emerging data from these trials to optimize our development and commercialization plans for these programs.

MTAP-deletion frequency in multiple solid tumor types

A partial deletion of chromosome 9p21, driven by loss of the tumor suppressor gene CDKN2A, is the most common homozygous deletion in human cancer. MTAP is adjacent to CDKN2A and is lost along with it in 80-90% of CDKN2A-deleted tumors, thus MTAP is one of the most commonly deleted genes across all cancer types. Based on The Cancer Genome Atlas (TCGA) data and data from a 2014 publication by Lee et al, there are at least 15 cancer types where MTAP loss occurs in more than 10% of patients, including approximately 10% of non-squamous NSCLC, 20% of squamous NSCLC, 25% of bladder cancers, 30% to 55% of MPNST and 40% of GBM. Given that we believe this is a large and important opportunity for patients with cancer, we are developing both TNG908 and TNG462.

Figure 3. The frequency of MTAP deletion across tumor types as determined from analysis of TCGA and an indication specific publication



PRMT5 mechanism of action

PRMT5 has long been a therapeutic target of interest for cancer given its role in regulating proteins involved in multiple essential cellular functions, including RNA splicing, cell cycling, cell death, and metabolic signaling. PRMT5 is a protein arginine methyltransferase that modifies the activity of these proteins, which are critical for growth and viability of both normal and cancer cells.

PRMT5 methylates target proteins by removing a methyl group from SAM, the co-factor and methyl donor which is necessary for PRMT5 activity, and transferring that methyl group to a specific residue on target proteins. This methyl modification, or “mark,” alters the function of the target protein, thereby regulating the cell processes for which the protein is important.

The function of PRMT5 is regulated in several ways, including by the endogenous inhibitor MTA. MTA directly competes with SAM for binding to the PRMT5 active site but does not have a methyl donor. Thus, when present, MTA inhibits PRMT5 function.

MTA-cooperative PRMT5 inhibition as a novel synthetic lethal mechanism in cancers with MTAP-deletion

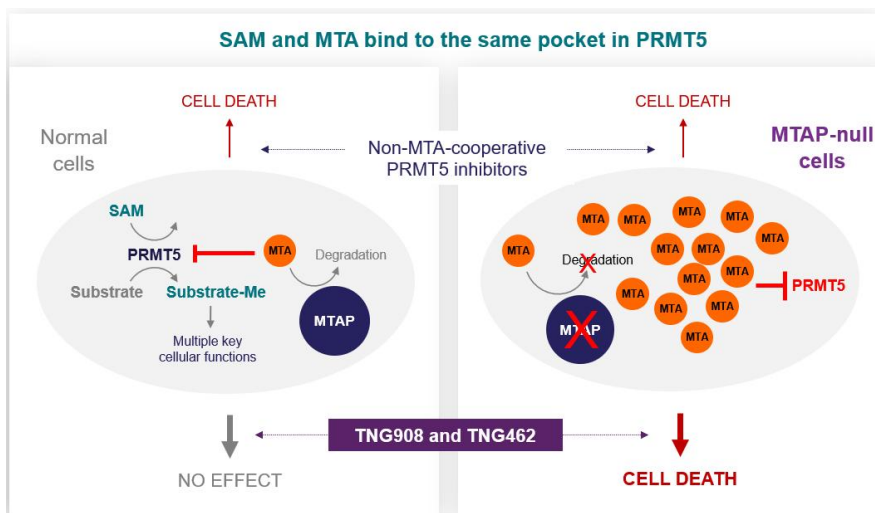
Our differentiated approach with TNG908 and TNG462

The challenge for PRMT5 inhibitors that are not MTA-cooperative is that they kill rapidly growing normal cells (bone marrow cells in particular) as effectively as cancer cells and therefore the level of inhibition needed to kill cancer cells is reduced by on-target, dose-limiting bone marrow toxicity. To address this problem, we designed TNG908 and TNG462 to be selectively active (synthetic lethal) in cancer cells that have a homozygous deletion of MTAP, which is not deleted in normal cells.

TNG908 and TNG462 bind PRMT5 cooperatively with MTA, whereas the non-MTA-cooperative PRMT5 inhibitors previously evaluated in clinical trials are either SAM-cooperative or SAM-competitive. In normal cells (MTAP WT), MTA is rapidly degraded by MTAP. When MTAP is deleted in cancer cells, intracellular MTA is markedly elevated compared to normal cells (Figures 4 and 5 below). TNG908 and TNG462 preferentially bind PRMT5 in the presence of MTA and “lock” the enzyme into the inactive state which prevents PRMT5 from methylating target proteins critical for cell survival. As a

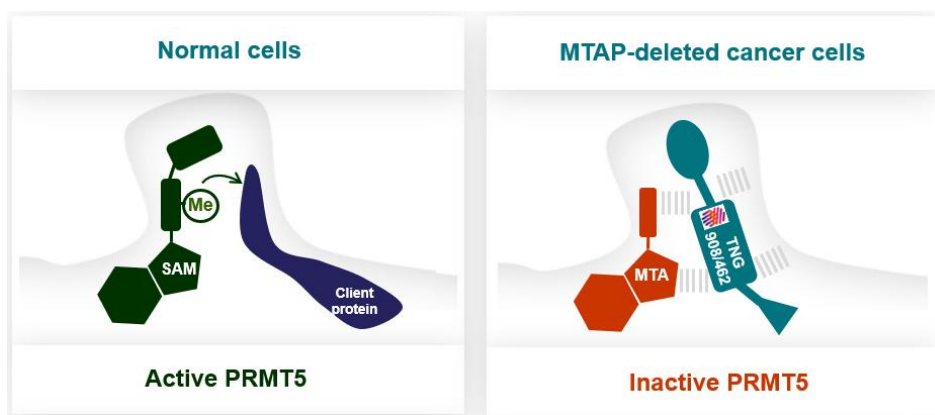
result, TNG908 and TNG462 selectively kill MTAP-deleted tumor cells with elevated MTA levels while sparing normal cells.

Figure 4. Schematic of PRMT5 and MTAP functions



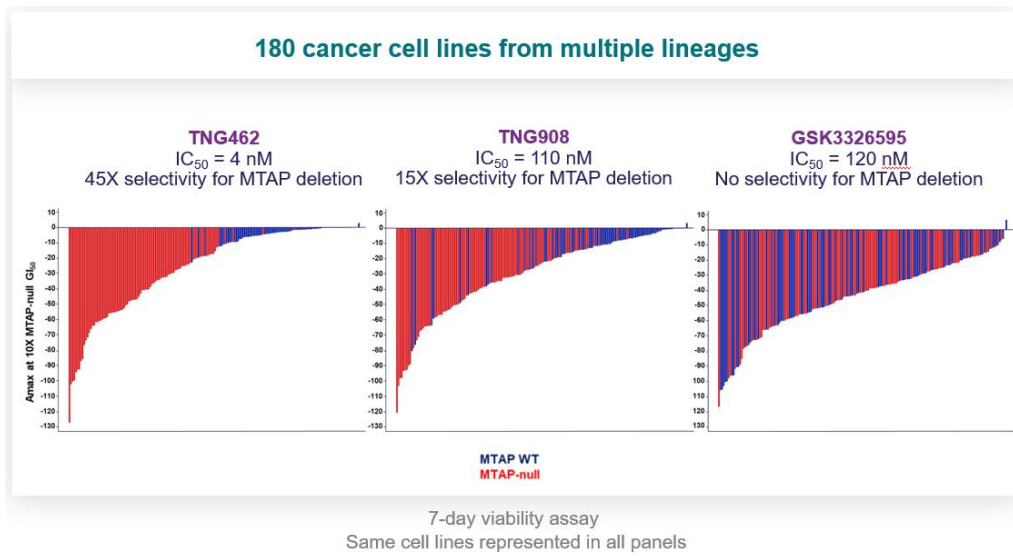
PRMT5 is an essential enzyme for all cell types, and MTAP deletion in cancer cells results in tumor specific sensitivity to PRMT5 inhibition. MTA-cooperative PRMT5 inhibitors, such as TNG908 and TNG462, may provide a wide therapeutic index by preferentially inhibiting PRMT5 in MTAP-deleted cancer cells, while relatively sparing normal tissue.

Figure 5. TNG908 and TNG462 have an MTA-cooperative mechanism of action that is selective for MTAP-deleted cancer cells



We compared the potency and selectivity of TNG908 and TNG462 to a non-MTA-cooperative PRMT5 inhibitor, GSK3326595, in a panel of 180 cancer cell lines representing multiple histologies, including NSCLC, bladder cancer, pancreatic cancer, mesothelioma, cancers of the central nervous system, leukemia and lymphoma. TNG908 and TNG462 demonstrated significant MTAP-selective inhibition of viability, while GSK3326595 showed no selectivity for MTAP-null cell lines over MTAP WT (Figure 6).

Figure 6. TNG462 and TNG908 demonstrate strong MTAP selectivity in 180 cancer cell lines as compared to GSK3326595



PRMT5 catalyzes SDMA residues of substrate proteins, a modification that can be detected and quantified by SDMA-specific antibodies as a direct measurement of PRMT5 activity. Therefore, SDMA quantification can be used as a pharmacodynamic biomarker for PRMT5 inhibitors. TNG908 and TNG462 both inhibit PRMT5 90-100% in the MTAP-null HAP1 cell line with marked selectivity over the MTAP WT cell line (Figure 7). The degree of PRMT5 inhibition and selective viability are consistent with data generated in isogenic xenograft models that differ only by presence or absence of the MTAP gene (Figure 8).

Figure 7. PRMT5 inhibition by TNG908 and TNG462 is dose-dependent and MTAP-selective. *In vitro* in-cell western data demonstrating dose-dependent reduction of SDMA levels after 24 hours of TNG908 or TNG462 treatment in HAP1 MTAP-isogenic cancer cell lines

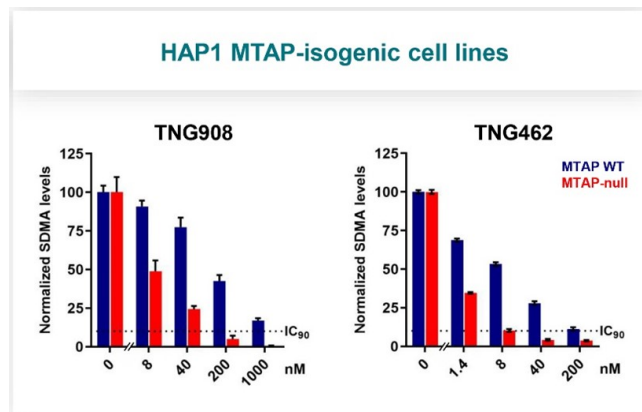
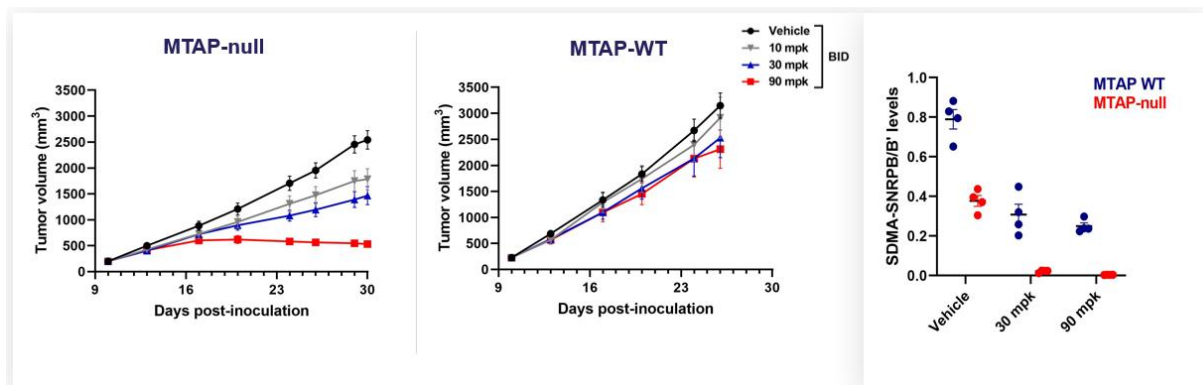


Figure 8. TNG908 demonstrates strong, MTAP-selective anti-tumor activity in xenograft models. TNG908 selectively inhibits PRMT5 in MTAP-null cancer in vivo



PRMT5 preclinical data overview

TNG908 and TNG462 are both highly selective for PRMT5 against a panel of 38 methyltransferases at 10 μ M, showing they do not inhibit any other methyltransferases, even well above the predicted clinical efficacious exposure range. Both TNG908 and TNG462 have excellent drug-like properties and are formulated for oral administration. Dose-dependent PRMT5 inhibition and anti-tumor efficacy have been shown in MTAP-null xenograft models, which demonstrate that both molecules suppress tumor growth in an on-target manner.

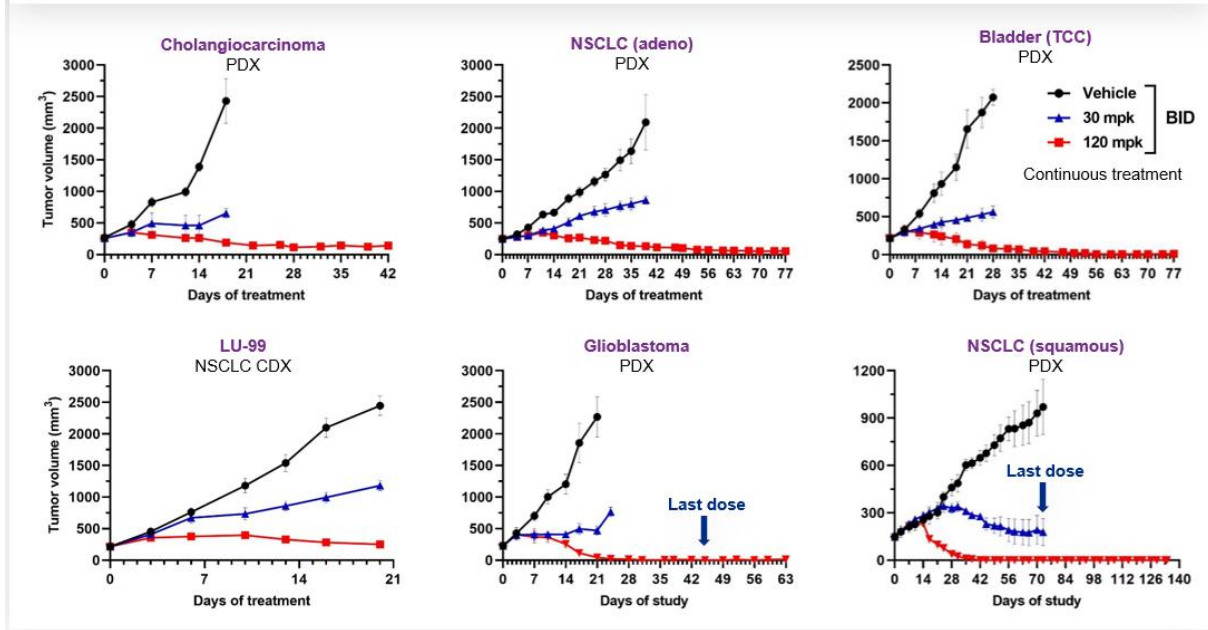
TNG908 and TNG462 drive dose-dependent, on-target, anti-tumor activity including deep and durable regressions in MTAP-null xenograft models regardless of histology. TNG462 has demonstrated increased potency and MTAP-deletion selectivity as compared to TNG908. Additionally, due to improved pharmacokinetic properties, TNG462 will be dosed once daily in the Phase 1/2 clinical trial.

TNG908 preclinical data summary

In our preclinical studies, TNG908 demonstrated 15-fold greater potency in MTAP-deleted cancer cells versus normal cells and robust efficacy in vitro and in vivo. Consistent with these findings, TNG908 demonstrated significant and dose-dependent anti-tumor activity in over 50 xenograft models representing multiple tumor lineages (sample data shown in Figure 9) that did not have a bias to specific histologies. These histology-agnostic responses included strong and durable regressions in a number of models including PDX models of cholangiocarcinoma, NSCLC, bladder cancer and GBM. Notably, in both the NSCLC (squamous) and GBM PDX models shown in Figure 9, complete responses were observed while on TNG908-treatment and maintained when therapy was discontinued in all mice (NSCLC-squamous PDX) and in 4/5 mice (GBM PDX).

Figure 9. TNG908 demonstrates strong anti-tumor activity with regressions in MTAP-deleted xenograft models

TNG908 IC50 110 nM, 15X selectivity for MTAP deletion

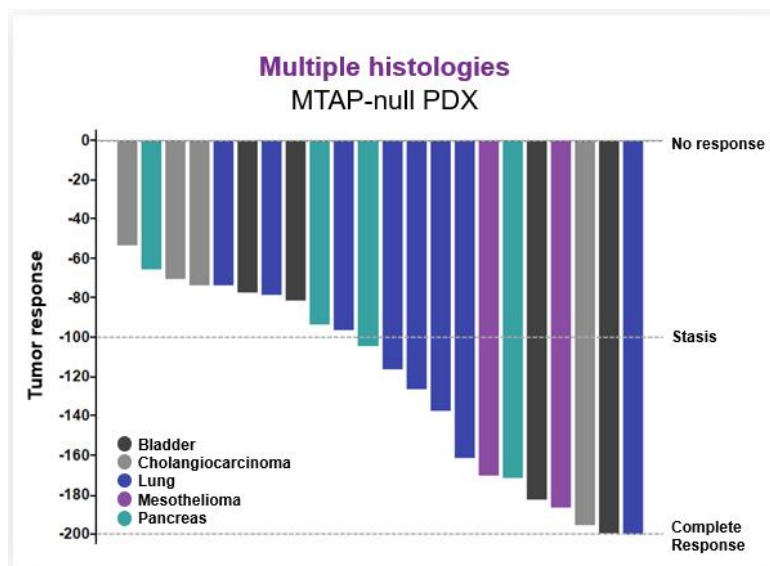


In preclinical non-human primate studies, TNG908 has exposure in CSF that is equivalent to plasma when corrected for protein-binding. In addition to the strong anti-tumor activity demonstrated in subcutaneous MTAP-null GBM xenograft models, we also have shown strong efficacy and prolonged survival in a GBM xenograft model that was inoculated in the brain. We believe these data uniquely position TNG908 as a potential treatment option for patients with MTAP-deleted tumors of the central nervous system (CNS), including GBM and CNS metastases of MTAP-deleted solid tumors.

TNG462 preclinical data summary

TNG462 has the same mechanism of action as TNG908 with improved potency and selectivity in MTAP-deleted cancer cell lines. In preclinical studies, TNG462 is 45 times more selective for MTAP-deleted cells (3-fold greater than TNG908) and 28 times more potent than TNG908, which may translate to a wider therapeutic index and stronger target inhibition than TNG908. TNG462 has improved pharmacokinetic properties relative to TNG908 that support once daily dosing in the clinic. Similar to TNG908, TNG462 drives strong anti-tumor activity without bias towards any specific histology. Deep and durable regressions were demonstrated in PDX models derived from cholangiocarcinoma, mesothelioma, lung, bladder and pancreatic cancer (sample data shown in Figure 10). In the preclinical models, TNG462 treatment also suppresses tumor growth even after removal of therapy in a NSCLC (squamous) PDX model.

Figure 10. TNG462 demonstrates strong anti-tumor activity with regressions in MTAP-deleted xenograft models



Preclinical combination data

While we expect TNG908 and TNG462 both will show strong single-agent efficacy, we plan to evaluate these molecules clinically in combination with other agents in the future. Based on strong preclinical data showing significant in vivo combination benefit, combinations of potential interest include CDK4/6, MAT2A, and KRAS inhibitors and potentially other oncogene-targeted therapies.

- Essentially all MTAP-deleted tumors also have a CDKN2A deletion and CDKN2A deletion may sensitize cancers to CDK4/6 inhibition, thus combining TNG462 or TNG908 with a CDK4/6 inhibitor may further enhance the clinical benefit of either inhibitor alone. We have demonstrated the efficacy of this combination in preclinical in vivo studies.
- MAT2A inhibitors reduce intracellular levels of the activating PRMT5 co-factor, SAM, and increase the ratio of MTA to SAM in MTAP-deleted cells. Strong synergy has been demonstrated preclinically with both TNG908 and TNG462 with a MAT2A inhibitor, suggesting that this could be a beneficial clinical combination in MTAP-deleted tumors.
- Approximately 30% of MTAP-deleted lung adenocarcinomas and 85% of MTAP-deleted pancreatic adenocarcinomas are also KRAS-mutant, therefore combining TNG908 or TNG462 with a KRAS inhibitor in these patients may have clinical benefit. Preclinical in vivo studies further support testing these combinations in clinical trials.

Planned clinical trials

TNG908 Phase 1/2

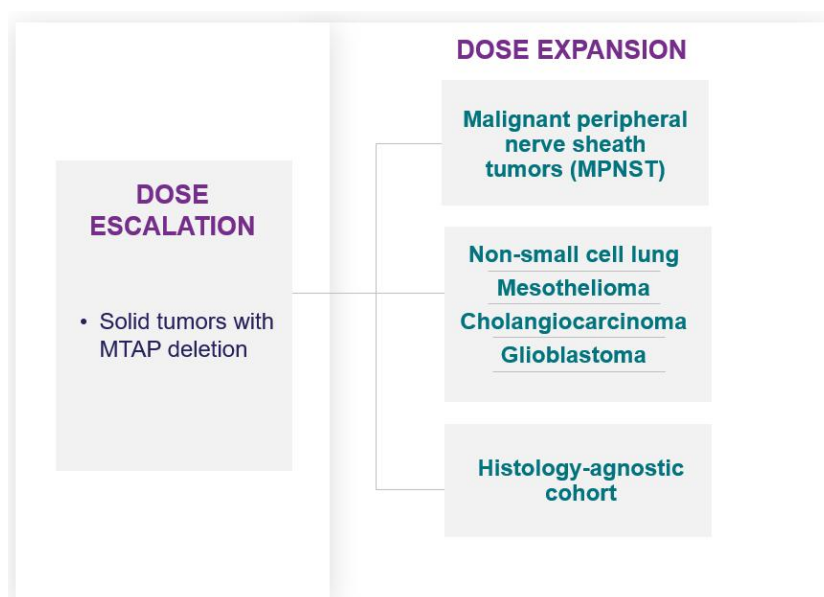
The Phase 1/2 first-in-human trial is evaluating the oral administration of TNG908 monotherapy in patients with MTAP-deleted tumors (See Figure 11 below). As TNG908 is designed to selectively inhibit PRMT5 in cancers with MTAP deletion, we are limiting enrollment to patients with MTAP-deleted cancers.

We are actively enrolling patients in the dose escalation phase and evaluating safety, pharmacokinetics and pharmacodynamics and efficacy in patients with locally advanced or metastatic solid tumors of any histology with an MTAP deletion. Following determination of the optimal efficacious dose, we will evaluate the efficacy of TNG908 in multiple histology-specific expansion arms including MPNST, NSCLC, mesothelioma, cholangiocarcinoma and GBM. In parallel, we will enroll a histology-agnostic cohort to provide optionality for a registration strategy in all tumors regardless of histology if broad activity is observed. Given that MTAP deletion is common in multiple indications, we may expand into additional histology-specific cohorts based on activity observed in the Phase 1/2 trial.

The indication specific cohorts were selected based on the unmet medical need for new therapies in prevalent histologies, including NSCLC, mesothelioma, cholangiocarcinoma and GBM, as well as indications where there are limited treatment options with no standard of care such as MPNST.

In the first quarter of 2022, the FDA cleared the IND for the Phase 1/2 trial and granted Fast Track designation to TNG908. We are actively enrolling patients in the Phase 1/2 clinical trial of TNG908. Based on a recent protocol amendment, GBM patients will be added to the ongoing trial. We expect to provide an update on the ongoing dose escalation portion of the trial, focusing on the proof-of-mechanism, in the second quarter of 2023.

Figure 11. TNG908 First-in-human trial schema.



TNG462 Phase 1/2

In the first quarter of 2023, the FDA cleared the IND for the Phase 1/2 trial and granted Fast Track designation to TNG462. We plan to initiate a Phase 1/2 clinical trial in mid-2023. The clinical trial for TNG462 is similar to the TNG908 trial, wherein all cancers must have an MTAP deletion. Similar to TNG908, the dose expansion portion of the clinical trial will include a histology-agnostic cohort. Unlike TNG908, GBM patients will be excluded from the clinical trial as TNG462 is not expected to cross the blood-brain barrier.

TNG260, CoREST-Selective Inhibitor

Overview

CoREST was discovered as a drug target with the potential to reverse the immune evasion associated with STK11 mutations using our immune evasion target discovery platform. This platform uses high throughput in vivo CRISPR-based target discovery screens to identify druggable targets that do not kill cancer cells directly, but rather attract immune cells to destroy them in the context of specific tumor suppressor gene loss.

TNG260 is a novel small molecule inhibitor of the CoREST deacetylase complex that reverses checkpoint inhibitor resistance in STK11 mutant preclinical models. TNG260 is being developed in combination with an anti-PD-1 antibody and is designed to reverse immune evasion in STK11-mutant cancers, with the aim of restoring sensitivity to immune checkpoint inhibition. In preclinical studies, selective CoREST inhibition by TNG260 in combination with an anti-PD-1 antibody resulted in complete regressions in ~60% of mice as a result of the transcriptional reprogramming of STK11-mutant tumor cells. In STK11-mutant cancers, TNG260 directly alters tumor cell cytokine secretion, markedly reduces recruitment of immune suppressive T regulatory cells, upregulates components of the antigen presentation machinery as well as PD-L1 on the tumor cell surface, which together lead to a more immunogenic tumor microenvironment. Preclinically, TNG260 in combination with an anti-PD-1 antibody resulted in complete tumor regressions and prevented regrowth in STK11-mutant

tumors, inducing immune memory. STK11 loss-of-function mutations occur in approximately 15% of NSCLC, 15% of cervical, 10% carcinoma of unknown primary, 5% of breast and 3% of pancreatic cancers. We plan to file an IND for TNG260 in the first half of 2023.

Mechanism of action

STK11 mutant cancers have several key features that contribute to an immune checkpoint resistant tumor microenvironment, including low PD-L1 expression, low T effector cell infiltration, and high levels of immune suppressor T regulatory cells. Treatment with an immune checkpoint inhibitor, such as anti-PD-1, is not sufficient to overcome the immune evasive environment of STK11-mutant tumors, leading to very limited clinical response in these patients. Inhibition of the CoREST complex by TNG260 has been shown to lead to changes in expression of immune-related genes that favor a more active immune environment. For example, TNG260 treatment leads to increased expression of CXCL9, CXCL10, and CXCL11, which are cytokines responsible for recruiting T effector cells, therefore increasing the anti-tumor immune response when combined with anti-PD-1 antibody. Additionally, the combination of TNG260 with an anti-PD-1 antibody in preclinical studies leads to decreased expression of CCL1 and CCL22, which are chemokines responsible for recruiting immune suppressive regulatory T cells to the tumor environment. Together, this leads to an uncoupling of the levels of T effector and regulatory T cells in the tumor, which contributes to a more active immune microenvironment and re-sensitization to anti-PD-1 treatment.

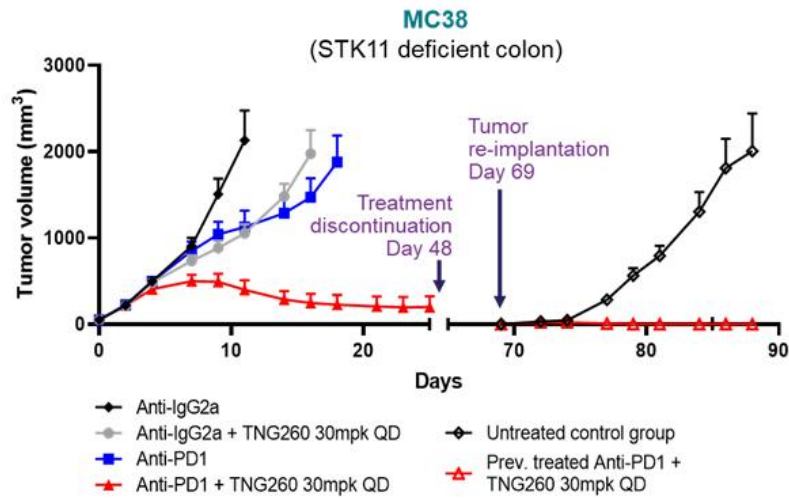
Target discovery

Our state-of-the-art in vivo CRISPR discovery platform enabled the discovery of STK11 as a tumor suppressor gene that drives immune evasion when not functional in cancer cells. We engineered a syngeneic mouse tumor model in which STK11 loss-of-function drives resistance to immune checkpoint blockade. Applying our in vivo CRISPR screen in this STK11 loss-of-function model, HDAC1 was identified as a target that reversed anti-PD-1 resistance caused by STK11 deletion. Though HDAC1 is a component of three major regulatory complexes, we observed that TNG260 is highly selective and only inhibits the CoREST complex and spares the other two complexes (Sin3 and NuRD).

Preclinical data summary

In preclinical models, TNG260 demonstrated strong genetic and pharmacologic validation showing reprogramming of the tumor microenvironment and strong sensitization to anti-PD-1 therapy in STK11-deficient tumor models. In a syngeneic mouse tumor model where STK11 mutations drive resistance to immune checkpoint blockade, CoREST inhibition by TNG260 in combination with an anti-PD-1 antibody resulted in complete tumor regressions in five out of eight treated mice. Treatment was stopped on Day 48 and the five of eight mice that were completely tumor-free at that time remained tumor-free for 21 days with no further treatment. Furthermore, when tumor cells were re-implanted in these mice on day 69, they were rejected, compared to a treatment-naïve group of animals where tumors grew as expected. This demonstrated the induction of immune memory in the animals with complete responses to TNG260 with anti-PD-1 antibody (Figure 12).

Figure 12: Pharmacologic proof-of-concept for CoREST inhibition in STK11 mutant MC38 mice with TNG260 in combination with an anti-PD-1 antibody

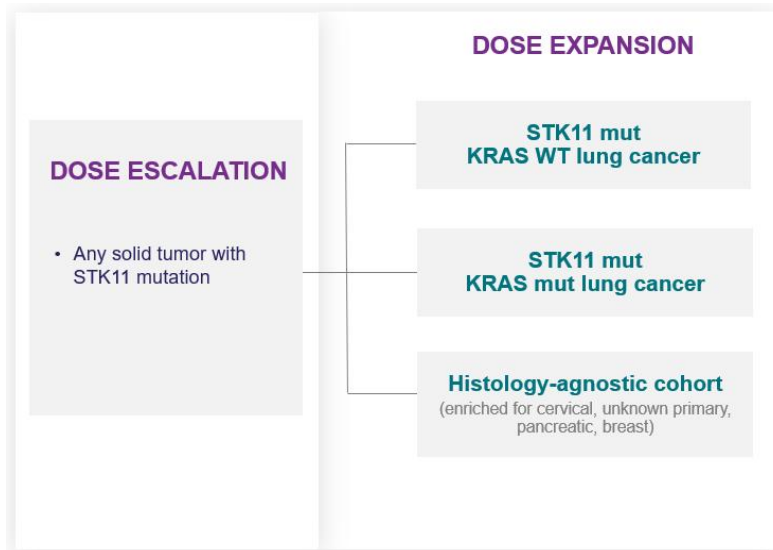


Planned clinical trials

Our Phase 1/2 first-in-human trial of TNG260 will evaluate the oral administration of TNG260 in combination with pembrolizumab (anti-PD-1 antibody) in patients with STK11-mutant solid tumors (Figure 12). As TNG260 is designed to work in combination with anti-PD-1 antibodies in tumors with STK11 loss, enrollment will be limited to patients with STK11 mutated tumors.

The dose escalation phase of this clinical trial will evaluate safety, pharmacokinetics, pharmacodynamics, and efficacy of TNG260 in combination with pembrolizumab in patients with locally advanced or metastatic cancer of any solid tumor histology with an STK11 mutation. Since efficacy with TNG260 requires combination with an anti-PD-1 antibody, TNG260 will be evaluated in combination with pembrolizumab. Following determination of the optimal efficacious dose, we will evaluate the efficacy of TNG260 plus pembrolizumab in indication-specific expansion arms including STK11 mutated NSCLC. In parallel, we will enroll a solid tumor, histology-agnostic cohort including cervical, pancreatic and breast cancer as well as carcinoma of unknown primary. We plan to file an IND for TNG260 in the first half of 2023.

Figure 12. TNG260 in combination with pembrolizumab first-in-human trial schema



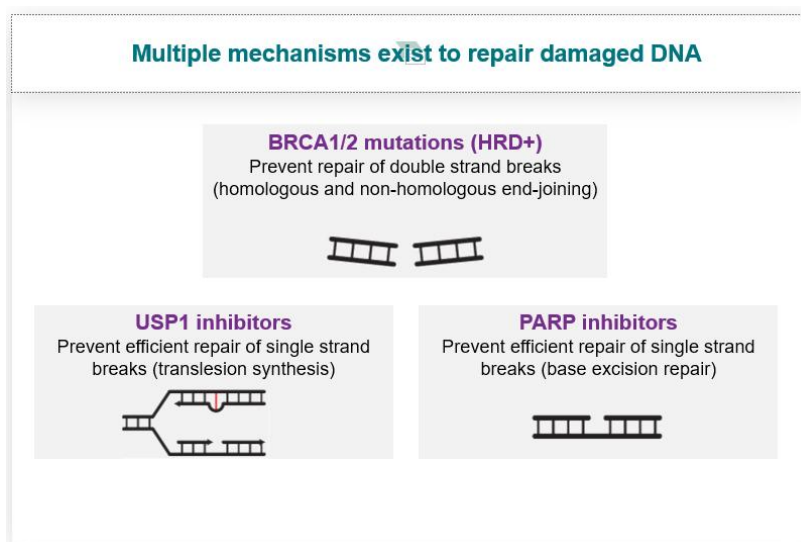
Overview

TNG348 is a novel allosteric inhibitor of USP1 for treatment of BRCA-mutant and other HRD+ cancers. USP1 was initially identified as a strong synthetic lethal target for BRCA1 loss-of-function using CRISPR-based screens in a panel of BRCA1-mutant versus wild-type cancer cell lines. In vivo preclinical studies of TNG348 have shown single agent efficacy and combination benefit with PARP inhibitors in BRCA1, BRCA2-mutant and other HRD+ cell-line and patient derived xenografts, including those that are intrinsically resistant to PARP inhibitors. These preclinical data further demonstrate that TNG348 is synergistic with PARP inhibition across a panel of human ovarian and breast cancer cell lines, including both PARP inhibitor sensitive and resistant models. Clinically, we expect TNG348 to have both single agent activity and combination benefit with PARP inhibitors in PARP inhibitor-naïve and PARP inhibitor-resistant BRCA1/2 mutant cancers and other HRD+ cancers. As such, USP1 has the potential to treat a patient population that is at least comparable in size to the PARP inhibitor market. BRCA1 or BRCA2 mutations are present in approximately 15% of ovarian cancers, 10% of breast cancers, 10% of prostate cancers, 5% of endometrial cancers and 5% of pancreatic cancers and additionally, BRCA wild-type HRD+ mutations are present in approximately 40% of ovarian, 15% of breast, 3% of prostate and 2% of pancreatic cancers. We expect to file an IND for TNG348 in mid-2023.

Mechanism of action

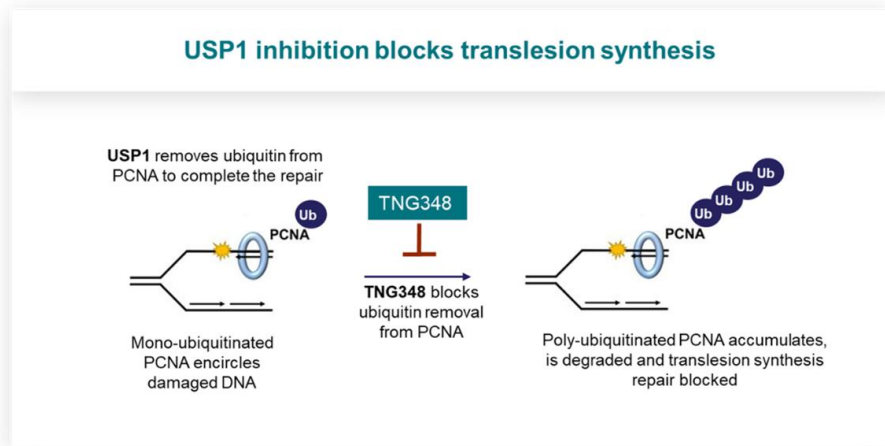
While normal cells have multiple mechanisms to repair damaged DNA and prevent the associated cell death, tumors with BRCA1/2 mutations lack one of those mechanisms, the ability to repair double strand breaks. BRCA1/2 mutant and other HRD+ cancers rely in part on translesion synthesis (TLS) and base excision repair (BER) for DNA damage repair and cell survival. USP1 and PARP inhibitors exploit these dependencies by preventing efficient translesion synthesis and base excision repair respectively (See Figure 18). Clinically, blocking DNA damage repair to induce cancer cell death is a validated therapeutic strategy in oncology as exemplified by PARP inhibitors for the treatment of BRCA1/2 mutant cancers.

Figure 13. Overview of DNA damage repair mechanism and how genetic alterations causing homologous recombination deficiency, such as BRCA1/2 loss, leads to a dependency on translesion synthesis (USP1) and base excision repair (PARP) pathways



USP1 is a deubiquitinating enzyme (DUB) that co-localizes with PCNA to DNA replication forks to ensure high-fidelity DNA replication. When mono-ubiquitinated PCNA (ub-PCNA) encounters DNA damage, USP1 removes ubiquitin from PCNA, switching synthesis to low fidelity TLS polymerases for gap filling and repair (See Figure 14). By inhibiting USP1, TNG348 blocks the ubiquitin removal from PCNA, driving PCNA poly-ubiquitination and degradation. This results in incomplete translesion synthesis repair. Ultimately, the replication stress induced by USP1 inhibition leads to decreased DNA synthesis, cell cycle arrest, and induction of cell death as detailed in our recent peer reviewed publication (Antione et al. Molecular Cancer Therapeutics, 2023).

Figure 14. TNG348 blocks an important DNA damage repair pathway known as translesion synthesis. By inhibiting USP1 activity, TNG348 prevents the posttranslational modification of PCNA required to bypass DNA damage using low fidelity TLS polymerases for gap filling and repair



Preclinical data summary

The DNA damage repair pathways regulated by USP1 are not currently targeted by any marketed drug. Based on genome-wide CRISPR-Cas9 screens in the presence of our USP1 inhibitors, we validated that the activity of TNG348 converges on ubiquitination of PCNA, which represent a highly differentiated mechanism relative to other DNA damage repair enzyme inhibitors, including PARP inhibitors (Figures 13 and 14). Based on in vitro cell line profiling and ex vivo studies in patient-derived organoid cultures, we expect TNG348 to have both single agent activity and combination benefit with PARP inhibitors in PARP inhibitor-naïve and PARP inhibitor-resistant cancers. (See Figure 15 and Figure 16). Because USP1 inhibition blocks TLS and PARP inhibition blocks BER, the drug combination is highly synergistic resulting in tumor regression in multiple patient-derived xenograft models that are not sensitive to either single agent alone (Figure 17).

Figure 15. TNG348 profiling using 7-14 day clonogenic assays across a panel of sixty-one breast and ovarian cancer cell lines, including BRCA1/2 mutant and HRD+ models, show single agent activity and strong combination synergy with PARP inhibitors.

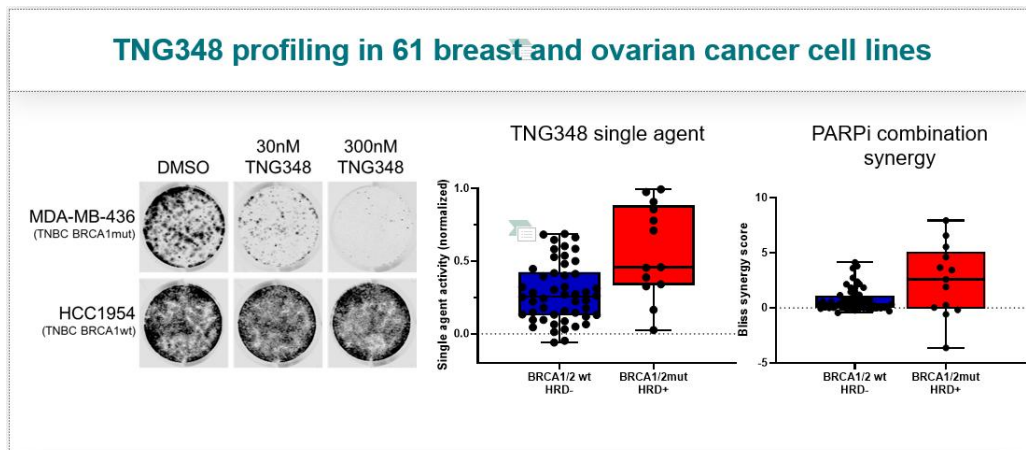


Figure 16. PARPi-resistant patient-derived organoids are sensitive to USP1 inhibition and are synergistic with niraparib

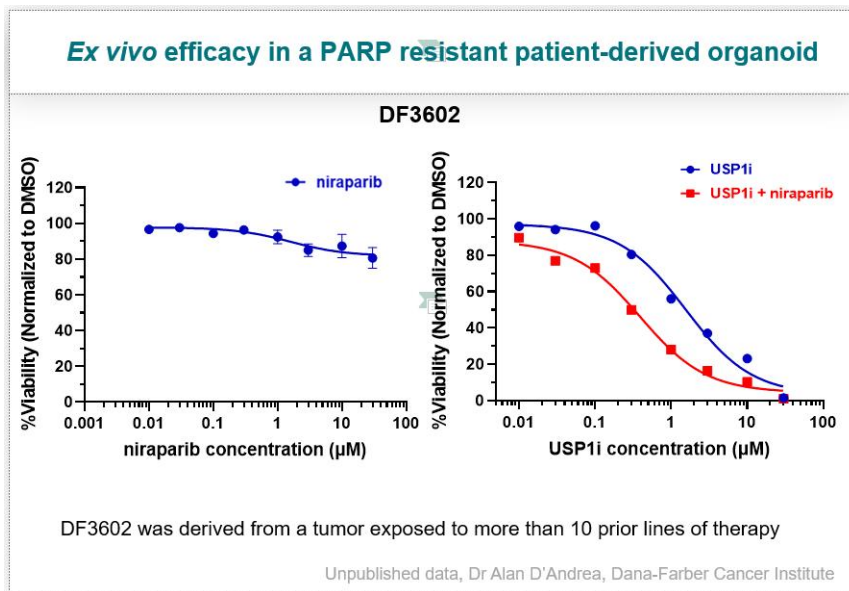
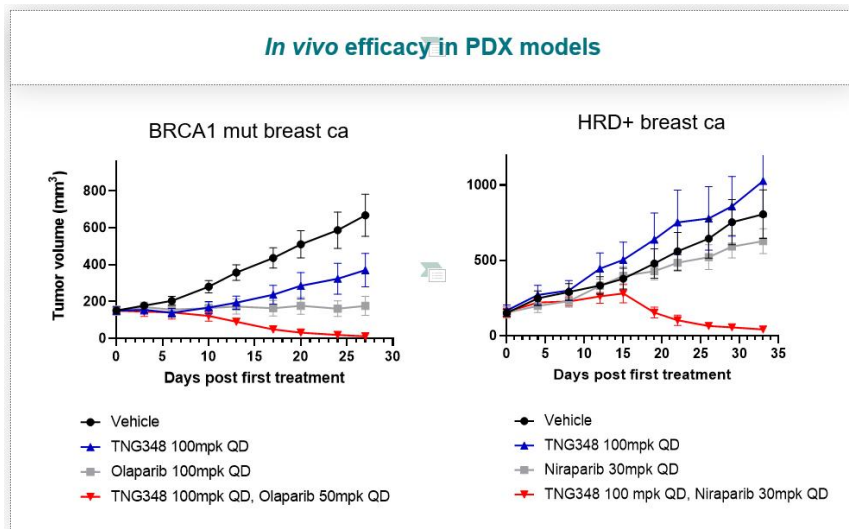


Figure 17. TNG348 demonstrates significant combination benefit with PARP inhibitor in breast cancer patient derived xenograft models harboring homologous recombination repair defects



Collaboration and License Agreements

Collaboration and License Agreement with Gilead Sciences

In August 2020, we entered into an amended and restated research collaboration and license agreement, which we refer to as the Gilead Agreement, with Gilead. The Gilead Agreement expanded our 2018 collaboration with Gilead, or the 2018 Gilead Agreement. Pursuant to the Gilead Agreement we use our proprietary functional genomics-based discovery platform to identify and develop novel immune evasion targets during a seven-year period ending in August 2027, or the Research Term. During the Research Term, Gilead has the option to obtain exclusive, worldwide licenses to develop and commercialize products directed to up to 15 targets validated in the collaboration. Prior to exercising its option for a program, Gilead may “extend” such program, in which case we will further collaborate with Gilead during the Research Term to discover and develop immuno-oncology treatments directed to such target(s), potentially through early clinical development and be eligible to receive research extension payments from Gilead. Gilead will retain its option rights to any such extended

program. For up to five programs licensed by Gilead, we have the option to co-develop and co-promote the lead product for such program in the United States, subject to certain exceptions, and eligible to receive milestone payments and royalties on ex-U.S. sales.

Under the terms of the Gilead Agreement, we received an upfront payment of \$125.0 million in addition to an upfront payment of \$50.0 million received under the 2018 Gilead Agreement. We also received a \$20.0 million equity investment in connection with the Gilead Agreement, and as of December 31, 2022, we received \$21.1 million in license fees and \$22.0 million in research option-extension fees. We are eligible to receive up to an additional \$410.0 million per program in license, research extension, and clinical, regulatory and commercial milestone payments. We are also eligible to receive tiered royalties in the first decile on net sales by Gilead on a country-by-country and product-by-product basis until the later of (i) the expiration of the last valid claim of our patents or, in some instances, certain of Gilead's patents, in each case covering such product in such country or (ii) ten years after the first commercial sale of such product in such country. For those products that we opt to co-develop and co-promote in the United States, we and Gilead will equally split profits and losses from the sales of such products in the United States, as well as development costs for such products attributable to the United States.

Either party may terminate the Gilead Agreement if the other party materially breaches the terms of such agreement, subject to specified notice and cure provisions, or enters into bankruptcy or insolvency proceedings. Additionally, Gilead may terminate the agreement for any or no reason, in its entirety or on a program-by-program basis, upon specified written notice. If we terminate the Gilead Agreement for Gilead's material breach, or Gilead terminates the Gilead Agreement without cause, then Gilead is obligated to negotiate with us in good faith for a specified period regarding the transfer by Gilead of certain assets and the provision by Gilead of certain assistance to enable us to continue the research, development and commercialization of products under any terminated programs.

To date, Gilead has licensed two of our programs and has research option-extended two programs under the Gilead agreements.

Our collaboration with Gilead excludes our lead programs, PRMT5, CoREST, USP1 as well as a growing pipeline of novel targets identified in our non-immune related target discovery screens. We also retain the right to identify and validate targets outside the scope of our collaboration with Gilead (all cell-autonomous targets, exclusive of those in immune evasion contexts), and to develop and commercialize products directed to such targets, on our own or in collaboration with third parties.

License Agreement with Medivir AB

In March 2020, we entered into a license agreement, or the Medivir Agreement, with Medivir AB, or Medivir, pursuant to which we obtained a worldwide, royalty-bearing, exclusive license under certain current and/or future patents and know-how of Medivir, to research, develop and commercialize products that are covered by such licensed patents or otherwise modulate USP1.

Under the terms of the Medivir Agreement, we are obligated to pay Medivir in connection with development, regulatory and commercial activities. We have agreed to make certain milestone payments of (i) \$1.4 million in the aggregate for the first licensed product that achieves specified clinical milestones plus \$25.0 million for the first licensed product that achieves specified regulatory approval and sales milestones, in each case, in either of the first two specified genetic contexts and (ii) \$0.7 million in the aggregate if that first licensed product achieves specified clinical milestones plus \$5.0 million if that first licensed product achieves specified regulatory and sales milestones for a third genetic context or the second licensed product achieves such specified development, regulatory and sales milestones in either of the first two specified genetic contexts. We have the right to reduce these milestone payments by a specified amount in the event the licensed product is not covered by Medivir's patents or if payments are due to a third party for a license under such third party's intellectual property rights. We are also obligated to pay Medivir a low single-digit royalty on net sales of any product covered by a licensed patent.

Payments in respect of net sales or sublicense in a country shall remain in force on a product-by-product, country-by-country basis, with respect to products that are not covered by a licensed patent or certain of our patents, for ten years from the date of first commercial sale in such country, and products that are covered by a licensed patent or certain of our patents, until the expiration date of the last to expire of the licensed patents covering such product or its manufacture or use in the applicable country. No milestones have been achieved to date.

The Medivir Agreement expires on the date of expiration of all royalty obligations. Either party may terminate the Medivir Agreement earlier upon an uncured material breach of the other party.

Manufacturing

Our lead investigational products are small molecule inhibitors that can be readily manufactured without requiring any specialized equipment or processes. We do not own or operate, and currently have no plans to establish any manufacturing facilities. We rely, and expect to continue to rely, on third-party Contract Development and Manufacturing Organizations, or CDMOs for the manufacturing, packaging, labeling and distribution of our investigational products for preclinical and clinical testing, as well as for commercial manufacturing if any of our investigational products obtain marketing approval. A team of internal experts oversee activities at contracted CDMOs with the goal of ensuring our investigational products are being manufactured under current good manufacturing practices, or cGMP. Currently, all manufacturing of our product candidates drug substance and drug product to be used in our planned clinical trial in the U.S. is conducted by one manufacturer. We believe that the contracted CDMO has the capacity to support our planned registrational studies, in addition to the first-in-human studies for our product candidates. The operations of the CDMO manufacturing drug substance and drug product are located outside the U.S. and, therefore, in addition to the sole-source risks related to this CDMO, we may also encounter challenges related to supply chain, climate issues, pandemic and geopolitical risks. We plan to expand and diversify our supply chain by identifying and contracting other CDMOs with the capacity and expertise to support our product candidates and other investigational products in our pipeline and to manufacture commercial supply of our drugs (if those therapies obtain regulatory approval).

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business and our product candidates, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets relating to our proprietary target discovery technology platform and on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of precision oncology that may be important for the development of our business and product candidates. We additionally may rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions, where available. Patent rights and regulatory protections are key factors that determine the period of market exclusivity for products in our industry. It is during the period of market exclusivity that, we believe, our potential future products have their greatest commercial value.

Our commercial success may depend in part on our ability to: obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to limit third parties from making, using, selling, offering to sell, or importing our product candidates (and any future products that may be approved for marketing by regulatory authorities) may depend on the extent to which we have rights under valid and enforceable licenses, patents, or trade secrets that cover these activities. In some cases, enforcement of these rights may depend on third-party licensors. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same and to the extent such patents are commercially useful in protecting our commercial products or methods of manufacturing, such patents may be challenged or invalidated or otherwise become less useful in protecting our commercial products and methods of manufacturing.

Because a significant portion of a pharmaceutical product's patent protection can elapse during the course of developing and obtaining regulatory approval of the product, certain countries, including the U.S., provide compensatory mechanisms to extend patent terms for pharmaceutical products. Patent expiration dates noted in the following paragraphs refer to statutory expiration dates and do not take into account any potential patent term adjustment or extension that may be available, or any potential disclaimers that may be needed to obtain certain patents that may reduce the term of such patents to correspond to that of earlier-expiring patents. There is no guarantee that any of our product candidates would be eligible for patent term extensions.

PRMT5 inhibitors

We exclusively own three patent families covering the composition of matter, form and methods of use for our product candidates TNG908, TNG462 and other structurally related PRMT5 inhibitors. For the first family, a US patent has been granted, and patent applications are pending in the United States, Argentina, Pakistan, Taiwan, Australia, Brazil,

Canada, China, Eurasia, Europe, Israel, India, Japan, Korea, Mexico, Malaysia, New Zealand, Singapore, Thailand and South Africa. Any patents granted in this family would be expected to expire no earlier than 2041. A Patent Cooperation Treaty application is pending in the second family, and any patents granted in this family would be expected to expire no earlier than 2042. A provisional United States patent application is pending in the third family, and any patents granted in this family would be expected to expire no earlier than 2043.

Additionally, we exclusively own six patent families covering other PRMT5 inhibitors and their methods of use with expiration dates ranging from 2039 to 2043. A US patent has been granted and a US patent application is pending in the first family. A US patent application is pending in the second family. Patent Cooperation Treaty applications are pending in the remaining four families.

USP1 inhibitors

We own two patent families covering USP1 inhibitors and methods of use thereof. Patent Cooperation Treaty applications are pending in both families. Any patents issuing from each of these two patent families are expected to expire no earlier than 2042. One of the patent families is exclusively owned by us, and the remaining one is jointly owned by us and Medivir AB and exclusively licensed to us under the Medivir Agreement.

CoREST inhibitors

We exclusively own two patent families relating to our CoREST inhibitor program, including composition of matter and methods of use thereof. A Patent Cooperation Treaty application is pending in the first family, and a provisional application is pending in the second family. Any issued patents, if granted, covering the composition of matter for our CoREST inhibitor, or methods of use thereof, are expected to expire no earlier than 2042.

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, clinical trials, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, recordkeeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drugs. We, along with our vendors, contract research organizations, or CROs, clinical investigators and contract development and manufacturing organizations, or CDMOs, 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 product 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, the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, its implementing regulations, and other federal statutes and regulations. Drugs are also subject to other federal, state and local statutes and regulations. If we fail to comply with applicable FDA or other regulatory requirements at any time with respect to product development, clinical testing, approval or any other regulatory requirements relating to product manufacture, processing, handling, storage, quality control, safety, pharmacovigilance, 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.

Our product candidates must be approved for therapeutic indications by the FDA before they may be marketed in the United States. For drug product candidates regulated under the FD&C Act, FDA must approve a New Drug Application, or NDA. The process generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice, or GLP, requirements;
- completion of the manufacture, under cGMP conditions, of the drug substance and drug product to be used in human clinical trials along with required analytical and stability testing;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually and when certain changes are made (for example, we received clearance of our IND application for TNG908 in the first quarter of 2022);

- approval by an institutional review board, or IRB, or independent ethics committee at each clinical trial site before each trial may be initiated at that site;
- 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;
- preparation and submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA to file the application 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 cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of 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, where applicable, consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States.

Preclinical studies and clinical trials for drugs

Before testing any drug in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of product 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 regulation 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. An IND includes the general investigational plan and the protocol(s) for clinical studies, the results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. 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 conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks, and imposes a full or partial clinical hold. A clinical hold can also be imposed once a trial has already begun, thereby halting the trial until any safety concerns or deficiencies articulated by FDA are corrected.

The clinical stage of development involves the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, who generally are 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, inclusion 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 compared 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 results for clinical trials other than Phase 1 investigations, must be submitted within specific timeframes for publication on www.ClinicalTrials.gov, a clinical trials database maintained by the National Institutes of Health.

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, FDA may nevertheless accept the results of the study in support of an NDA if the study was conducted in accordance with GCP

requirements, and the FDA is able to validate the data through independent analysis and 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 or be combined.

- *Phase 1* — Phase 1 clinical trials involve initial introduction of the investigational product in a limited population of healthy human volunteers or patients with the target disease or condition. These studies are typically designed to test the safety, dosage tolerance, absorption, metabolism, distribution, and excretion of the investigational product in humans, 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 drug's potential efficacy, to determine the 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 labeling. Generally, two adequate and well-controlled Phase 3 trials are required by the FDA for approval of an NDA.

In the first quarter of 2022, we received clearance of our IND application for TNG908 to initiate a Phase 1/2 clinical trial. In the first quarter of 2023, we received clearance of our IND application for TNG462 to initiate a Phase 1/2 clinical trial.

In March 2022, the FDA released final guidance titled "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 development costs and time.

Post-approval trials, sometimes referred to as Phase 4 clinical trials or post-marketing studies, 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 completion of Phase 4 clinical trials as a condition of NDA approval.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators within 15 days 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 product candidate and 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 product 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 product 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 package requesting approval to market the product for one or more indications. An NDA must contain proof of the drug's safety and efficacy for the requested indications and the marketing

application is required to 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 drug to the satisfaction of the FDA. The FDA must approve an NDA before a drug may be marketed in the United States.

The FDA reviews all submitted NDAs to ensure they are sufficiently complete to permit substantive review 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 product is safe and effective for the indications sought and whether the facility in which it is manufactured, processed, packaged or held meets standards, including cGMP requirements, designed to assure and preserve the product's continued identity, strength, 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 6 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 substantial user fee.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy, or REMS, if it believes such a strategy is necessary to ensure that the benefits of the drug outweigh its risks. A REMS can include use of risk evaluation and mitigation strategies such as medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, special monitoring 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 are adequate to assure consistent production of the 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 indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA. The FDA may require additional clinical or preclinical testing or recommend other actions, such as requests for additional information or clarification, that the applicant might take 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 product with specific prescribing information for one or more indications.

Even if the FDA approves a product, 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 product'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 drug intended to treat a rare disease or condition, which is a disease or condition with either a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States when 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. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent 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, although companies developing orphan-designated products are eligible for certain incentives, including tax credits for qualified clinical testing and waiver of application fees.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to 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 product 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 exclusivity.

Expedited development and review programs for drugs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval, and the purpose of these programs is to get important new drugs to patients more quickly than standard FDA review timelines typically permit.

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 applies to the combination of the product candidate and the specific indication for which it is being studied. 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. Rolling review means that the FDA may review portions of the marketing application before the sponsor submits the complete application. In the first quarter of 2022 and 2023, the FDA granted Fast Track designation for TNG908 and TNG462, respectively.

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, alone or in combination with one or more other drugs, 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 as well as more intensive FDA interaction and guidance.

Products 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. Any product submitted to the FDA for approval that has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition may be eligible for priority review. Under priority review, the FDA's goal date to take action on the marketing application is six months compared to ten months for a standard review. 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, in a diligent manner, adequate and well-controlled post-approval confirmatory studies to verify and describe the product's clinical benefit and, under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA may require, as appropriate, that such trials be underway prior

to approval or within a specific time period after the date accelerated approval is granted. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or an indication approved under Accelerated Approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product.

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, these FDA programs do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval, though they may expedite the development or review process.

Pediatric information and pediatric exclusivity

Under the Pediatric Research Equity Act, or PREA, as amended, certain NDAs and NDA supplements must contain data that can be used to assess the safety and efficacy of the product candidate 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 PREA requires that a sponsor who is planning to submit a marketing application for a product candidate 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. The FDA and the sponsor must reach an agreement on the PSP. Unless otherwise required by regulation, PREA does not apply to a drug for an indication for which orphan designation has been granted, except that PREA will apply to an original NDA for a new active ingredient that is orphan-designated if the drug is a molecularly targeted cancer product intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer.

A drug can also obtain pediatric exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity may be granted based on the voluntary completion of a pediatric study that adequately responds to 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 continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, reporting of adverse experiences and promotion and advertising requirements. FDA's advertising and promotion requirements 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 approved products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies enforce the laws and regulations prohibiting the promotion of off-label uses, including not only by company employees but also by agents of the company or those speaking on the company's behalf, 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. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties, including liabilities under the False Claims Act where products are reimbursed under federal health care programs. Promotional materials for approved drugs must be submitted to the FDA in conjunction with their first use or first publication. Further, for certain modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain prior FDA approval of an 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, as well as the manufacturing process for making the drug to confirm continued compliance with cGMP. Manufacturers and certain subcontractors must register their establishments with the FDA and applicable state agencies and are subject to periodic unannounced inspections for compliance with regulatory requirements. Changes to the manufacturing process are strictly regulated and, depending on the nature of the change, may require prior FDA approval before implementation. In addition, manufacturers and other parties involved in the drug supply chain must comply with product tracking and tracing requirements and notify the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution. Accordingly, manufacturers must

continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other regulatory requirements.

The FDA may withdraw approval of a product if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. 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;
- the issuance of 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.

Regulation of companion diagnostics

Companion diagnostics provide information that is essential for the safe and effective use of a corresponding drug. A companion diagnostic may be used to help 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. Companion diagnostics are regulated as medical devices by the 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 the 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 PMA.

The FDA has issued several guidance documents regarding the co-development of drugs and companion diagnostic tests, including a 2014 final guidance titled “Guidance for Industry: In Vitro Companion Diagnostic Devices”, a 2016 draft guidance titled “Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product,” and a 2018 draft guidance titled “Developing and Labeling In Vitro Companion Diagnostic Devices for a Specific Group or Class of Oncology Therapeutic Products. Once cleared or approved, the companion diagnostic device must adhere to applicable post-marketing requirements including the FDA’s quality system regulation (QSR), adverse event reporting, recalls and corrections, and product marketing requirements and limitations. Like drug manufacturers, companion diagnostic manufacturers are subject to unannounced FDA inspections at any time during which the FDA will conduct an audit of the product(s) and the company’s facilities for compliance with regulatory requirements.

Other regulatory matters

Manufacturing, sales, promotion and other activities of product candidates following product approval, where applicable, and 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 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 will seek to obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers and physicians may expose us to certain liabilities 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 future. 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 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. 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. 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 and civil monetary penalties laws, including the federal False Claims Act, or FCA, imposes criminal and civil penalties, including through civil whistleblower 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. 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 federal False Claims Act also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery.
- The federal civil monetary penalties laws 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.
- HIPAA, which 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 federal Anti-Kickback Statute, a person or entity may be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, impose, among other things, specified requirements on covered entities and their respective 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.
- Federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products
- 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, as well as certain non-physician providers such as physician assistants and nurse practitioners) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

- Analogous state and foreign laws and regulations, including, but not limited to, state anti-kickback and false claims laws, may be broader in scope than the provisions described above and may apply regardless of payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and 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; restrict marketing practices or require disclosure of marketing expenditures and pricing information. State and foreign laws may 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.

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.

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 product 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 CMS. 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. 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, 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, which will require additional expenditure above and beyond the costs required to obtain FDA or other comparable regulatory approvals. Some product 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 (when a product candidate is approved for marketing). Levels of coverage and reimbursement for a product can differ significantly from payor to payor.

The containment of healthcare costs has become a priority of federal, state and foreign governments (and other third-party payers), 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.

In the European Union, 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 upon. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union 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. European Union member states may approve a specific price for a product or 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 European Union have increased the amount of 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 European Union. 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.

Current and future healthcare reform legislation

In the United States and certain 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 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. The ACA includes provisions of importance to our potential product candidates that:

- created an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs;
- expanded eligibility criteria for Medicaid, 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;
- 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.
- 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 pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several 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, and review the relationship between pricing and manufacturer patient programs. President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. In February 2023, HHS issued a proposal in response to an October 2022 executive order from President Biden that includes a proposed prescription drug

pricing model that will test whether targeted Medicare payment adjustments will sufficiently incentivize manufacturers to complete confirmatory trials for drugs approved through FDA's accelerated approval pathway. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

The Inflation Reduction Act of 2022, or IRA, includes several provisions that may impact our business to varying degrees, including provisions that reduce the out-of-pocket cap for Medicare Part D beneficiaries from \$7,050 to \$2,000 starting in 2025, thereby effectively eliminating the coverage gap; impose new manufacturer financial liability on certain drugs under Medicare Part D; and allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition. Specifically, under the IRA, a single-source pharmaceutical product qualifies for selection for participation in the drug price negotiation program if it is (i) a small-molecule drug for which at least seven years have passed since the date of approval from the FDA and there is no generic on the market (as of the date of selection); or (ii) a biologic for which 11 years have passed since the date of FDA licensure and there is no biosimilar on the market (as of the date of selection). Given that any negotiated price does not take effect until approximately two years after selection, small-molecule drug and biologic manufacturers are afforded at least nine years and 13 years, respectively, before they may be obligated to sell their product under Medicare Part B and Part D, as applicable, at CMS-negotiated pricing. The IRA also requires companies to pay rebates to Medicare to the extent that drug pricing increases faster than inflation, and it also further delayed until January 1, 2032 the implementation of the HHS rebate rule that would have limited the fees that pharmacy benefit managers can charge.

We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. Federal Government will pay for healthcare drugs and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs (if approved for marketing) or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

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.

Other United States 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 that 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, manufacturing, commercial sales, promotion and distribution of our potential future products. For instance, in 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* — The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid throughout the EEA. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products (gene therapy, somatic cell therapy and tissue engineered products) and products with a new active substance indicated for the treatment of certain diseases, which includes products for the treatment of cancer. For medicines that do not fall within one of the mandatory categories, an applicant still has the option of submitting an application for a centralized marketing authorization to the European Medicines Agency, or 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. If pursuing marketing authorization of a product candidate for a therapeutic indication under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use, or CHMP, is responsible for conducting an initial assessment of whether a product meets the required quality, safety and efficacy requirements, and whether a product has a positive benefit/risk ratio. Under the centralized procedure the maximum timeframe for the evaluation of a marketing authorization application, or 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. Clock stops may extend the timeframe of evaluation of a MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of a MAA under the accelerated assessment procedure is 150 days, excluding clock stops, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.
- *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:
 - o Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EEA Member State for a medicinal product that has not yet been authorized in any EEA Member State and that does not fall within the mandatory scope of the centralized procedure.
 - o In the mutual recognition procedure, a medicine is first authorized in one EEA Member State, in accordance with the national procedures of that country. Following this, additional marketing authorizations can be sought from other EEA Member States in a procedure whereby the countries concerned recognize the validity of the original, national marketing authorization.

In both cases, as with the centralized procedure, the competent authorities of the EEA Member States assess the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy before granting the marketing authorization.

Now that the United Kingdom has left the European Union, Great Britain is no longer covered by the EEA procedures for the grant of marketing authorizations described above (under the Northern Ireland Protocol, centralized European Union marketing authorizations continue to be recognized in Northern Ireland) and a separate marketing authorization is therefore required to market drugs in Great Britain. For three years from January 1, 2021, the UK's regulator, the MHRA, may adopt decisions taken by the European Commission on the approval of new marketing authorizations through the centralized procedure, and the MHRA will have regard to marketing authorizations approved in a country in the EEA (although in both

cases a marketing authorization will only be granted if any Great Britain-specific requirements are met). This is known as the EC Decision Reliance Procedure. On January 24, 2023, the MHRA announced that a new international recognition framework will be put in place from January 1, 2024, which will have regard to decisions on the approval of marketing authorizations made by the European Medicines Agency, or EMA, and certain other regulators. On February 27, 2023, the UK government and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the “Windsor Framework”. This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA will be responsible for approving all medicinal products destined for the UK market (Great Britain and Northern Ireland) and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. A single UK-wide marketing authorization will be granted by the MHRA for all medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. Once the Windsor Framework is approved by the EU-UK Joint Committee, the UK Government and the European Union will enact legislative measures to enact it into law.

In the EEA, new products for therapeutic indications that are authorized for marketing (i.e., innovator 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 referencing the preclinical and clinical trial data contained in the dossier of the innovator product when applying for a generic or biosimilar marketing authorization in the EEA during a period of eight years from the date on which the innovator product was first authorized in the EEA. The additional two-year period of market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EEA until ten years have elapsed from the initial authorization of the reference product in the European Union. The overall ten-year 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. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on a MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials

The criteria for designating an “orphan medicinal product” in the EEA are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, in the EEA a medicinal product may be designated as orphan if it meets the following criteria: (i) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; and (ii) either (a) such condition affects no more than five in 10,000 persons in the EEA when the application is made, or (b) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EEA to justify the investment needed for its development; and (iii) there exists no satisfactory method of diagnosis, prevention or treatment of such condition, 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, unless certain conditions are met. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric studies. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

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 national competent authority, or NCA, 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, or EC, 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 applicable directives. All suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

Government regulation of data collection outside of the United States

In the event we conduct clinical trials in the European Union, we will be subject to additional privacy restrictions. The collection and use of personal health data in the European Economic Area, or EEA (being the European Union plus Norway, Iceland, and Liechtenstein), is governed by the General Data Protection Regulation, or the GDPR, which became effective on May 25, 2018. The GDPR applies to the processing of personal data by any company established in the EEA and to companies established outside the EEA to the extent they process personal data in connection with the offering of goods or services to data subjects in the EEA or the monitoring of the behavior of data subjects in the EEA. The GDPR enhances data protection obligations for data controllers of personal data, including stringent requirements relating to the consent of data subjects, expanded disclosures about how personal data is used, enhanced requirements for securing personal data, requirements to conduct privacy impact assessments for “high risk” processing, limitations on retention of personal data, mandatory data breach notification and “privacy by design” requirements, and creates direct obligations on service providers acting as processors. The GDPR also imposes strict rules on the transfer of personal data outside of the EEA to countries that do not ensure an adequate level of protection, like the United States. Failure to comply with the requirements of the GDPR and the related national data protection laws of the European Union Member States and Norway, Iceland and Liechtenstein, which may deviate slightly from the GDPR, may result in fines of up to 4% of a company’s global revenue for the preceding financial year, or €20,000,000, whichever is greater. Moreover, the GDPR grants data subjects the right to claim material and non-material damages resulting from infringement of the GDPR. Given the breadth and depth of changes in data protection obligations, maintaining compliance with the GDPR will require significant time, resources and expense, and we will be required to put in place controls and processes ensuring compliance with the new data protection rules. There has been limited enforcement of the GDPR to date, particularly in biopharmaceutical development, so we face uncertainty as to the exact interpretation of the new requirements on any future trials and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the new law. Further, the United Kingdom’s decision to leave the European Union, means that it has in force its own legislation which is aligned with the GDPR, known as the Data Protection Act 2018. The requirements are similar except that the United Kingdom is now regarded as a “third country” for the purposes of transfers of personal data from the EEA. Transfers continue to flow freely from the United Kingdom to the EEA; however, as part of the agreement between the United Kingdom and the European Union, the United Kingdom intends to obtain an adequacy decision from the European Commission to ensure personal data can continue to flow freely from the European Union to the United Kingdom.

Data protection authority activity differs across the European Union, with certain authorities applying their own agenda which shows there is uncertainty in 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 European Union, 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.

Competition

We face direct competition from pharmaceutical and biotechnology companies leveraging the principle of synthetic lethality as well as companies developing therapies for the same target pathway and the same indications. Well-established companies that are developing or may develop therapies based on synthetic lethality include AstraZeneca, Amgen, GlaxoSmithKline, Bristol Myers Squibb, Merck KGaA and Pfizer. Smaller and earlier-stage companies focused on synthetic lethality include Artios Pharma, KSQ Therapeutics, IDEAYA Biosciences, Mirati Therapeutics, Repare Therapeutics and Servier Pharmaceuticals.

Our PRMT5 inhibitor programs, which includes TNG908 and TNG462, will face direct competition from companies that have clinical-stage, MTA-cooperative PRMT5 inhibitors that are selective for MTAP-deleted cancers. We are aware that Mirati Therapeutics and Amgen are in Phase 1/2 clinical trials with MTA-cooperative PRMT5 inhibitor programs, using the same mechanism of action as TNG908 and TNG462. Currently, there are no MTA-cooperative PRMT5 inhibitors that are authorized for marketing by any regulatory authority.

Indirect competition may come from MAT2A inhibitor programs that are uniquely different than the TNG908 and TNG462 mechanism of action but are synthetic lethal with MTAP-deletions. MAT2A is an enzyme upstream of PRMT5 essential for the metabolism of the PRMT5 co-factor SAM that acts on the same pathway as TNG908. We are aware that

IDEAYA Biosciences (IDE397) has a clinical program and Servier Pharmaceuticals (S95035) has a preclinical MAT2A inhibitor program.

We are not aware of any competition from other companies developing a similar mechanism as TNG260, our CoREST inhibitor program.

Competition for TNG348, our USP1 inhibitor program, comes from KSQ Therapeutics, which has a USP1 program in clinical development. Additionally, in March 2023, Debiopharm acquired global rights to a USP1 inhibitor in late preclinical development.

We face competition more broadly across the oncology market for safe, efficacious, and reimbursable cancer treatments. The most common methods of treating patients with cancer are surgery, radiation, and drug therapy, including chemotherapy, hormone therapy, biologic therapy (such as monoclonal and bispecific antibodies), immunotherapy, cell-based therapy and targeted therapy, or a combination of any such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates, if any are approved, may compete with these existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our product candidates that we successfully introduce to the market may pose challenges. In addition, many companies are developing new oncology therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development.

Many of our competitors, either alone or with their collaborators, have significantly greater resources, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement, and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove significant competitors, particularly through collaborative arrangements with large and established companies. Additionally, mergers and acquisitions may result in even more resources being concentrated in our competitors.

Employees and Human Capital Resources

Attracting and retaining qualified and experienced employees in research and development, clinical, manufacturing, quality and other positions is crucial to our ability to compete effectively. Competition for these employees is intense in the pharmaceutical industry in which we operate. Our ability to recruit and retain such employees depends on a number of factors, including the growth of our organization, the culture and work environment we have created, our organizational values and goals and our corporate philosophy; talent development and career opportunities; and compensation and benefits.

As of December 31, 2022, we had 110 full-time employees, 84 employees are engaged in research and development and 26 are engaged in business development, finance, legal, and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements.

Talent Acquisition and Employee Development:

Our principal talent acquisition goal is to attract, retain, and develop the highest quality talent. As we build our organization beyond drug discovery and drug development, our goals have been extended to include establishing an employee base that will allow us to efficiently move our pipeline products through clinical trials, regulatory approvals and into the market where we can help patients and their families and, simultaneously, to have a workforce that provides diverse backgrounds and ideas, are trained to operate and act at the highest standards of ethics and integrity, and are dedicated to achieve the highest level of innovation and to advance oncology treatments through the use of synthetic lethality. To support our talent acquisition, our human resources programs are designed to develop talent to prepare them for leadership positions in the future; reward employees through competitive benefits programs, including competitive pay, incentive compensation, and an equity program that aligns the incentives of our employees with the interests of our shareholders; enhance our culture through efforts aimed at making the workplace more engaging and inclusive; and retain and develop talent that embody our core values.

Diversity:

While Tango is early in its corporate development, our employees represent a broad set of backgrounds, perspectives and experiences. We attribute our early growth and success to the diversity that our employees bring with them to their professional roles. We are committed to the goals of diversity, equity and inclusion, which is the foundation upon which we are building a leading synthetic lethality business that is pushing the advances in oncology care, all with the objective of benefiting patients. We are building a work environment where employees can express themselves and have a voice in how we operate. Among other things, members of our management meet in small group sessions with all employees throughout the year and the feedback in these meetings is used to drive our professional development programs, our compensation structure, our organizational development and our culture.

Tango has also recently established a Diversity, Equity and Inclusion (DE&I) Council in which a broad, cross-section of our employees are members. The DE&I Council is responsible for initiatives that prioritize building a diverse workforce and creating an environment that is equitable and inclusive for all employees and employee candidates. The DE&I Council has led company-wide education efforts to inform our employees and our management team of the challenges employees face in the work environment so actions can be taken throughout the organization to support a range of diversity, equity and inclusion causes.

Further, the Nominating and Corporate Governance Committee charter sets forth specific guidelines that the Committee will use in evaluating future individuals for nomination to the Board of Directors. Among the identified factors the Committee is to consider in nominating a candidate is the diversity of a candidate. The Board recognizes that diversity plays an important role in its functioning and operations.

These and similar programs are important to develop a sense of belonging for all employees and for our Board of Directors.

Employee Engagement:

We survey our employees on an annual basis to assess overall engagement of our workforce, and compare our engagement results against prior year results, as well as a set of benchmark companies. These companies are in the biotech sector and of similar size (number of employees). We use these results, both our internal results and the comparative results against the benchmark companies, to assess our employee engagement performance during the preceding year and to determine areas of focus going forward.

Following the 2021 engagement survey, we were able to implement a number of initiatives in response to employee feedback, including updating our vacation policy and adopting policies designed to improve employee wellness. In our most recent survey, conducted in 2022, we continued to generate results that were generally higher than our benchmark dataset, which supports our view that we have positive employee engagement. We identified areas where we are performing well, such as our efforts around innovation and social connection. As is the case with every survey, we also used the data to identify areas where we want to focus our efforts for improvement, including employee empowerment. As was the case in 2022, we will take these 2022 results, and a task force has been formed to enable actions that will further improve our engagement.

We also conduct regular townhall meetings with our employees that are intended to keep our employees updated on important corporate initiatives and to obtain input from employees on these initiatives. We also use periodic employee surveys so we can quickly obtain employee feedback on new programs or policies that are under consideration.

Item 1A. Risk Factors.

Investing in our securities involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all other information in this Annual Report on Form 10-K, including our financial statements and the related notes and the “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” The occurrence of one or more of the events or circumstances described in these risk factors, alone or in combination with other events or circumstances, may have a material adverse effect on our business, reputation, revenue, financial condition, results of operations and future prospects, in which event the market price of our common stock could decline, and you could lose part or all of your investment. The material and other risks and uncertainties summarized above and described below are not intended to be exhaustive and are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of a number of factors, including the risks described below. See also the section titled “Note Regarding Forward-Looking Statements” above.

Risks Related to Our Limited Operating History, Financial Position, and Capital Requirements

We are a precision oncology company with a limited operating history.

We are a precision oncology company with a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Since the Company’s inception, we have devoted substantially all of our efforts to organizing and staffing our company, acquiring and developing intellectual property, business planning, raising capital, conducting discovery, research and development activities, and providing general and administrative support for these operations. We have no products approved for commercial sale and therefore have never generated any revenue from product sales, and we do not expect to in the foreseeable future. The revenue that we have generated from our collaboration agreement is also not sufficient to fund our operations. We have not obtained regulatory approvals for any of our product candidates, and there is no assurance that we will obtain approvals in the future. We have two investigational new drug, or IND, applications, for TNG908 and TNG462 that were cleared by the FDA in the first quarters of 2022 and 2023, respectively. Other than TNG908 and TNG462, all of our product candidates are still in preclinical development. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on cash and cash equivalent holdings, our stockholders’ equity and working capital. If we were to expend our cash resources more quickly than we anticipate as we advance into and through the approval process, our cash runway may be shorter than the target we may disclose from time to time.

We have incurred significant net losses since our inception and anticipate that we will continue to incur losses for the foreseeable future.

We have incurred significant net losses since our inception. As of December 31, 2022, we had an accumulated deficit of \$269.5 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect our research and development expenses to increase significantly in connection with the commencement and continuation of clinical trials of our product candidates. In addition, if we obtain regulatory approval for our product candidates, we will incur significant sales, marketing and manufacturing expenses. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

We expect our operating results to fluctuate significantly in the future as our business advances

The amount of our future losses is uncertain and our quarterly and annual 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 on-going and future clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;

our ability to obtain INDs for our pipeline product candidates, successfully open clinical trial sites and recruit and retain subjects for clinical trials, and any delays caused by difficulties in such efforts;

our ability to obtain regulatory approval for our product 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 product candidates and any future product candidates and research-stage programs, which may change from time to time;
the cost of manufacturing our product candidates and products, should they receive regulatory approval, which may vary depending on FDA and other comparable foreign regulatory requirements, the quantity of production and the terms of our agreements with manufacturers;
expenditures that we will or may incur to develop additional product candidates;
the level of demand for our product candidates should they receive regulatory approval, which may vary significantly;
the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future therapeutics that compete with our product candidates;
the changing and volatile U.S. and global economic environments, including as a result of the COVID-19 pandemic; and
future accounting pronouncements or changes in our accounting policies.

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 when we have met any previously publicly stated guidance we may provide.

We have no products approved for commercial sale and have not generated any revenue from product sales.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from product sales, and we do not expect to generate any revenue from the sale of products in the near future. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- successfully complete our planned preclinical studies for our novel precision oncology development programs;
- timely file INDs for our programs, and obtain clearance of these INDs to allow for commencement of such future clinical trials;
- timely complete patient enrollment and patient dosing in our TNG908 and TNG462 clinical trials;
- successfully complete our TNG908 and TNG462 clinical trials and any future clinical trials;
- initiate and successfully complete all safety and efficacy studies required to obtain U.S. and foreign regulatory approval for our product candidates;
- make and maintain arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- obtain and maintain patent and trade secret protection or regulatory exclusivity for our product candidates;
- launch commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- obtain and maintain acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- position our products to effectively compete with other therapies;
- obtain and maintain healthcare coverage and adequate reimbursement for our products, if and when approved;
- enforce and defend intellectual property rights and claims;
- implement measures to help minimize the risk and disruption of COVID-19 to our employees as well as patients and subjects to be enrolled in our clinical trials; and
- maintain a continued acceptable safety profile of our products following approval.

Further, our most advanced program is a PRMT5 inhibitor, TNG908. Given the large number of patients with MTAP-deleted cancers who may benefit from a PRMT5 inhibitor, and the resulting business opportunity, we also developed a next-generation PRMT5 inhibitor, TNG462, with increased potency, MTAP-deletion selectivity, as well as longer target coverage.

TNG462, our next-generation PRMT5 inhibitor, is 45-fold more potent in cells with an MTAP deletion than those without and induces deep tumor regressions in preclinical models of multiple cancer types. The clinical development path for TNG462 is expected to be similar to TNG908, evaluating safety and efficacy in multiple tumor types in a future Phase 1/2 clinical trial. GBM will be excluded from the clinical trial as TNG462 does not cross the blood-brain barrier in preclinical non-human primate models. If clinical evaluation of TNG462 supports this hypothesis, we may elect to promote TNG462 as our lead PRMT5 inhibitor, which may result in a delay to our development timeline for the lead PRMT5 program of approximately 12 to 18 months (in this case, we could continue clinical development of TNG908, however, the focus would be on GBM, which constitutes only a subset of the larger MTAP-deleted cancer patient population). If we elect to promote TNG462, it may result in the delay in receiving potential revenue from product sales, if approved by regulatory authorities.

We will need to raise substantial additional funding. If we are unable to raise capital when needed or on terms acceptable to us, we would be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts.

The development of pharmaceutical products is capital-intensive. We are currently advancing our precision oncology programs through clinical and preclinical development. We received FDA clearance of our IND applications for TNG908 and TNG462 in the first quarters of 2022 and 2023, respectively. We are actively enrolling patients in the TNG908 Phase 1/2 clinical trial, which is evaluating safety and efficacy in multiple indications. We expect to initiate the Phase 1/2 clinical trial for TNG462 in mid-2023 which will evaluate safety and efficacy in multiple indications. We plan to file an IND for TNG260, our selective CoREST inhibitor, in the first half of 2023. We also plan to file an IND for TNG348, our USP1 inhibitor, in mid-2023. Consequently, we expect our expenses to significantly increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate and complete clinical trials of, and seek regulatory approval for, our product candidates. As a result, we will be required to raise substantial additional funding in the future in order to continue our operations.

In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We may also need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our current or future product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we have, and will continue to, incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts.

We expect that our existing cash, cash equivalents and marketable securities will fund our operating expenses and capital expenditure requirements at least into 2025. However, our future capital requirements will depend on and could increase significantly as a result of many factors (which may result in exhausting such cash resources prior to 2025), including:

- the scope, progress, results and costs of product discovery, preclinical and clinical development, and clinical trials for our product 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 product candidates;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under our existing collaboration agreements or any additional collaboration agreements we may establish;
- 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 in-license other product candidates and technologies;
- the costs of securing manufacturing arrangements for clinical and commercial production;
- our ability to hire and retain skilled scientific and operational personnel to meet our development, clinical and commercial objectives;
- costs related to the development of any companion diagnostics we may use in the future; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our product candidates.

Our commercial revenue, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

As a result of disruptions in the financial markets in general, and the recent decrease in biopharmaceutical stock prices and market capitalizations in particular, as well as the ongoing COVID-19 pandemic, equity and debt financing may be 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 acceptable to us, if at all.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product that has received regulatory approval 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.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through one or a combination of private and public equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. 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. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our existing common stockholders will be diluted, and the terms of those securities may include liquidation or other preferences that may materially adversely affect your rights as a common stockholder. 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, acquiring, selling or licensing intellectual property rights, and making capital expenditures, declaring dividends, repurchase shares of our common stock, or other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to meet certain milestones in connection with debt financing and the failure to achieve such milestones by certain dates may force us to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us which could have a material adverse effect on our business, operating results and prospects.

We also could be required to seek funds through arrangements with additional collaborators or otherwise at an earlier stage than otherwise would be desirable. If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or product candidates, grant licenses on terms that may not be favorable to us or grant rights to develop and market our product candidates that we would otherwise prefer to develop and market ourselves, any of which may have a material adverse effect on our business, operating results and prospects.

Risks Related to the Development of our Precision Oncology and Other Programs and Product Candidates

We have never successfully completed any clinical trials and we may be unable to do so for any product candidates we develop. Certain of our programs are still in preclinical development and may never advance to clinical development.

We have not yet demonstrated our ability to successfully register, initiate, enroll and complete clinical trials, including large-scale, pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. We received FDA clearance of two IND applications for TNG908 and TNG462. We may not be able to file any future INDs for any of our other product candidates on the timelines we expect, if at all. Further, timelines for developing and filing INDs are subject to significant uncertainties and projected timelines can be improved upon or delayed. For example, we extended the timeline for filing an IND for our USP1 inhibitor program as we continued work on a development candidate, TNG348, that has improved pharmaceutical properties. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that require us to suspend or terminate clinical trials. Any guidance we receive from the FDA or other regulatory authorities is subject to change. These regulatory authorities could change their position, including on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional clinical trials or result in the imposition of stricter approval conditions than we currently expect. Successful completion of our clinical trials is a prerequisite to submitting an NDA to the FDA, a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, or other marketing applications to regulatory authorities in other jurisdictions, for each product candidate and, consequently, the regulatory approval of each product candidate. While the INDs for TNG908 and TNG462 were cleared by the FDA, it is possible that an adequate number of patients may not be enrolled on a timely basis, or at all, and the studies may not be completed (and preliminary, initial or final trial results may not be available) on time. Similarly, future clinical trials may not begin on time or be completed on schedule, if at all.

If we are required to conduct additional preclinical studies or clinical trials of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other

testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety and/or efficacy concerns, we may, among other things:

- be delayed in obtaining regulatory approval for our product candidates;
- not obtain regulatory approval at all;
- obtain regulatory approval for indications or patient populations that are not as broad as intended or desired;
- be subject to post-marketing testing requirements; or
- have the product removed from the market after obtaining regulatory approval.

Our programs are focused on the development of oncology therapeutics for patients with genetically defined or biomarker-driven cancers, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs is novel and may never lead to approved or marketable products.

The discovery and development of oncology therapeutics for patients with genetically defined or biomarker-driven cancers is a rapidly evolving area, and the scientific discoveries that form the basis for our efforts to discover and develop product candidates are relatively new. Our proprietary functional genomics discovery approach is based on the genetic concept of synthetic lethality. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. Although we believe, based on our preclinical work, that the genetic markers targeted by our programs drive the formation and spread of certain cancers, clinical results may not confirm this hypothesis or may only confirm it for certain alterations or certain tumor types. The patient populations for our product candidates are limited to those with specific target alterations and may not be completely defined but are substantially smaller than the general treated cancer population, and we will need to screen and identify these patients with targeted alterations. Successful identification of patients is dependent on several factors, including achieving certainty as to how specific alterations respond to our product candidates and the ability to identify such alterations. Furthermore, even if we are successful in identifying patients with specific targets, we cannot be certain that the resulting patient populations with each mutation will be as large as we anticipate, large enough to allow us to successfully obtain approval for each such mutation and commercialize our product candidates and achieve profitability.

Clinical product development involves a lengthy and expensive process, with an uncertain outcome.

Our preclinical studies, our TNG908 and TNG462 clinical trials and future clinical trials may not be successful. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining regulatory approval from regulatory authorities for the sale of any product candidate, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and outcomes are uncertain. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim or preliminary results of a clinical trial do not necessarily predict final results (or be indicative of safety and efficacy if commercialized and used in a broader population). Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain regulatory approval of their product candidates.

If we or third-parties are unable to successfully develop screening technology for biomarkers that enable patient selection, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates.

A key component of our strategy includes the use of next-generation sequencing to guide patient selection and/or to confirm target engagement of our product candidates. In some cases, third-parties provide this technology. It is not always the case, however, that the biomarker we have identified for patient selection is on the panel offered by certain next generation technology sequencing providers. If not already commercially available, we may collaborate with sequencing companies for the development of biomarkers associated with our product candidates. We may have difficulty in establishing or maintaining such development relationships, and we will face competition from other companies in establishing these collaborations.

There are also several risks associated with biomarker identification and validation. We, in collaboration with any diagnostic partners, may not be able to identify predictive biomarkers or pharmacodynamic biomarkers for one or more of our programs. We may not be able to validate potential biomarkers (e.g., certain genetic mutations) or their functional relevance preclinically in relevant in vitro or in vivo models. Data analytics and information from databases that we rely on for identifying or validating some of our biomarker-target relationships may not accurately reflect potential patient

populations. Potential biomarkers, even if validated preclinically, may not be functionally effective or validated in human clinical trials.

If next generation sequencing companies experience any delays including the biomarkers we have identified for patient selection on their panels or tests, or if they do not include those biomarkers on their panels or tests, our clinical trials may be delayed or may not identify sufficient patients to complete the trial and our clinical trials may be unsuccessful and our therapies will not advance to approval.

If we are unable to successfully validate, develop and obtain regulatory approval for diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these product candidates.

In connection with the clinical development of our product candidates for certain indications, we may engage third parties to develop or otherwise obtain access to in vitro companion diagnostic tests to identify patient subsets within a disease category who may derive selective and meaningful benefit from our product candidates. Such companion diagnostics may be used during our clinical trials as well as in connection with the commercialization of our products that receive regulatory approval. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. The FDA and comparable foreign regulatory authorities regulate in vitro companion diagnostics as medical devices and, under that regulatory framework, will likely require the conduct of clinical trials to demonstrate the safety and effectiveness of any diagnostics we or third parties may develop, which we expect will require separate regulatory clearance or approval prior to commercialization.

We intend to rely on third parties for the design, development and manufacture of companion diagnostic tests for our therapeutic product candidates that may require such tests. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining approval for these companion diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our future collaborators may encounter difficulties in developing, obtaining regulatory clearance or approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our therapeutic product candidates themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we are unable to successfully develop companion diagnostics for these therapeutic product candidates, or experience delays in doing so, the development and commercialization of these therapeutic product candidates may be adversely affected, these therapeutic product candidates may not obtain regulatory approval, and we may not realize the full commercial potential of any of these therapeutic products that obtain regulatory approval.

Interim, top-line, and initial data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to confirmation, audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose interim, top-line or initial data from our current and future clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data, including audit and verification procedures, and as results from additional clinical trial participants become available and trial participants spend additional time on therapy. For example, we may report responses in certain patients that are unconfirmed at the time and which do not ultimately result in confirmed responses to treatment after follow-up evaluations. We may also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, initial, interim and top-line data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between initial or interim data and final data could significantly harm our business prospects and may cause the price of our common stock to fluctuate or decline.

Further, regulatory agencies and others may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could adversely impact the potential of the particular program, the likelihood of obtaining regulatory approval of the particular product candidate, the

scope of product label, and commercialization of any approved product. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is derived from information that is typically extensive, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

We may from time to time indicate the intent to publicly disclose certain clinical trial data at a future date. We have, for example, noted that we will provide an update on the ongoing dose escalation portion of the TNG908 clinical trial, focusing on proof-of-mechanism. Due to the factors described above, and elsewhere in these *Risk Factors*, we may be unable to report that data on or before the time indicated to investors, we may not have the data to provide the information previously indicated and, even if we do provide such clinical trial data, the final results from that phase of the clinical trial may be different from what we disclose initially.

If the initial, interim or top-line data that we report differ from final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be significantly impaired, which could materially harm our business, operating results, prospects or financial condition.

We may incur additional costs or experience delays in initiating or completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We may experience delays in initiating or completing our preclinical studies or clinical trials, including as a result of delays in obtaining, or failure to obtain, the FDA's clearance to initiate clinical trials under future INDs. Additionally, we cannot be certain that preclinical studies or clinical trials for our product candidates will not require redesign, will enroll an adequate number of subjects on time, or will be completed on schedule, if at all. We may experience numerous unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or prevent our ability to receive regulatory approval or commercialize our product candidates, including the following:

- we may receive feedback from regulatory authorities that require us to modify the design or implementation of our preclinical studies or clinical trials or to delay or terminate a clinical trial;

- regulators or IRB, or ethics committees may delay or may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- preclinical studies or clinical trials of our product candidates may fail to show safety or efficacy or otherwise produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials, or we may decide to abandon product research or development programs;

- preclinical studies or clinical trials of our product candidates may not produce differentiated or clinically significant results across tumor types or indications;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants 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, fail to maintain adequate quality controls, be unable to provide us with sufficient product supply to conduct or complete preclinical studies or clinical trials, fail to meet their contractual obligations to us in a timely manner, or at all;

- our clinical trial sites or investigators 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 in order to ensure our trials generate statistically significant results;

- we may elect to, or regulators or IRBs or ethics committees may require us or our investigators to, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our clinical trials are being exposed to unacceptable health risks;

- the cost of clinical trials of our product candidates may be greater than we anticipate;

- clinical trials of our product candidates may be delayed due to complications associated with the evolving COVID-19 pandemic which we have experienced in connection with our TNG908 clinical trial as described below;

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;

- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our product candidates;

- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and

regulatory developments with respect to our competitors' products, including any developments, litigation or public concern about the safety of such products.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions at which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination or clinical hold due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, adverse findings upon an inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA may disagree with our clinical trial design or our interpretation of data from clinical trials or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

Moreover, principal investigators for our current or future clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected the interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site, and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of regulatory approval of one or more of our product candidates.

Our product development costs will also increase if we experience delays in testing or regulatory approvals. We do not know whether any of our current or future clinical trials will begin as planned, or whether any of our current or future clinical trials will need to be restructured or will be completed on schedule, if at all. Significant preclinical study or clinical trial delays, including those caused by the COVID-19 pandemic, also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates and may significantly harm our business, operating results, financial condition and prospects.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities, or as needed to provide appropriate statistical power for a given trial. In particular, because we are focused on patients with specific genetic mutations for the development of our precision oncology programs and because some of the indications we are pursuing are orphan indications that have small populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. For example, following the FDA's clearance of our IND application for the Phase 1/2 clinical trial of TNG908, we and our third-party CRO have initiated multiple clinical trial sites, and we are actively enrolling patients in the trial. While we expect to continue to enroll patients in our TNG908 clinical trial, we have experienced slower than expected enrollment, due to limited site resources resulting from COVID-19, and may experience slower enrollment as a result of limited trial populations due to competitive trials or other factors beyond our control. Delays in enrollment may affect the timing of any results from the TNG908 Phase 1/2 trials (as well as the timing for dose escalation and dose expansion) and therefore the regulatory approval (if any) for TNG908 may extend beyond the period we have targeted or beyond the timeline expected by investors.

The patient eligibility criteria defined in our trial protocols, including biomarker-driven identification, may limit the patient populations eligible for our clinical trials to a greater extent than competing clinical trials for the same indication that do not have biomarker-driven patient eligibility criteria. We also rely on the willingness and ability of clinicians to screen their patients for biomarkers to indicate which patients may be eligible for enrollment in our clinical trials.

In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications as do our product candidates, and patients who would otherwise be eligible for our clinical trials may choose instead to enroll in clinical trials of our competitors' product candidates (for example, two INDs for other companies have been cleared by the FDA for clinical trials of MTA-cooperative PRMT5 inhibitors for the treatment of cancer patients, such trials have already

enrolled patients and those trials are using some of the same clinical trial sites that we use). Further, the IND for TNG462, our next generation MTA-cooperative PRMT5 inhibitor, was cleared by the FDA in January 2023 and we expect to initiate the Phase 1/2 clinical trial for TNG462 in mid-2023. The patient population eligible for the TNG462 clinical trial will be largely the same as for the TNG908 clinical trial. As a result, our own trials may compete to enroll patients among a limited population and each trial may experience delays or limited enrollment. Furthermore, as noted above, our ability to enroll patients may be significantly delayed by the ongoing COVID-19 pandemic (including due to lack of resources and personnel at trial sites), and we cannot accurately predict the extent and scope of such delays at this point.

In addition to the competitive trial environment, the eligibility criteria of our clinical trials will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure to assure their cancer is either severe enough or not too advanced to include them in a study. The process of finding patients may prove costly. We also may not be able to identify, recruit or enroll a sufficient number of patients to complete our clinical studies because of the perceived risks and benefits of the product candidates under study, the availability and efficacy of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective patients, and the patient referral practices of physicians. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies, reporting initial and final trial results and obtaining regulatory approval of potential products may be delayed.

Further, if we are unable to identify patients with the targeted genetic mutations for our clinical trials, this could compromise our ability to seek designations under applicable FDA expedited review and development programs, including Breakthrough Therapy Designation and Fast Track Designation (to the extent these are available to us), or otherwise seek to accelerate clinical development and regulatory timelines. Patient enrollment may be affected by other factors, including:

- the severity of the disease under investigation;
- the efforts to obtain and maintain patient consents and facilitate timely enrollment in clinical trials;
- the ability to monitor patients adequately during and after treatment;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- reporting of the initial results of any of our clinical trials; and

factors we may not be able to control, including the impacts of the COVID-19 pandemic, that may limit patients, principal investigators or staff or clinical site availability.

We anticipate that certain of our current product candidates and future product candidates could be used in combination with third-party drugs or biologics, some of which are still in development, and we have limited or no control over the supply, regulatory status, or regulatory approval of such other drugs or biologics.

Certain of our current product candidates and any future product candidates may have the potential to be administered in combination with existing standards of care such as checkpoint inhibitor immunotherapies, chemotherapies, targeted therapies or radiotherapy. Our ability to develop and ultimately commercialize our current programs and product candidates and any future programs or product candidates for use in combination with other therapies will depend on our ability to access such drugs or biologics on commercially reasonable terms for the clinical trials and their availability for use with our commercialized product, if approved. We cannot be certain that current or potential future commercial relationships will provide us with a steady supply of such drugs or biologics on commercially reasonable terms or at all.

Any failure to maintain or enter into new successful commercial relationships, or the expense of purchasing checkpoint inhibitor immunotherapies or other potential combination or comparator therapies in the market, may delay our development timelines, increase our costs and jeopardize our ability to develop our current product candidates and any future product candidates as commercially viable therapies. If any of these occur, our business, financial condition, operating results, stock price and prospects may be materially harmed.

Moreover, the development of product candidates for use in combination with another product or product candidate may present challenges that are not faced for single agent product candidates. The FDA or comparable foreign regulatory authorities may require us to use more complex clinical trial designs in order to evaluate the contribution of each product and product candidate to any observed effects. It is possible that the results of such trials could show that any positive previous trial results are attributable to the other therapy and not our current product candidates and any future product candidates. Even if successful, such trials may cause delays in the time to obtain regulatory approval, thereby limiting any exclusive periods we have to market the product candidate. Moreover, following product approval, the FDA or comparable foreign regulatory authorities may require that products used in conjunction with each other be cross labeled for combined use. To the extent that we do not have rights to the other product, this may require us to work with a third party to satisfy such a requirement. Moreover, developments related to the other product may impact our clinical trials for the combination as well

as our commercial prospects should we receive regulatory approval. Such developments may include changes to the other product's safety or efficacy profile, changes to the availability of the other product, quality, manufacturing and supply issues with respect to the other product, and changes to the standard of care.

Results from earlier preclinical studies of our programs and product candidates are not necessarily predictive of the results of later preclinical studies and clinical trials of our programs and product candidates. If we cannot replicate the results from our earlier preclinical studies of our programs and product candidates in our later preclinical studies and clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

Any results from our earlier preclinical studies of our programs or our product candidates may not necessarily be predictive of the results from later preclinical studies and clinical trials. Similarly, even if we are able to complete our planned preclinical studies and clinical trials of our product candidates according to our current development timeline, the results from such preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway, or safety, pharmacokinetic or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical, nonclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain regulatory approval.

We may not be able to file INDs for our precision oncology and other programs to commence clinical trials on the timelines we expect, and even if we are able to, the FDA may not permit us to proceed.

We have received FDA clearance of our IND applications for TNG908 and TNG462 and we are actively enrolling patients in our Phase 1/2 clinical trial for TNG908. We expect to initiate the Phase 1/2 clinical trial for TNG462 in mid-2023. Additionally, we plan to file an IND for: (i) TNG260, our selective CoREST inhibitor, in the first half of 2023 and (ii) TNG348, our USP1 inhibitor, in mid-2023. However, we may not be able to file such INDs or INDs for future product candidates for our precision oncology or other programs on the timelines we expect. We have in the past, for example, extended the timeline for filing an IND for our USP1 inhibitor program as we continued to work on the development candidate in order to improve its pharmacologic properties.

Further, we may experience manufacturing delays or other delays with IND-enabling studies. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate clinical trials. These risks also apply to amendments we submit to existing INDs or to a new IND. Any failure to file INDs on the timelines we expect or to obtain regulatory approvals for our planned clinical trials may prevent us from initiating or completing our clinical trials or commercializing our product candidates on a timely basis, if at all.

Our clinical trials or those of our current or future collaborators may reveal significant adverse events not seen in our preclinical or nonclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.

Before obtaining regulatory approvals for the commercial sale of any products, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. Clinical testing is expensive and can take many years to complete, and outcomes are inherently uncertain. Failure can occur at any time during the clinical trial process. Because our precision oncology programs and our product candidates are in an early stage of development, there is a high risk of failure, and we may never succeed in developing marketable products. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials also may fail to show the desired safety and efficacy profile despite having progressed through nonclinical studies and initial clinical trials. If the results of our current and future preclinical studies and clinical trials are inconclusive with respect to the safety, pharmacokinetics or efficacy of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be prevented from, or delayed in, obtaining regulatory approval for such product candidates. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. There may be side effects experienced

during clinical trials in connection with the use of oncology therapies. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects as a result of the use of our therapy (or due to other factors). In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Product liability claims can be expensive to defend and result in significant damages and harm to our reputation. While we do have insurance to cover certain product liability claims, including in connection with certain injury during clinical trials, the coverage may not cover all injuries, be sufficient to cover all expenses related to any injury and we may be required to pay damages from our own resources and the amount of such damages may be significant.

Further, our product candidates could cause undesirable side effects in clinical trials related to on-target toxicity. If on-target toxicity is observed, or if our product candidates have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In addition, our product candidates could cause undesirable side effects that we have not yet observed. Many compounds that initially showed promise in early-stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound. There can be no assurance that any of our current or future clinical trials will ultimately be successful or support further clinical development or regulatory approval of any of our product candidates.

Certain of our product candidates will be used, and future product candidates may be used, in combination with one or more cancer therapies. The uncertainty resulting from the use of our product candidates in combination with other cancer therapies may make it difficult to accurately predict side effects in future clinical trials. As is the case with many treatments for cancer and rare diseases, it is likely that there may be side effects associated with the use of our product candidates. If significant adverse events or other side effects are observed in our clinical trial of our product candidate in combination with another therapy, we may have difficulty recruiting patients to our clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of one or more product candidates altogether. We, the FDA or other applicable regulatory authorities, or an IRB may suspend or terminate clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Even if the side effects do not preclude combination products from obtaining or maintaining regulatory approval, undesirable side effects may inhibit market acceptance of the approved products due to its tolerability versus other therapies. Any of these developments could materially harm our business, operating results, financial condition and prospects.

Some of our product candidates modulate pathways for which there are currently no approved or effective therapies, and utilize novel binding locations, which may result in greater research and development expenses, regulatory issues that could delay or prevent approval, or discovery of unknown or unanticipated adverse effects.

Some of our product candidates modulate pathways for which there are currently no approved or effective therapies, which may result in uncertainty regarding our current and future development efforts and ability to obtain regulatory approval for such candidates. We select programs for cancer driver targets based on what we believe is compelling biological rationale. We explore new programs based on extensive preclinical data analysis which sometimes cannot predict efficacy or safety in humans.

Some of our product candidates utilize novel binding locations, which may result in greater research and development expenses, regulatory issues that could delay or prevent drug candidate development and approval, or discovery of unknown or unanticipated adverse effects. We utilize structural biology in tight integration with our medicinal chemistry and biology capabilities to predict and design the compounds that we believe will achieve the most desirable characteristics, including potency, selectivity, bioavailability, and drug-like properties. A disruption in any of these capabilities may have significant adverse effects in our ability to expand our pipeline of product candidates, and we cannot predict whether we will continue to have access to these capabilities in the future to support our pipeline development. In addition, there can be no assurance that we will be able to identify, design and synthesize the necessary compounds or that these or other problems related to the development of product candidates will not arise in the future, which may cause significant delays or raise problems we may not be able to resolve.

Regulatory approval of novel product candidates such as ours can be more expensive, riskier and take longer than for other, more well-known or extensively studied pharmaceutical or biopharmaceutical product candidates due to our and regulatory agencies' lack of experience with them. The novelty of the mechanism of action of any of our product candidates may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. The novel mechanism of action also means that fewer people are trained in or experienced with product candidates of this type, which

may make it more difficult to find, hire and retain personnel for research, development and manufacturing positions and to identify clinical trial investigators to use our product candidates in trials. If our inhibitors utilize a novel mechanism of action that has not been the subject of extensive study compared to more well-known product candidates, there is also an increased risk that we may discover previously unknown or unanticipated adverse effects during our preclinical studies and clinical trials. Any such events could adversely impact our business prospects, operating results and financial condition.

We conduct clinical trials for our product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We currently conduct certain clinical trials outside the United States, and expect we will continue to do so in the future, and these jurisdictions may include countries in Europe, Australia or other foreign jurisdictions. For example, a separate clinical trial for TNG908 has commenced in France. The acceptance of trial data from clinical trials conducted outside the United States by the FDA, or comparable foreign regulatory authorities, may be subject to certain conditions. In cases where data from clinical trials conducted outside the United States are intended to serve as the sole basis for regulatory approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless: (i) the data are applicable to the United States population and United States medical practices, (ii) the trials were performed by clinical investigators of recognized competence and pursuant to Good Clinical Practices, or GCP, regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving regulatory approval or clearance for commercialization in the applicable jurisdiction.

Although we intend to explore other therapeutic opportunities in addition to the programs and product candidates that we are currently developing, we may fail to identify viable new product candidates for clinical development for a number of reasons. If we fail to identify additional product candidates, our business could be materially harmed.

The ongoing success of businesses in the biopharmaceutical industry depend, to a large extent, on the ability to continue to introduce new products, especially as exclusivity rights to given therapies or indications expire. Research programs to pursue the development of our existing and planned product candidates for new or additional indications and to identify new product candidates and disease targets require substantial technical, financial and human resources whether or not they are ultimately successful. Our screening technology and research programs may fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications and/or product candidates (or the development of a chemical compound or formulation that has the desired effect cannot be developed);
- potential product candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective products; or
- it may take greater human and financial resources than we possess to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, thereby limiting our ability to develop, diversify and expand our potential product portfolio.

Because we have limited financial and human resources, we intend to initially focus on research programs and product candidates for a limited set of indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to develop suitable product candidates through internal research programs, which could materially adversely affect our future growth and prospects.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities. Before we can commercialize any of our product candidates, we must obtain regulatory approval. We received clearance of our IND applications for TNG908 and TNG462. We are actively enrolling patients in our Phase 1/2 clinical trial for TNG908 and we expect to initiate the Phase 1/2 clinical trial for TNG462 in mid-2023. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. It is possible that our product candidates, including any product candidates we may seek to develop in the future, will never obtain regulatory approval. We have limited experience in filing and supporting the applications necessary to gain regulatory approvals and expect to rely on third-party CROs and/or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended pharmacokinetics, side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use. In addition, regulatory authorities may find fault with our manufacturing process or facilities or that of third-party contract manufacturers. We and our third-party manufacturers that we expect to rely on for commercial production of our therapies, if approved, may also face greater than expected difficulty in manufacturing our product candidates.

The process of obtaining regulatory approvals, both in the United States and abroad, is expensive and often takes many years. If the FDA or a comparable foreign regulatory authority requires that we perform additional preclinical studies or clinical trials, approval may be delayed, if obtained at all. The length of such a delay varies substantially based upon a variety of factors, including the type, complexity and novelty of the product candidate involved. Changes in regulatory approval policies during the development period, changes in or enactment of additional statutes or regulations, or changes in regulatory review policies for each submitted NDA, premarket approval application, or PMA, or equivalent application types, may cause delays in the approval or rejection of an application. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication or a related companion diagnostic is suitable to identify appropriate patient populations;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA, or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change such that our clinical data are insufficient for approval; and
- due to the factors identified above in this and other risk factors;

Even if we were to obtain regulatory approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, thereby narrowing the commercial potential of the product candidate. In addition, regulatory authorities may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

If we experience delays in obtaining, or if we fail to obtain, approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenue will be materially impaired.

The COVID-19 pandemic, or a similar pandemic, epidemic, or outbreak of an infectious disease, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates and the initiation and completion of clinical trials.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. Beginning in 2020 and continuing through the date of this filing, a novel strain of a virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes COVID-19 has spread across the world. Despite progress with distribution and administration of vaccines, COVID-19 and its effects continue to evolve, and countries continue to respond with the implementation of various responses. The extent to which the coronavirus impacts our operations or those of our third-party partners, including our preclinical studies and clinical trial operations, will depend on future developments, which are highly uncertain and cannot be predicted with confidence and could adversely impact our preclinical or clinical trial operations in the United States and our future clinical trial sites in foreign jurisdictions, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography. For example, similar to other biopharmaceutical companies, we may experience delays in initiating IND-enabling studies, protocol deviations, delays in enrolling our clinical trials, or dosing of patients in our clinical trials as well as in activating new trial sites. COVID-19 may also affect employees of third-party CROs located in affected geographies that we expect that we will rely upon to carry out our clinical trials. Any negative impact COVID-19 has to patient enrollment or treatment or the execution of our product candidates could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, and have a material adverse effect on our financial results.

Additionally, timely enrollment in planned clinical trials and the reporting of clinical trial results is dependent upon clinical trial sites which could be adversely affected by global health matters, such as pandemics. We are conducting, and plan to conduct, clinical trials for our product candidates in geographies which are currently affected by the COVID-19 pandemic, including our clinical trial for TNG908, a Phase 1/2 clinical trial in which we are actively enrolling patients in the United States and in France. The impact of the COVID-19 pandemic on the resources at clinical trial sites, among other factors, may impact the enrollment and progression (including dose escalation and dose expansion) of the Phase 1/2 trials for TNG908 and TNG462 and any future clinical trials we may conduct. Some factors from the COVID-19 pandemic that may delay or otherwise adversely affect enrollment in the clinical trials of our product candidates, including TNG908 and TNG462, as well as our business generally, include:

- the potential diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- the potential negative effect on the operations of our third-party manufacturers;
- interruption in global shipping affecting the transport of clinical trial materials, such as patient samples, investigational drug product and conditioning drugs and other supplies used in our clinical trials;
- staffing shortages at clinical trial sites, both healthcare professionals (e.g. physicians, nurses) and support staff, caused by the COVID-19 pandemic and the challenges of finding replacements may adversely impact the timing and on-going performance of a clinical trial;
- changes in local regulations as part of a response to the COVID-19 pandemic, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether; and
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines.

Our employees, including our lab personnel, are currently working at our office headquarters. We have, in the past, taken temporary precautionary measures intended to help minimize the risk of the virus to our employees, including temporarily requiring certain of our employees to work remotely, suspending all non-essential travel worldwide for our employees, implementing COVID-19 testing policies for employees in certain instances and discouraging employee attendance at industry events and in-person work-related meetings, which could negatively affect our business.

Risks Related to Commercialization

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 products in the biopharmaceutical and related industries is highly competitive. We compete in the segments of the pharmaceutical, biotechnology, and other related markets that address structural biology-guided chemistry-based drug design to develop therapies in the fields of cancer and genetic diseases. There

are many other companies focusing on precision oncology to develop therapies in the fields of cancer and other diseases. Specifically, with respect to TNG908 and TNG462 (each of which received FDA clearance of our respective IND applications), we are aware that Mirati Therapeutics, Inc. and Amgen each have a clinical MTA-cooperative PRMT5 inhibitor program that have commenced clinical trials, using the same mechanism of action as TNG908 and TNG462 (and there are other indirect competitors in the PRMT5 inhibition space as well).

We also compete more broadly across the market for cost-effective and reimbursable cancer treatments. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach (as noted above), and others are based on entirely different approaches. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes, such as Amgen. We face competition with respect to our current product candidates, and expect that we will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology 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.

Any product candidates that we successfully develop and commercialize will compete with currently approved therapies and new therapies that may become available in the future from segments of the pharmaceutical, biotechnology and other related markets. We believe principal competitive factors to our business include, among other things, our ability to identify biomarkers and third-party genetic screening services that include the applicable biomarkers in their test panels, ability to successfully transition research programs into clinical development, and the scalability of the platform, pipeline, and business. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, level of generic competition and novel competition that utilize the same mechanism of action and availability of reimbursement from government and other third-party payors.

Many of the companies that we compete against or which we may compete against in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and marketing, promoting and selling approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic 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. If barriers to entry do not remain in place, other companies may be able to more directly or effectively compete with us.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we or our collaborators may develop. Our competitors also may obtain FDA or other regulatory approval for their products sooner than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market.

If the market opportunities for our programs and product candidates are smaller than we estimate or if any regulatory approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.

The incidence and prevalence for target patient populations of our programs and product candidates have not been established with precision. TNG908 and TNG462, our first two product candidates to have INDs cleared by the FDA, are both oral small molecule inhibitors of PRMT5. We are developing TNG908 for the treatment of patients with solid tumors with MTAP deletion, a genetic alteration which occurs in 10% to 15% of all human tumors, including NSCLC, mesothelioma, cholangiocarcinoma, and GBM, as well as indications where there are limited treatment options with no standard of care, including MPNST. Our next-generation PRMT5 product candidate, TNG462, is being developed for the same patient population as TNG908 with the exception of GBM as TNG462 does not cross the blood-brain barrier in preclinical non-human primate models. Additionally, TNG260 is a first-in-class, CoREST inhibitor, which reverses the immune evasion effect of STK11 loss-of-function mutations. STK11 loss-of-function mutations are a genetic alteration in approximately 15% of NSCLC, 15% of cervical, 10% carcinoma of unknown primary, 5% of breast and 3% of pancreatic cancers. TNG348 is a USP1 inhibitor that is a strong synthetic lethal target for BRCA1/2 mutations, which are present in approximately 15% of ovarian, 10% of breast, 10% of prostate, 5% of endometrial and 5% of pancreatic cancers and additionally, BRCA wild-type HRD+ mutations which are present in approximately 40% of ovarian, 15% of breast, 3% of

prostate and 2% of pancreatic cancers. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our estimates.

The total addressable market opportunity will ultimately depend upon, among other things, the diagnosis criteria included in the final label (if approved for marketing), the indications for which our product candidates are approved for sale, acceptance by the medical community and patient access, product pricing and reimbursement. The number of patients with the cancers and solid tumors for which our product candidates may be approved as treatment may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. We may not be successful in our efforts to identify additional product candidates. Due to our limited resources and capital, we must prioritize development of certain product candidates, which may prove to be the wrong choice and may adversely affect our business.

If our current product candidates or any future product candidates do not achieve broad market acceptance, the revenue that we generate from their sales may be limited, and we may never become profitable.

We have never commercialized a product candidate for any indication. Even if our current product candidates and any future product candidates are approved by the appropriate regulatory authorities for marketing and sale, they may not gain acceptance among physicians, patients, third-party payors, and others in the medical community. If any product candidates for which we obtain regulatory approval do not gain an adequate level of market acceptance, we may not generate significant revenue and may not become profitable or may be significantly delayed in achieving profitability. Market acceptance of our current product candidates and any future product candidates by the medical community, patients and third-party payors will depend on a number of factors, some of which are beyond our control. For example, physicians are often reluctant to switch their patients, and patients may be reluctant to switch, from existing therapies even when new and potentially more effective or safer treatments enter the market. If public perception is influenced by claims that the use of certain precision oncology product candidates or immunotherapies and targeted therapies is unsafe, whether related to our or our competitors' products, our potential future products may not be accepted by the general public or the medical community. Future adverse events in precision oncology, immuno-oncology or the biopharmaceutical industry could also result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or approvals of our product candidates.

Efforts to educate the medical community and third-party payors on the benefits of our current product candidates and any future product candidates may require significant resources and may not be successful. If our current product candidates or any future product candidates are approved but do not achieve an adequate level of market acceptance, which will depend on a number of factors, we could be prevented from or significantly delayed in achieving profitability.

Risks Related to Our Reliance on Third Parties

We expect to rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We do not have the ability to independently conduct clinical trials. We expect to rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct or otherwise support clinical trials for our product candidates, including our Phase 1/2 clinical trials of TNG908 and TNG462, and for any other product candidates that emerge from our precision oncology programs. We may also rely on academic and private non-academic institutions to conduct and sponsor clinical trials relating to our product candidates.

Since we will rely on third parties for execution of clinical trials for our product candidates, we will control only certain aspects of their activities that will be important for the conduct of the trial (and such control that we do exercise may be based on contractual provisions that may be breached by the third-party). For example, for the Phase 1/2 clinical trials of TNG908 and TNG462, we will rely on one CRO (and expect that we will rely on that same CRO in connection with our TNG260 clinical trial if the IND for such therapy is approved by the FDA) for the conduct of the trials and, depending on the trial, one or a very limited number of manufacturers to manufacture the study drug to be used during the course of the trials. We are responsible for ensuring that each of our clinical trials is conducted and the study drug is manufactured in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on a CRO or CDMO will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties, suspension/hold or termination of trials and other penalties up to and including criminal prosecution.

We, our principal investigators and our CROs are required to comply with regulations, including GCP for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any products in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we, our principal investigators or our CROs fail to comply with applicable GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our current or future clinical trials will comply with GCP. In addition, our clinical trials generally must be conducted with product candidates produced under cGMP regulations. Our failure or the failure of our principal investigators, third party manufacturers or CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process, significantly increase our expenditures and could also subject us to enforcement action. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we have designed our Phase 1/2 clinical trials of TNG908 and TNG462 and intend to design the future clinical trials for our product candidates, the operational details of these trials will be executed by CROs and we expect CROs will conduct all of our future clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, are outside of our direct control. Our reliance on third parties to conduct future clinical trials also results in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may have staffing difficulties, fail to comply with contractual obligations, experience regulatory compliance issues, undergo changes in priorities or become financially distressed or form relationships with other entities, some of which may be our competitors.

If the principal investigators or CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates or our development program may be materially and irreversibly harmed. If we are unable to rely on clinical data collected by our principal investigators or CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party principal investigators or CROs terminate, we may not be able to enter into arrangements with alternative investigators (or clinical trial sites) and CROs. If principal investigators or CROs do not successfully carry out their contractual obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such principal investigators or CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, our product candidates. As a result, we believe that our financial results and the commercial prospects for our product candidates in the subject indication would be harmed, our costs could increase and our ability to generate future revenue, if any, could be delayed.

We have entered into collaborations and we may seek to establish additional collaborations in the future, and we might not realize the anticipated benefits of such collaborations. If we are not able to establish additional collaborations on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.

Our product development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with other pharmaceutical and biotechnology companies, like our existing collaboration with Gilead, for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's own evaluation of a potential collaboration. Factors a potential collaborator will use to evaluate a collaboration may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of

competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, as well as industry, and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all and it may be difficult to recruit and retain the expertise needed to launch and commercialize a new drug therapy. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

In addition, any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Research, development, commercialization and/or strategic collaborations, including the existing collaboration that we have with Gilead, are subject to numerous risks that may impact the success of a collaboration, which include the following:

- collaborators may have significant control or discretion in determining the efforts and resources that they will apply to a collaboration, and might not commit sufficient efforts and resources or might misapply those efforts and resources;
- we may have limited influence or control over the approaches to research, development and/or commercialization of product candidates in the territories in which our collaboration partners lead research, development and/or commercialization;
- collaborators might not pursue research, development and/or commercialization of collaboration product candidates or might elect not to continue or renew research, development and/or commercialization programs based on nonclinical and/or clinical trial results, changes in their strategic focus, availability of funding or other factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators might delay, provide insufficient resources to, or modify or stop research or clinical development for collaboration product candidates or require a new formulation of a product candidate for clinical testing;
- collaborators with sales, marketing and distribution rights to one or more product candidates might not commit sufficient resources to sales, marketing and distribution or might otherwise fail to successfully commercialize those product candidates;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;
- disputes might arise regarding the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our collaborators and us and our partners or with those we engage in connection with sponsored research;
- collaborators might not properly maintain or defend our intellectual property rights or might use our intellectual property improperly or in a way that jeopardizes our intellectual property or the potential commercial benefit of our product candidates or exposes us to potential liability;
- collaboration activities might result in the collaborator having intellectual property covering our activities or product candidates, which could limit our rights or ability to research, develop and/or commercialize our product candidates;
- collaborators might not be in compliance with laws applicable to their activities under the collaboration, which could impact the collaboration and us;
- disputes might arise between a collaborator and us that could cause a delay or termination of the collaboration or result in costly litigation that diverts management attention and resources; and
- collaborations might be terminated, which could result in a need for additional capital to pursue further research, development and/or commercialization of our product candidates.

In addition, funding provided by a collaborator might not be sufficient to advance product candidates under the collaboration. For example, although Gilead provided us with \$175.0 million upfront payments and a \$20.0 million equity investment in connection with our collaboration, we might need additional funding to advance product candidates prior to the completion of the clinical milestones of the collaboration agreement with Gilead.

If a collaborator terminates a collaboration or a program under a collaboration, including by failing to exercise a license or other option under the collaboration, whether because we fail to meet a milestone or otherwise, any potential revenue from the collaboration would be significantly reduced or eliminated. In addition, we will likely need to either secure other funding to advance research, development and/or commercialization of the relevant product candidate or abandon that program (or abandon a different program to allocate resources to the program rejected by the collaborator), the development of the relevant product candidate could be significantly delayed, and our cash expenditures could increase significantly if we are to continue research, development and/or commercialization of the relevant product candidates.

Additionally, disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing of the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation

Any one or more of these risks, if realized, could reduce or eliminate future revenue from product candidates under our collaborations, and could have a material adverse effect on our business, financial condition, results of operations and/or growth prospects.

We contract with third parties for the manufacture of our product candidates for preclinical development and expect to continue to do so for clinical testing and commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical development and clinical testing, as well as for the commercial manufacture of our products if any of our product candidates receive regulatory approval. In some cases, we rely on one party to manufacture our preclinical and clinical products and we exercise limited direct control over this manufacturer (and it would be time consuming and expensive to move production to a new manufacturer, if we were able to do so at all). This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products, if approved, or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. For example, we rely on a limited number of CDMOs to perform certain chemistry-related work on our preclinical product candidates. One such CDMO is located in Ukraine, which was invaded by Russia in February 2022 and, as a result, their work on our behalf of was interrupted. Another CDMO, with operations in Shanghai, was impacted when lock-down procedures were recently implemented due to COVID-19 and was unable to operate at full capacity. Events such as those in Ukraine and China may delay development of our future product candidates, which have been temporary and limited to date, but such delays may materially impact the timing for moving products into development candidate stage and IND-enabling studies, as well as initiating trials, in the future.

The facilities used by our contract manufacturers to manufacture our product candidates must be inspected by the FDA pursuant to pre-approval inspections that will be conducted after we submit our marketing applications to the FDA. We do not control the manufacturing process of, and will be completely dependent on, our contract manufacturers for compliance with cGMP in connection with the manufacture of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to pass regulatory inspections and/or maintain regulatory compliance for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority finds deficiencies with or does not approve these facilities for the manufacture of our product candidates or if it finds deficiencies or withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

If any CDMO with whom we contract fails to perform its obligations, we may be forced to enter into an agreement with a different CDMO, which we may not be able to do on reasonable terms, if at all, and such new agreement may result in significantly greater costs to us. In such scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original CDMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CDMOs for any reason, we will be required to verify that the new CDMO

maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CDMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CDMO may possess technology related to the manufacture of our product candidate that such CDMO owns independently. This would increase our reliance on such CDMO or require us to obtain a license from such CDMO in order to have another CDMO manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

Further, our failure, or the failure of our third-party manufacturers to comply with applicable regulations could 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 product candidates or products, if approved, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business and supplies of our product candidates.

Our product candidates and any products that we may develop may compete with other product candidates and approved products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

The third parties upon whom we rely for the supply of the active pharmaceutical ingredients and drug product to be used in our product candidates are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.

The active pharmaceutical ingredients, or API, and drug product we expect to use in all of our product candidates are supplied to us from single-source suppliers, in some cases the same manufacturer produces the API and drug product. Our ability to successfully develop our product candidates, and to ultimately supply our commercial products in quantities sufficient to meet the market demand (and to meet requirements in connection with our planned clinical trials), depends in part on our ability to obtain the API and drug product for these products in accordance with regulatory requirements and in sufficient quantities for clinical testing and commercialization. We are also unable to predict how changing global economic conditions or global health concerns such as the ongoing COVID-19 pandemic, as well as potential supply chain disruptions or cost increases related thereto, will affect our third-party suppliers and manufacturers. Any negative impact of such matters on our third-party suppliers and manufacturers may also have an adverse impact on our results of operations or financial condition.

For all of our product candidates, we intend to identify and qualify additional manufacturers to provide such API and drug product prior to submission of an NDA to the FDA and/or an MAA to the EMA. We are not certain, however, that our single-source suppliers will be able to meet our demand for products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers.

Establishing additional or replacement suppliers for the API and drug product used in our product candidates, if required, may not be accomplished quickly (or at all). If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory inspection or approval, which could result in further delay. While we seek to maintain adequate inventory of the API and drug product used in our product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain such API and drug product from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects.

Risks Related to Our Intellectual Property

If we cannot obtain new patents, maintain our existing patents and protect the confidentiality and proprietary nature of our trade secrets and other intellectual property, our business and competitive position may be harmed.

Our success depends in part on our ability to obtain and maintain patent and regulatory protections for our products candidates, to preserve our trade secrets and other proprietary rights and to prevent third parties from infringing on our rights and our proprietary technology.

We have procured patent rights, through both ownership and license, that cover our product candidates, and expect apply for additional patent protections in the future. However, our patent applications may not result in the issuance of patents in the U.S. or other countries. In addition, a patent may be issued in one country, but a counterpart patent may not be issued in another country, which is not uncommon in the biopharmaceutical industry.

Even if a patent is issued, that is not conclusive as to its inventorship, scope, validity or enforceability and therefore that patent may not afford adequate (or any) protection for our product candidates or future approved products. On the basis of such inconclusiveness, third parties may challenge our patents. Furthermore, patents have a limited lifespan. In the United States and most other jurisdictions in which we have undertaken patent filings, the natural expiration of a patent is generally twenty years after it is filed, assuming all maintenance fees are paid. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, patents we may own or in-license may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our current or future product candidates, including generic versions of such drugs. Nor can we be certain that we will obtain any patent term extension as permitted under the "Hatch-Waxman Amendments" which 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.

If any of our patents are narrowed, invalidated, revoked or become unenforceable, competitors may develop and market products similar or identical to ours that do not conflict with or infringe our patents rights, which could have a material adverse effect on our financial condition. Even if we obtain and maintain patents, our business may be significantly harmed if the patents are not broad enough to protect our products from copycat or similar products.

In addition, if there are challenges to our intellectual property by third parties, we may in the future enter into agreements with those parties that provide certain intellectual property rights to our future marketed products or products in our pipeline. If we do enter into such agreements, we may not be the exclusive provider of a therapy and, as a result, we expect that any potential revenue from the sales of such therapies would be materially and negatively impacted.

We may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although we generally require all of our employees, consultants and advisors and any other third parties who have access to our proprietary know-how, information or technology to assign or grant similar rights to the inventions they make in the course of their work to us, we cannot be certain that we have executed such agreements with all parties who may have contributed to our intellectual property, nor can we be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy.

We have, and expect that we will continue, to finance or collaborate in research and development projects conducted by third parties, including government organizations, hospitals, universities or other educational or research institutions, or other for-profit companies. Such third parties may be unwilling to grant us certain rights to technology or products developed through such projects. Disputes may also arise as to the rights to technology or products developed in collaboration with such third parties and we may not be able to secure the proprietary rights to any technology generated in such collaboration.

Significant legal questions exist concerning the extent and scope of patent protection for biopharmaceutical products and processes in the U.S. and elsewhere. Accordingly, there is no certainty that patent applications owned or licensed by us will issue as patents, or that our issued patents will afford meaningful protection against competitors. Once issued, patents are subject to challenge through both administrative and judicial proceedings in the U.S. and other countries. Such proceedings include re-examinations, inter partes reviews, post-grant reviews and interference proceedings before the U.S. Patent and Trademark Office, as well as opposition proceedings before the European Patent Office and other non-U.S. patent offices. Certain countries have laws that provide stronger bases for challenging third party patent rights than are available to challenge patents in other countries. Therefore, we may be able to defend our patents against a third-party claim in one country but counterpart patents may be invalidated in other countries and we may be able to invalidate a third-party patent in one country but not invalidate its counterpart patents in other countries. Further, in jurisdictions outside the United States, a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license. Accordingly, any actual or purported co-owner of our patent rights could seek monetary or equitable relief requiring us to pay it compensation for, or refrain from, exploiting these patents due to such co-ownership. Litigation may be required to enforce, defend or obtain our patent and other intellectual property rights. Any administrative proceeding or litigation could require a

significant commitment of our resources and, depending on outcome, could adversely affect the scope, validity or enforceability of certain of our patent or other proprietary rights.

Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents, with respect to either the same compounds, methods, formulations or other subject matter, in either case that we may rely upon to dominate our patent position in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until at least 18 months after the earliest priority date of patent filing, or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in patents we may own or in-license patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty.

Some of the sensitive technology, techniques and proprietary compounds used in our business are protected as trade secrets. Among other things, we enter into 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 (or for which we determine we will not seek patent protection). Although we seek to 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 (or that the terms of such agreements are enforceable). In our business, we rely on collaboration with, or discuss the potential for collaboration with, suppliers, outside scientists and other biopharmaceutical companies. Collaboration and discussion of potential collaboration or inadvertent disclosure of a trade secret present a strong risk of exposing our trade secrets. If our trade secrets were exposed, we may lose the protection and potential exclusive rights afforded by trade secret law, and such exposure may likely help our competitors and allow them to access technology without restriction and adversely affect our business prospects.

In addition, the patent prosecution 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. Due to expense of patent filings, we also may not file in every jurisdiction in which patents may be issued (and, therefore, we may not be able to assert patents rights in every country in the future). Further, with respect to certain pending patent applications covering our current or future product candidates, prosecution has yet to commence. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the relevant patent office(s) may be significantly narrowed by the time they issue, if they ever do. 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 to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Similarly, trademarks and trade names we utilize in our business may be challenged, infringed, diluted or declared generic or determined to be infringing on other marks. These marks can be important for name recognition in markets. If we are unable to secure and protect our trademarks and trade names, our business could be harmed.

If we are found to be infringing third party patents, we may be forced to pay damages to the patent owner and/or obtain a license to continue the manufacture, sale or development of our products. If we cannot obtain a license, we may be prevented from the manufacture, sale or development of our products or product candidates, which may adversely affect our business.

Parts of our technology, techniques, proprietary compounds and potential product candidates, including those which are or may be in-licensed or developed in collaboration with third parties, may be found to infringe patents owned by or granted to others. We may in the future receive notices claiming our products (if approved) and product candidates infringe third party patents (and notices offering the right to license certain technology to us) and third parties may in the future file civil lawsuits against us claiming infringement of their intellectual property rights.

Third parties may claim that the manufacture, use or sale of our products or product candidates infringes patents owned or granted to such third parties. We may become aware of patents owned by third parties that might be claimed by such third parties to be infringed by the development and commercialization of our products (if approved) or our

investigational compounds. In such cases we may take certain actions with respect to some of these, for example we may try to invalidate the patents or obtain licenses to a technology or invention.

Any holder of patents covering similar technology to our technology could sue us for damages, which may be material in amount, and seek to prevent us from manufacturing, selling or developing our products (and we may be, in certain cases, prevented from initiating product launches in certain jurisdictions or required to withdraw the product from the market after it has been launched). Intellectual property disputes, can be costly and time consuming to defend and there is no guarantee that we would prevail in such lawsuit. If we cannot successfully defend against any infringement claims, we may seek to invalidate the patent or seek a license to the technology prior to or during legal actions in order to reduce the risks in connection with the product launches (or at a later time after product introduction) and to reduce further costs and the risk of a court determination that our technology, techniques, proprietary compounds or potential product candidates infringe the third party's patents. A required license may be costly or may not be available on acceptable terms, if at all. A costly license, or inability to obtain a necessary license, could have a material adverse effect on our business.

In some instances, we believe we may prevail in a patent infringement action. There can, however, be no assurance that the court will agree with our position or that it will decide any infringement case in our favor. Nor can we be certain that, if we do not prevail in litigation, that we may be able to obtain a license to any third-party patent on commercially reasonable terms (or at all); successfully develop non-infringing alternatives on a timely basis (or at all); or license alternative non-infringing technology, if any exists, on commercially reasonable terms (or at all). Any impediment to our ability to manufacture, use or sell approved forms of our future products (if approved by regulatory authorities) or our product candidates could have a material adverse effect on our business and prospects.

It is possible that we could lose market exclusivity for a product earlier than expected, which may harm our competitive position.

In our industry, much of an innovative product's commercial value is realized while it has market exclusivity. Market exclusivity for our future products (if approved for sale by regulatory authorities) will likely depend in large part on patent rights and certain regulatory forms of protection. As noted above, patent protection can be uncertain as to the validity, scope and enforceability of many issued patents. Absent relevant patent protection for a product, once regulatory exclusivity periods expire, generic versions of the product can be approved and marketed.

The market exclusivity of our products may be impacted by competitive products that are either innovative or generic copies. In our industry, the risk of generic challenges has been increasing. U.S. law includes an approval pathway for generic versions of innovative small molecule products. Under the pathway, the FDA may approve products that are generic copies of innovative small molecule therapies on the basis of less extensive data than is required for a full new drug application. The law provides a mechanism to challenge the patents that protect an innovator's products. Such litigation may begin as early as four years after the innovative small product is first approved by the FDA. Pathways for generic products also exist in many other markets, including Europe and Japan. Competition, including from generics approved for marketing, would likely result in a decrease in volume of sales of our products, as well as a decrease in prices and lower margins for our products (if approved for marketing by regulatory authorities).

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 in-license, our trade secrets or other proprietary rights. In addition, any patents or other proprietary rights we may own or in-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 (and we may not be able to prevent the commercialization of the competitor product). In addition, in an infringement proceeding, a court may decide that one or more of any patents we may own or in-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 in-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 in-license (or any other proprietary rights we may own). 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings relating to our proprietary rights could have a material adverse effect on our ability to compete in the marketplace and may negatively impact our stock price.

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 in-license. These proceedings are expensive and an unfavorable outcome could result in a loss of our current patent rights (or technology covered under current patent applications) 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.

Even in cases in which we or our licensors or strategic partners initiate legal proceedings against a third party to enforce a patent covering one of our current or future product candidates, the defendant could (and in pharmaceutical patent litigation the defendant often does) make a counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. If such counterclaims are successful, the exclusivity related to the product may be lost and our business would be harmed.

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 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for research and 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.

We may be subject to damages or settlement costs resulting from claims that we or our employees have violated the intellectual property rights of third parties, or are in breach of our agreements. We may be accused of, allege or otherwise become party to lawsuits or disputes alleging wrongful disclosure of third-party confidential information by us or by another party, including current or former employees, contractors or consultants. In addition to diverting attention and resources to such disputes, such disputes could adversely impact our business reputation and/or protection of our proprietary technology.

The intellectual property landscape relevant to our product candidates and programs is crowded, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. We cannot assure you that our current or future product candidates and other technologies that we have developed, are developing or may develop in the future do not or will not infringe, misappropriate or otherwise violate existing or future patents or other intellectual property rights owned by third parties. For example, many of our employees were previously employed at other biotechnology or pharmaceutical companies. Although we try to ensure that our employees, consultants and advisors 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 these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's former employer. We may also be subject to claims that patents and applications we have filed to protect inventions of our employees, consultants and advisors, even those related to one or more of our current or future product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims.

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

substantial damages for infringement, misappropriation or other violations, which we may have to pay if a court decides that the product candidate or technology at issue infringes, misappropriates 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 current product candidate, including TNG908 and TNG462, or future product candidates, or from using our proprietary technologies, unless the third party licenses its product rights to us, which it is not required to do, on commercially reasonable terms or at all;

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 products, or the license to us may be non-exclusive, which would permit third parties to use the same intellectual property to compete with us;

redesigning our current or future product candidates or processes so they do not infringe, misappropriate or violate third-party intellectual property rights, which may not be possible or may require substantial monetary expenditures and time; and

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. 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.

We may be unable to obtain patent or other intellectual property protection for our current or future product candidates or our future products, if any, in all jurisdictions throughout the world, and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

We may not be able to pursue patent coverage of our current or future product candidates in all countries. Filing, prosecuting and defending patents on current or future product candidates in all countries throughout the world would be prohibitively expensive, and 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 where intellectual property rights enforcement is not as strong as that in the United States. These products may compete with our current or future product candidates and in jurisdictions where we do not have any issued patents our patent applications or other intellectual property rights may not be effective or sufficient to prevent them from competing. Much of our patent portfolio is at the very early stage. We will need to decide whether and in which jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines.

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 pharmaceutical products, which could make it difficult for us to stop the infringement of any patents we may own or in-license or marketing of competing products in violation of our proprietary rights generally. 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.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents we may own or license that are relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

If we fail to comply with our obligations in any agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We may from time to time be party to license and collaboration agreements with third parties to advance our research or allow commercialization of current or future product candidates. For example, in March 2020 we entered into a License Agreement with Medivir with respect to certain technology related to USP1. Such agreements may impose numerous obligations, such as development, diligence, payment, commercialization, funding, milestone, royalty, sublicensing, insurance, patent prosecution, enforcement and other obligations on us and may require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the

licenses. In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technologies covered by these license agreements.

Further, the terms of these agreements can be complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business

Any termination of these licenses, or if the underlying patents fail to provide the intended exclusivity, could result in the loss of significant rights and could harm our ability to commercialize our current or future product candidates, and competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of certain of our current or future product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe, misappropriate or otherwise violate intellectual property rights of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our current or future product candidates, and what activities satisfy those diligence obligations;
- the priority of invention of any patented technology; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our future licensors and us and our partners.

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

Patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase uncertainties of the scope of our patent protection and the costs related to obtaining and enforcing our patents. 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. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

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.

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 United States 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 rights under patents that we might obtain in the future. Further, other countries and jurisdictions, such as the European Union, periodically review their intellectual property laws and they

may also take similar actions that impact the laws and regulations governing patents and they may implement changes that could weaken our ability to obtain new patents or to enforce our rights under patents that we might obtain in the future

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might subject us to infringement claims or adversely affect our ability to develop and market our current or future product candidates.

We cannot guarantee that any of our or our licensors' patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending patent application in the United States and abroad that is relevant to or necessary for the commercialization of our current or future product candidates in any jurisdiction. For example, U.S. patent applications filed before November 29, 2000 and certain U.S. patent applications filed after that date that will not be filed outside the United States remain confidential until patents issue. As mentioned above, patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our current or future product candidates could have been filed by third parties without our knowledge. Additionally, identification of third-party patent rights that may be relevant to our operations is difficult because patent searching is imperfect due to, for example, differences in terminology among patents or incomplete databases. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our current or future product candidates or the use of our current or future product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our current or future product candidates. We may incorrectly determine that our current or future product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our current or future product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our current or future product candidates.

If we fail to identify and correctly interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims which can result in the adverse consequences related to infringement as described in the preceding risk factors.

Intellectual property rights do not guarantee commercial success of current or future product candidates or other business activities. Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

The degree of future protection afforded by our intellectual property rights, whether owned or in-licensed, is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- patents, should they issue, that we may own or in-license, may not provide us with any competitive advantages, may be narrowed in scope, or may be challenged and held invalid or unenforceable;

- others may be able to develop and/or practice technology, including compounds that are similar to the chemical compositions of our current or future product candidates, that is similar to our technology or aspects of our technology but that is not covered by the claims of any patents we may own or in-license, should any patents issue;

- we, or our future licensors or collaborators, might not have been the first to make the inventions or to file the patent covered by a patent application that we own or may in-license;

- others may independently develop similar or alternative technologies without infringing, misappropriating or otherwise violating our intellectual property rights;

- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and may then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such trade secrets or know-how;

- we may not be able to maintain the confidentiality of our trade secrets or other proprietary information;

- we may not develop or in-license additional proprietary technologies that are patentable; and

- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

Risks Related to Government Regulation

Our future commercial success depends on gaining regulatory approval for new products and obtaining approvals for new indications.

We invest significant amounts in developing new products and technologies. Our success and revenue growth, if any, will depend in part on our identification, development and commercialization of new products and technologies, and approval of additional indications for our any products under development. Product development is very expensive, takes significant time and involves a high degree of risk. Only a small number of research and development programs result in the commercialization of a product.

Our ability to grow our business may be adversely affected if we are delayed or unable to successfully develop the products in our pipeline, if we are unable to gain regulatory approval of such product candidates, and expand the indications that may be treated by such product candidates, and gaining regulatory approval to sell and market such product candidates in additional jurisdictions.

We must also maintain all such regulatory approvals for the period of time that we sell the product in each such jurisdiction. Our failure to obtain, or a delay in obtaining, approval or our failure to maintain approvals once obtained, will prevent us from selling products and generating revenues for those products in such jurisdiction where we do not hold such approvals

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Assuming that our product candidates prove to be safe and effective in clinical trials, we expect that we will file for marketing approval for such product candidates in the United States and we may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product 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 fail to receive applicable regulatory approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and future potential revenue may be less than expected by investors and analysts.

Obtaining and maintaining regulatory approval of our product 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 regulatory approval of a product candidate, 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 nonclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In short, the foreign regulatory approval process involves all of the risks associated with FDA approval. 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 may intend to charge for our products will also be subject to approval.

We may seek priority review designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months from the date of filing, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in an expedited regulatory review or approval process or necessarily

confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

We may seek orphan drug designation for certain of our product candidates, and we may be unsuccessful or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

As part of our business strategy, we may seek orphan drug designation for certain of our product candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a product intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population of 200,000 or more in the United States where there is no reasonable expectation that the cost of developing the product will be recovered from sales in the United States. 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. The FDA granted Orphan Drug Designation to TNG908 for the treatment of malignant peripheral nerve sheath tumors (MPNST) and malignant glioma, including GBM.

Similarly, in Europe, the European Commission, upon the recommendation of the EMA's Committee for Orphan Medicinal Products, grants orphan designation to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in Europe and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation is granted for drugs intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in Europe would be sufficient to justify the necessary investment in developing the drug. In Europe, orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a product with an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

Obtaining orphan drug exclusivity may not effectively protect a product candidate from competition because different products having different chemical compositions can be approved for the same condition and the same therapies can be approved for different conditions but used off-label. Even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, 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 if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a product nor gives the product any advantage in the regulatory review or approval process. While we may seek orphan drug designation for our product candidates, we may never receive such designations. Even if we do receive such designations, there is no guarantee that we will enjoy the benefits of those designations.

A breakthrough therapy designation and fast track designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development, regulatory review or approval process, and each designation does not increase the likelihood that any of our product candidates will receive regulatory approval in the United States.

We may seek a breakthrough therapy designation for some of our 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 the 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. Product candidates designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated

approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the 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 therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification and rescind the designation or decide that the time period for FDA review or approval will not be shortened.

We may also seek fast track designation for some of our product candidates and, in the case of TNG908 and TNG462, we have been granted fast track designation by the FDA. If a drug is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you 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. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

We may seek accelerated approval of our current or future product candidates using the FDA's accelerated approval pathway. Accelerated approval by the FDA, even if granted for our current or any other future 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 regulatory approval.

We may seek accelerated approval of our current or future product candidates, where applicable, using the FDA's accelerated approval pathway. A product 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 or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA requires 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. Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be under way prior to approval or within a specified time period after the date accelerated approval was granted. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. In addition, the FDA currently requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact 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. Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of traditional FDA approval.

The FDA, the EMA and other regulatory authorities may implement additional regulations or restrictions on the development and commercialization of our product candidates, and such changes can be difficult to predict.

The FDA, the EMA and regulatory authorities in other countries have each expressed interest in further regulating biotechnology products. Agencies at both the federal and state level in the United States, as well as U.S. Congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our product candidates. Adverse developments in clinical trials of products conducted by others may cause the FDA or other oversight bodies to change the requirements for conducting clinical trials or for approval of any of our product candidates. These regulatory review agencies and committees and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory agencies and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay

or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

Inadequate funding for the FDA, the SEC and other U.S. government agencies or the EMA or comparable foreign regulatory authorities, including from government shut downs, or other disruptions to these agencies' operations, 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 the FDA, the EMA or comparable foreign regulatory authorities 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 and accept the payment of user fees, and enact statutory, regulatory and policy changes. Average review times at the FDA or other regulatory authorities have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business.

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 the FDA, the EMA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in prior years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, 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.

Separately, since March 2020 when foreign and domestic inspections were largely placed on hold due to the COVID-19 pandemic, the FDA has been working to resume pre-pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre-approval inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to 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 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications.

Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA and other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, 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.

Healthcare legislative 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 and statutes could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) changes to the method in which drug prices are determined for Medicare and Medicaid participants or other potential patients in the U.S. (or by which drug prices are determined in other countries and regions), (iii) additions or modifications to product labeling (if, and when, a product is approved for sale); (iv) the recall or discontinuation of our products (if any products are approved by applicable regulatory authorities); or (v) additional record-keeping requirements. If any such changes were to be imposed, they could adversely

affect the operation of our business. For additional information, see the section entitled “Business – Current and future healthcare reform legislation.”

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any of our product candidates, if approved;
- the ability to set a price that we believe is fair for any of our product candidates, if approved;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical and biologic products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA’s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Further, reductions in reimbursement from Medicare and other government programs may also result in reductions in payments from private payers. 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.

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 product 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.

We expect that additional 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 product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Additionally, we expect to experience pricing pressures in connection with the sale of any future approved product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those drugs and decrease our ability to generate revenue.

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. For more information regarding insurance coverage and reimbursement please see “Business – Government Regulation – Insurance Coverage and Reimbursement.”

Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, 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.

Even if we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the U.S., the European Union or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

There is significant uncertainty related to the insurance coverage and reimbursement of newly-approved products. In the U.S., third-party payors, and governmental healthcare plans, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the U.S. for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates. Outside the U.S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other foreign jurisdictions have and will continue to put pressure on the pricing and usage of our product candidates (if approved by regulators).

Moreover, increasing efforts by governmental and third-party payors in the U.S. 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 product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

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 products on the market, once we begin commercializing our product 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 product candidates for which we may obtain regulatory approval. Our future arrangements with third-party payors, healthcare providers, 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 product candidates for which we obtain regulatory approval. See the section entitled “*Business – Other healthcare laws*.”

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 future sales of our product candidates (following regulatory approval of such therapy) by us or third-parties that we engage, 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, imprisonment, 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 not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. Further, defending against any such actions can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the above occur, our ability to operate our business and our results of operations could be adversely affected.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are 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. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with appropriately licensed and permitted third parties for the disposal of these materials and wastes. We cannot, however, eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of 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.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to post-market study requirements, marketing and labeling restrictions, and even recall or market withdrawal if unanticipated safety issues are discovered following approval. In addition, we may be subject to penalties or other enforcement action if we fail to comply with regulatory requirements.

Any regulatory approvals that we receive for our product candidates will require surveillance to monitor the safety and efficacy of the product candidate. If the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, import, export, adverse event reporting, storage, advertising, promotion, monitoring, and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and listing, as well as continued compliance with cGMP and GCPs for any clinical trials that we conduct post-approval and pharmacovigilance reporting obligations. Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics, and those supplying products, ingredients, and components of them, are required to register their establishments with the FDA and certain state agencies, and are subject to periodic announced and unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other regulatory requirements, including applicable product tracking and tracing requirements. Any regulatory approvals that we receive for our product candidates may also 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 studies, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. The FDA may also require a REMS in order to approve our product candidates, which could include 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. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- clinical trial holds;
- fines, warning letters or other regulatory enforcement action;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. 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 regulatory approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

European data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

We are conducting and plan to conduct additional clinical trials and enroll subjects in our current or future clinical trials in the U.S. and Europe, and therefore we will be subject to privacy restrictions. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the European Economic Area (“EEA”), including personal health data, is subject to the EU General Data Protection Regulation, or GDPR and similarly, processing of personal data regarding individuals in the UK is subject to the UK General Data Protection Regulation and the UK Data Protection Act 2018, or UK GDPR and together with the EU GDPR, “GDPR”. 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. While we have commenced the process of implementing procedures to comply with the GDPR, compliance with these regulations will be a rigorous and time-intensive process that we expect will increase our cost of doing business and require us to change certain of 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. Further, many countries interpret the application of the provisions of the GDPR in different manner, making compliance in certain countries and across the EEA challenging.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs.

As we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA’s accounting provisions.

Risks Relating to Employee Matters and Managing Anticipated Growth

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

We are highly dependent on many of our key employees and members of our executive management team as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment letter agreements with certain of our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and clinical trial and commercialization strategies. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Recruiting and retaining qualified scientific, clinical, medical, 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, including temporary loss due to illness, 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 products. 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, medical and clinical personnel from universities and research institutions. Failure to provide evidence of safety and efficacy of our product candidates in clinical trials, or delays experienced in such clinical trials, may make it more challenging to recruit and retain qualified scientific personnel.

In particular, we have experienced a very competitive hiring environment in Boston and Cambridge, Massachusetts. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success with which we can discover and develop product candidates and our business will be limited.

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 collect and use a variety of personal data, such as names, mailing addresses, email addresses, phone numbers. In addition, in connection with our TNG908 and TNG462 Phase 1/2 clinical trials, we (and our third party processors assisting with the clinical trial) will have access to, and may store, clinical and health information of the patients participating in the trial.

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 the compounds we are developing, our screening platform technology, 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 GDPR) and may cause a material adverse impact to our reputation, affect our ability to 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. 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 the losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, other expenses or lost revenue 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. By way of example, the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020, creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal data. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and in other states. Third parties that perform services on our behalf in connection with our research and development efforts and other operations may also hold proprietary or confidential information regarding our business on their information technology networks. The risks outlined above (and elsewhere in this risk factor) apply to any third-party service provider that holds our information, including the ability of unauthorized access to our confidential and proprietary information.

Further, the California Privacy Rights Act, or CPRA, was passed by California voters on November 3, 2020. The CPRA will create additional obligations with respect to processing and storing personal information that are scheduled to take effect on January 1, 2023 (with certain provisions having retroactive effect to January 1, 2022). Additionally, some observers have noted that the CCPA and CPRA could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business. Already, in the United States, we have witnessed significant developments at the state level, for example, comprehensive privacy laws akin to the CCPA have recently been passed in Colorado, Utah, Virginia and Colorado, and, with bills being proposed in several other states, it is quite possible that other U.S. states will follow suit. New privacy and data security laws have been proposed in more than half of the states in the U.S. and in the U.S. Congress. Further, in addition to the proposals for comprehensive consumer privacy laws, many states are considering more limited privacy bills that focus on specific issues such as biometric data. The existence of comprehensive privacy laws in different states in the country will make our compliance obligations more complex and costly.

A number of states have adopted privacy laws and several states have proposed new privacy laws, some of which are similar to the above discussed recently passed laws. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

To enable the transfer of personal data outside of the EEA or the UK, adequate safeguards must be implemented in compliance with European and UK data protection laws (for example, the European Commission approved Standard Contractual Clauses, or SCCs). In addition, transfers made pursuant to the SCCs (and other similar appropriate transfer safeguards) need to be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular regarding applicable surveillance laws and relevant rights of individuals with respect to the transferred personal data, to ensure an “essentially equivalent” level of protection to that guaranteed in the EEA in the jurisdiction where the data importer is based (“Transfer Impact Assessment”). On June 4, 2021, the EC issued new forms of SCCs for data transfers from controllers or processors in the EU/EEA (or otherwise subject to the GDPR) to controllers or processors established outside the EU/EEA. The new SCCs replace the SCCs that were adopted previously under the EU Data Protection Directive. The UK is not subject to the EC’s new SCCs but has published its own transfer mechanism, the International Data Transfer Agreement, or IDTA, along with a separate addendum to the EU SCCs), which enable transfers from the UK, and has also implemented a similar Transfer Impact Assessment requirement. The new IDTA or the U.K. addendum must be used for any new contract entered into as of September 21, 2022 and implemented in existing contracts that incorporate the prior version of the SCCs by March 21, 2024. Implementing these new safeguards will require significant effort and cost and may result in us needing to make strategic considerations around where EEA or UK personal data is utilized, processed and stored.

Although the UK is regarded as a third country under the EU GDPR, the European Commission has issued a decision recognizing the UK as providing adequate protection under the EU GDPR (“Adequacy Decision”) and, therefore, transfers of personal data originating in the EEA to the UK remain unrestricted. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The UK Government has also now introduced a Data Protection and

Digital Information Bill (“UK Bill”) into the UK legislative process. The aim of the UK Bill is to reform the UK’s data protection regime following Brexit. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regime and threaten the UK Adequacy Decision from the EU Commission. This may lead to additional compliance costs and could increase our overall risk. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties.

These and other future developments regarding the flow of data across borders could increase the cost and complexity of delivering our services in some markets and may lead to governmental enforcement actions, litigation, fines, and penalties or adverse publicity, which could adversely affect our business and financial position.

Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition and results of operations.

If we or third-party CMOs, CROs or other contractors or consultants fail to comply with U.S. and international data protection laws and regulations, it could result in government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we, our CRO operating our trials, or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we or such third-party have violated individuals’ privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2022, we had 110 full-time employees. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly as we function as a public company and in the areas of product development, regulatory affairs and, if any of our product candidates receives regulatory approval, sales, medical affairs, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we may not be able to effectively manage the planned expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

Risks Related to Our Common Stock

Our executive officers, directors, principal stockholders and their affiliates own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Based on our common stock outstanding as of December 31, 2022, our executive officers, directors and their affiliates and our principal stockholders beneficially held, in the aggregate, approximately 40% of our outstanding voting stock. These stockholders, acting together, would be able to significantly influence all matters requiring stockholder approval. For example, these stockholders would be able to significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. These stockholders may have interests, with respect to their common stock, that are different from those of other investors 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.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Under Sections 382 and 383 of the Internal Revenue Code, as amended, or the Code, if a corporation undergoes an “ownership change” (generally defined as a greater than 50 percentage point change (by value) in the ownership of its equity over a three-year period), the corporation’s ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income may be limited. We have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. The Company has performed an analysis of ownership changes through December 31, 2021, and determined that on February 6, 2017 and August 17, 2020, ownership changes had occurred. Based on this analysis, the Company’s ability to use its pre-change tax attributes to offset federal and state taxable income are subject to annual limitations and a portion of the attributes generated prior to February 6, 2017, will expire unutilized, which could potentially result in an increased future tax liability. The Company has adjusted its deferred tax assets and valuation allowance balance for the affected tax attribute carryforwards to reflect the expiration of the attributes.

Federal net operating loss carryforwards generated in taxable years beginning after December 31, 2017 will not be subject to expiration. However, any such net operating loss carryforwards may only offset 80% of our annual taxable income in taxable years beginning after December 31, 2020. There is also a risk that due to regulatory changes, such as suspensions on the use of net operating loss carryforwards or other unforeseen reasons, our existing net operating loss carryforwards could expire or otherwise be unavailable to offset future income tax liabilities, including for state tax purposes. In future years, if and when a net deferred tax asset is recognized related to our net operating loss carryforwards, the changes in the carryforward/carryback periods as well as the new limitation on use of net operating loss carryforwards may significantly impact our valuation allowance assessments for net operating loss carryforwards. For these reasons, we may not be able to utilize some portion of our net operating loss carryforwards, none of which are currently reflected on our balance sheet, even if we attain profitability.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Our certificate of incorporation and 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 board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- 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 the stockholders may 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, and special meetings of stockholders may not be called by any other person or persons;
- 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 then, in addition to any other vote required by law, only upon the approval of not less than 66 2/3% of all outstanding shares of our capital stock then entitled to vote in the election of directors;
- supermajority voting requirements to amend our bylaws by stockholder action (unless our board recommends that our stockholders approve such amendment(s)) and 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, which preferred stock may include rights superior to the rights of the holders of common stock.

These anti-takeover provisions and other provisions in our certificate of incorporation and 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.

Our bylaws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Pursuant to our bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall 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 a fiduciary duty owed by any of our directors, officers, or other employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware, or the DGCL, or our certificate of incorporation or bylaws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim governed by the internal affairs doctrine. We refer to the foregoing provision as 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. Our bylaws further provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. We refer to such provision as the Federal Forum Provision. Our bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital 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 U.S. federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, these forum selection clauses 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 the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. While the Delaware Supreme Court and courts in other states have upheld federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court, 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 us and/or our stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States 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 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 and representatives 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 also expect our non-U.S. activities to increase in time. We have, and we expect we will continue to, engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents, representatives or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

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 United States and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing 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, imposition of a monitor, possible exclusion from participation in 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.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

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

Our stock price has been and is likely to continue to be volatile. The stock market in general, and the market for biopharmaceutical companies in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- advancement of our preclinical programs, such as our targeted oncology programs, into clinical testing;
- results of clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States 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 programs and product candidates or preclinical and clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- 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 and third-party reimbursement decisions;
- market conditions in the pharmaceutical and biotechnology sectors;
- purchases or sales of our securities by our officers, directors or significant shareholders;
- limited trading volume;
- general economic, industry and market conditions; and
- the other factors described in this “*Risk Factors*” section.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, and particularly after we are no longer an “emerging growth company,” we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act and rules subsequently implemented by the SEC and The Nasdaq Global Market, or Nasdaq, have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, these rules and regulations have made it more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

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 relies in part on the research and reports that industry or financial analysts publish about us or our business. We do not control these analysts. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price target for our stock or publish inaccurate or unfavorable evaluations of our company or our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock or fail to publish reports covering our company regularly, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline. In addition, if we are the subject of negative publicity, whether from an analyst, academic, industry group or the general or financial press, our stock price may decline.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock has been and may continue to be volatile. The stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

General Risk Factors

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, could adversely affect our business operations, financial condition and results of operations.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank ("SVB") was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation ("FDIC") as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC indicated that all depositors of SVB would have access to all of their money after only one business day of closure, including funds held in

uninsured deposit accounts, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB, Signature Bank or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder. We did hold certain funds in a deposit account with SVB, and while we now have access to those funds, we did not have access for a short time leading up to the events on March 10, 2023.

Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to \$25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediately liquidity may exceed the capacity of such program. Additionally, there is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.

Although we assess our banking relationships as we believe necessary or appropriate, our access to our cash resources are adequate to fund our operations into at least 2025. But if the banks in which we hold our cash and cash equivalents were to experience bankruptcy or suspend operations, in such case, the amounts above the level insured by the FDIC may not be available to us immediately, or at all.

The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- Delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets; or
- Termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and/or projected business operations and financial condition and results of operations.

In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by parties with whom we conduct business, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

The tax regimes we are subject to or operate under are unsettled and may be subject to significant change. Changes in tax laws (including in response to the COVID-19 pandemic) or tax rulings, or changes in interpretations of existing laws, could cause us to be subject to additional income-based taxes and non-income taxes (such as payroll, sales, use, value-added, digital tax, net worth, property, and goods and services taxes), which in turn could materially affect our financial position and results of operations. Additionally, new, changed, modified, or newly interpreted or applied tax laws could increase our potential future customers' and our compliance, operating and other costs, as well as the costs of our products, if approved. As we expand the scale of our business activities, any changes in the U.S. taxation of such activities may increase our effective tax rate and harm our business, financial condition, and results of operations. Complying with these tax laws is complex and the statutes and regulations can be subject to varying interpretation which can make compliance challenging.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the United States and other countries are experiencing increased inflation and interest rates have increased in response to this inflation. These conditions in the U.S. and global economy have caused significant volatility and uncertainty in U.S. and international markets. A severe or prolonged economic downturn, a marked increase in interest rates and inflation could result in a variety of risks to our business, including, weakened demand for our product

candidates (if and when approved by regulatory authorities) and our ability to raise additional capital when needed on acceptable terms, if at all. In addition, our business may be generally exposed to the impact of political or civil unrest or military action, including the current conflict between Russia and Ukraine (where a vendor that performs chemistry related work on our pre-clinical product candidates is located) and, while we do not otherwise have direct exposure to Ukraine, our business and results of operations may be impacted based upon the events taking place there. A weak or declining economy could also strain our suppliers and the global supply chain, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

An active trading market for our common stock may not be sustained, and you may not be able to resell your shares at the price you paid.

Although our common stock is listed on The Nasdaq Global Market, an active trading market for our shares may not be sustained. In the absence of an active trading market for our common stock, investors may be unable to sell their shares.

Item 1B. Unresolved Staff Comments

Not Applicable.

Item 2. Properties

Our corporate headquarters is located at 201 Brookline Avenue, Boston, Massachusetts, where we lease and occupy approximately 64,805 square feet of office and laboratory space. The term of our amended lease with respect to this facility expires on January 31, 2033, however, under certain circumstances, this lease may terminate on an earlier date.

Item 3. Legal Proceedings

From time to time, we may become involved in litigation or other legal proceedings. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock currently trades on The Nasdaq Global Market under the symbol "TNGX".

Holders of Common Stock

As of March 20, 2023, there were approximately 35 stockholders of record of our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number of stockholders of record.

Dividend Policy

We currently intend to retain all available funds and future earnings, if any, to fund the development and expansion of our business. We have never declared or paid cash dividends on our common stock, and we do not expect to pay any cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, on our common stock will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, anticipated cash needs, and other factors that the board of directors may deem relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Unregistered Sales of Equity Securities

During the year ended December 31, 2022, we did not issue or sell any unregistered securities not previously disclosed in an Annual Report on Form 10-K or in a Current Report on Form 8-K.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. [Reserved]

Not applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing at the end of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in, or implied by, the forward-looking statements contained in the following discussion and analysis.

Unless otherwise indicated, references in this Management's Discussion and Analysis of Financial Condition and Results of Operations section to "Tango," "we," "us," "our" and other similar terms refer to our wholly-owned subsidiary Tango Therapeutics Sub, Inc. and its subsidiary prior to the closing of the business combination with BCTG Acquisition Corp. and to Tango Therapeutics, Inc. and its consolidated subsidiaries after giving effect to the Business Combination.

Overview

Tango Therapeutics was founded with a clear mission: discover the next generation of precision medicines to help patients with cancer through addressing the specific genetic alterations that fuel the cancer. We leverage our state-of-the-art target discovery platform to identify novel targets and develop new drugs directed at tumor suppressor gene loss in defined patient populations with high unmet medical need. Tumor suppressor gene loss remains a largely unaddressed target space specifically because these genetic events cannot be directly targeted. Our novel small molecules are designed to be selectively active in cancer cells with specific tumor suppressor gene loss, killing those cancer cells while sparing normal cells. We also are extending this target space beyond the classic, cell-autonomous effects of tumor suppressor gene loss to include the discovery of novel targets that reverse the effects of tumor suppressor gene loss that prevent the immune system from recognizing and killing cancer cells (immune evasion). We believe our approach will provide the ability to deliver the deep, sustained target inhibition necessary to optimize tumor response and clinical benefit as a result of the unique ability of synthetic lethal targeting to spare normal cells.

Our lead program, TNG908, is an MTA-cooperative inhibitor of PRMT5 designed to work selectively in cancer cells with an MTAP deletion. MTAP-deletion occurs in approximately 10% to 15% of all human tumors including NSCLC, mesothelioma, pancreatic cancer, cholangiocarcinoma and GBM. In preclinical studies, TNG908 demonstrated 15-fold greater potency in MTAP-deleted cancer cells versus normal cells and robust efficacy in vitro and in vivo. Patients are actively being enrolled in the Phase 1/2 clinical trial and we expect to provide an update on the ongoing dose escalation portion of the trial, focusing on proof-of-mechanism, in the second quarter of 2023.

Given the large number of patients with MTAP-deleted cancers who may benefit from a PRMT5 inhibitor, and the resulting business opportunity, we also developed a next-generation PRMT5 inhibitor, TNG462, with increased potency, MTAP-deletion selectivity, as well as longer target coverage. TNG462 is 45 times more potent in cells with an MTAP deletion than those without and induces deep tumor regressions in preclinical models of multiple cancer types which is expected to significantly increase the therapeutic index. The clinical development path for TNG462 is expected to be similar to TNG908, evaluating safety and efficacy in multiple tumor types in a Phase 1/2 clinical trial. GBM will be excluded from the clinical trial as TNG462 is not expected to cross the blood-brain barrier. We expect to initiate the Phase 1/2 clinical trial for TNG462 in mid-2023.

Discovered as part of our immune evasion target discovery platform, TNG260 is a first-in-class, CoREST inhibitor, which reverses the immune evasion effect of STK11 loss-of-function mutations. STK11 loss-of-function mutations are present in approximately 15% of NSCLC, 15% of cervical cancers, 10% of carcinoma of unknown primary, 5% of breast cancers and 3% of pancreatic cancers. In syngeneic models with an STK11 mutation and an intact immune system, the combination of TNG260 with an anti-PD-1 antibody resulted in sustained complete tumor regressions and the induction of immune memory against re-implantation of tumors. We plan to file an IND for TNG260 in the first half of 2023. We expect that TNG260 will be among the first oncology molecules to leverage the benefits of genetically-based patient selection (STK11-mutation) with checkpoint inhibitor therapy.

We are developing TNG348, a novel allosteric inhibitor of USP1 for treatment of BRCA1, BRCA2-mutant and other HRD+ cancers. BRCA1 or BRCA 2 mutations are present in approximately 15% of ovarian, 10% of breast, 10% of prostate, 5% of endometrial and 5% of pancreatic cancers and additionally, BRCA wild-type HRD+ mutations are present in approximately 40% of ovarian, 15% of breast, 3% of prostate and 2% of pancreatic cancers. In vivo preclinical studies for TNG348 have shown single agent efficacy and combination benefit with PARP inhibitors in BRCA1, BRCA2-mutant and

other HRD+ cell-line and patient derived xenografts, including those that are intrinsically resistant to PARP inhibition. These preclinical data further demonstrate that TNG348 is synergistic with PARP inhibition across a panel of human ovarian and breast cancer cell lines, including both PARP inhibitor sensitive and resistant lines. Clinically, we expect TNG348 to have single agent activity in PARP inhibitor -naïve and PARP inhibitor-resistant BRCA1/2 mutant and other HRD+ cancers, and to synergize with PARP inhibitors. We expect to file an IND for this program in mid-2023.

Business Combination

On April 13, 2021, the Company, BCTG Merger Sub Inc., a Delaware corporation, and Tango Therapeutics, Inc. (now known as Tango Therapeutics Sub, Inc., or Old Tango) signed a definitive merger agreement, or the Merger Agreement, memorializing the terms of BCTG's acquisition of 100% of Old Tango's issued and outstanding equity securities in exchange for \$550.0 million worth of consideration in the form of BCTG common stock, or the Business Combination. The Business Combination was approved on August 9, 2021 by shareholders of BCTG, resulting in BCTG acquiring 100% of our issued and outstanding equity securities on August 10, 2021. Upon the closing of the Business Combination, BCTG Merger Sub Inc. merged with and into Tango, with Tango as the surviving company in the Merger, and BCTG changed its name to "Tango Therapeutics, Inc.", or New Tango. For additional information on the Business Combination, see Note 3 to the audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

We received gross proceeds of \$167.1 million upon the closing of the Business Combination. Simultaneous with the closing of the Business Combination, Tango entered into agreements with certain investors, the PIPE Investors, pursuant to which these PIPE Investors purchased 18,610,000 shares of our common stock at \$10.00 per share, for aggregate gross proceeds of \$186.1 million, upon the closing of the PIPE financing. Total transaction costs and redemptions totaled \$26.9 million, resulting in total net proceeds of \$326.3 million.

Subject to the terms of the Merger Agreement, at the effective time of the Business Combination, each share of Old Tango redeemable convertible preferred stock issued and outstanding immediately prior to the effective time of the Business Combination was converted into a share of New Tango common stock, at the conversion ratio of 0.34. At the effective time of the Business Combination, each option to purchase Old Tango common stock became an option to purchase shares of New Tango common stock, subject to adjustment in accordance with the exchange ratio.

Financial Overview

Since the Company's (Old Tango) inception, we have focused primarily on organizing and staffing our company, business planning, raising capital, discovering product candidates, securing related intellectual property, and conducting research and development activities for our programs. To date, we have funded our operations primarily through equity financings and from the proceeds received from our collaboration agreement with Gilead. Since inception, we have raised an aggregate of \$166.9 million of gross proceeds from the sale of our preferred shares, \$342.1 million in gross proceeds through the closing of the Business Combination and PIPE Financing transactions (as described above) and another \$220.1 million through our collaboration with Gilead.

We believe that our existing cash, cash equivalents and marketable securities on hand as of December 31, 2022 of \$366.1 million will enable us to fund our operating expenses and capital expenditure requirements at least into 2025. Since inception, we have incurred significant operating losses. For the years ended December 31, 2022 and 2021, our net losses were \$108.2 million and \$58.2 million, respectively. We had an accumulated deficit of \$269.5 million as of December 31, 2022. We expect to continue to incur significant and increasing expenses and operating losses for the foreseeable future, as we advance our product candidates through preclinical and clinical development and seek regulatory approvals, manufacture drug product and drug supply, and maintain and expand our intellectual property portfolio. We also expect to hire additional personnel, pay for accounting, audit, legal, regulatory and consulting services, and pay costs associated with maintaining compliance with Nasdaq listing rules and the requirements of the U.S. Securities and Exchange Commission, director and officer liability insurance, investor and public relations activities and other expenses associated with operating as a public company. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our preclinical studies, our clinical trials, and our expenditures on other research and development activities.

We do not have any product candidates approved for sale and have not generated any revenue from product sales. We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for our product candidates, if ever. In addition, if we obtain regulatory approval for our product candidates and do not enter into a third-party commercialization partnership, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing, manufacturing and distribution activities. As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until we can generate significant revenue from product sales, if ever, we expect to finance our operations through a

combination of public or private equity offerings and debt financings or other sources, such as potential collaboration agreements, strategic alliances and licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on acceptable terms, or at all. Our failure to raise capital or enter into such agreements as, and when needed, could have a negative effect on our business, results of operations and financial condition.

Because of the numerous risks and uncertainties associated with pharmaceutical 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 revenues from the sale of our therapies, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

Revenue

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

Collaboration Agreements with Gilead Sciences

In October 2018, we entered into a collaboration agreement with Gilead (2018 Gilead Agreement). Pursuant to the terms of the 2018 Gilead Agreement, we received an initial upfront payment of \$50.0 million. The upfront payment was initially recorded as deferred revenue on our balance sheet and is recognized as revenue as or when the performance obligation under the contract is satisfied.

In August 2020, the 2018 Gilead Agreement was expanded into a broader collaboration via an amended and restated research collaboration and license agreement (Gilead Agreement). Pursuant to the terms of the Gilead Agreement, we received an upfront payment of \$125.0 million. Consistent with the treatment of the previously received upfront payment, this upfront payment was recorded as deferred revenue on our balance sheet and is recognized as revenue as or when the performance obligation under the contract is satisfied.

In December 2020 and September 2021, Gilead elected to extend two programs for research extension fees totaling \$24.0 million, which was added to our estimate of the transaction price to total \$199.0 million. A total of \$2.0 million of fees related to the research extensions have not been received as of December 31, 2022 as these were determined to be conditional upon the satisfaction of additional research obligations, and thus a contract asset, however, we determined that achievement of the entire research extension fees was probable and that a significant reversal in the amount of cumulative revenue recognized would not occur.

In April 2021, Gilead licensed a program for an \$11.0 million fee. The \$11.0 million license fee was received and recognized as revenue in the second quarter of 2021 since we have no continued involvement in the advancement of the program, Gilead can benefit from the license on its own and the license is separately identifiable from the research services.

As of December 31, 2022, \$82.6 million has been recognized as collaboration revenue related to the upfront and research extension payments from the Gilead agreements.

During the years ended December 31, 2022 and 2021, we recognized \$24.9 million and \$26.0 million, respectively, of collaboration revenue associated with the Gilead Agreements based on performance completed during each period.

Refer to Note 2 and Note 4 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding our revenue recognition accounting policy and our collaboration agreement with Gilead.

Operating Expenses

Research and Development Expenses

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

- employee-related expenses, including salaries, bonuses, benefits, stock-based compensation, other related costs for those employees involved in research and development efforts;
- external research and development expenses incurred under agreements with contract research organizations, or CROs, as well as consultants that conduct our preclinical studies and development services;
- costs related to manufacturing material for our preclinical and clinical studies;
- laboratory supplies and research materials;
- costs to fulfill our obligations under the collaboration with Gilead;
- costs related to compliance with regulatory requirements; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent, utilities and insurance.

Costs for certain activities are recognized based on an evaluation of the progress to completion of specific tasks using data such as information provided to us by our vendors and analyzing the progress of our preclinical studies or other services performed. Significant judgment and estimates are made in determining the accrued expense balances at the end of any reporting period.

Our direct external research and development expenses consist primarily of fees paid to CROs and outside consultants in connection with our preclinical and clinical development and manufacturing activities. Our direct external research and development expenses also include fees incurred under license agreements. We track these external research and development costs on a program-by-program basis once we have identified a product candidate.

We do not allocate employee costs, costs associated with our target discovery efforts, laboratory supplies, and facilities, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs and, as such, are not separately classified. We characterize research and development costs incurred prior to the identification of a product candidate as discovery costs. We use internal resources primarily to conduct our research and discovery activities as well as for managing our preclinical, development and manufacturing activities.

The following table summarizes our research and development expenses:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
TNG908 direct program expenses	\$ 12,818	\$ 11,012
TNG462 direct program expenses	7,206	—
TNG260 direct program expenses	4,906	—
TNG348 direct program expenses	9,874	8,009
Discovery direct program expenses	28,763	28,031
Unallocated research and development expenses:		
Personnel-related expenses	28,185	21,276
Facilities and other related expenses	14,154	9,308
Total research and development expenses	<u>\$ 105,906</u>	<u>\$ 77,636</u>

The successful development of our product candidates is highly uncertain. We plan to substantially increase our research and development expenses for the foreseeable future as we continue the development of our product candidates and manufacturing processes and conduct discovery and research activities for our preclinical programs. We cannot determine with certainty the timing of initiation, the duration or the completion costs of current or future preclinical studies and clinical trials of our product candidates or the timing of regulatory filings in connection with clinical trials or regulatory approval, due to the inherently unpredictable nature of preclinical and clinical development. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make

determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to the results of ongoing and future preclinical studies and clinical trials, regulatory developments and our ongoing assessments as to each product candidate's commercial potential. Our clinical development costs have, and are expected to increase significantly with the commencement and continuation of our clinical trials. We anticipate that our expenses will increase substantially, particularly due to the numerous risks and uncertainties associated with developing product candidates, including the uncertainty of:

- the scope, rate of progress, and expenses of our ongoing research activities as well as any preclinical studies, clinical trials and other research and development activities;
- establishing an appropriate safety profile with IND-enabling studies;
- successful enrollment in and completion of clinical trials;
- whether our product candidates show safety and efficacy in our clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- the progress of our collaboration with Gilead;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- commercializing product candidates, if and when approved, whether alone or in collaboration with others; and
- continued acceptable safety profile of products following any regulatory approval.

Any changes in the outcome of any of these variables 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 these product candidates. We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on other product candidates. For example, if the FDA, European Medicines Agency (EMA), or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate.

General and Administrative Expenses

General and administrative expense consists primarily of employee related costs, including salaries, bonuses, benefits, stock-based compensation and other related costs. General and administrative expense also includes professional services, including legal, accounting and audit services and other consulting fees as well as facility costs not otherwise included in research and development expenses, insurance and other general administrative expenses.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with operating as a public company.

Other Income (Expense), Net

Interest Income

Interest income consists of income earned and losses incurred in connection with our investments in money market funds, U.S. Treasury bills and U.S. government agency bonds.

Other Income (Expense), Net

Other income (expense), net consists of miscellaneous income and expense unrelated to our core operations.

Provision for Income Taxes

Our provision for income tax consists of an estimate for U.S. federal and state income taxes based on enacted rates, as adjusted for allowable credits, deductions, uncertain tax positions, changes in deferred tax assets and liabilities and changes in tax law. For the years ended December 31, 2022 and December 31, 2021, we recorded an income tax provision of \$0.1 million and \$0.3 million, respectively.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		Change
	2022	2021	
		(in thousands)	
Collaboration revenue	\$ 24,860	\$ 26,042	\$ (1,182)
License revenue	—	11,000	(11,000)
Total revenue	24,860	37,042	(12,182)
Operating expenses:			
Research and development	105,906	77,636	28,270
General and administrative	30,025	17,596	12,429
Total operating expenses	135,931	95,232	40,699
Loss from operations	(111,071)	(58,190)	(52,881)
Other income (expense):			
Interest income	1,456	495	961
Other income (expense), net	1,493	(248)	1,741
Total other income, net	2,949	247	2,702
Loss before income taxes	(108,122)	(57,943)	(50,179)
Provision for income taxes	(54)	(292)	238
Net loss	\$ (108,176)	\$ (58,235)	\$ (49,941)

Collaboration Revenue

Collaboration revenue of \$24.9 million and \$26.0 million for the years ended December 31, 2022 and 2021, respectively, was derived from the Gilead collaboration. The decrease of \$1.2 million is primarily due to lower research costs incurred under the collaboration during the year ended December 31, 2022 resulting in lower collaboration revenue recognized.

License Revenue

License revenue of \$11.0 million for the year ended December 31, 2021 was derived from the Gilead collaboration. The decrease of \$11.0 million is primarily due to Gilead licensing a program for \$11.0 million during the second quarter of 2021 as compared to no programs licensed during the year ended December 31, 2022.

Research and Development Expenses

Research and development expense was \$105.9 million for the year ended December 31, 2022 compared to \$77.6 million for the year ended December 31, 2021. The increase of \$28.3 million was primarily due to a \$15.9 million increase in preclinical, clinical development and manufacturing activities to advance our programs, mainly TNG462 and TNG260. Personnel-related costs increased \$6.9 million primarily due to an increase of share-based compensation expense and additional headcount to support our research and development activities. Additionally, facilities costs increased by \$2.3 million due to expenses incurred related to the new lease at 201 Brookline Avenue in Boston, Massachusetts.

General and Administrative Expenses

General and administrative expense was \$30.0 million for the year ended December 31, 2022 compared to \$17.6 million for the year ended December 31, 2021. The increase of \$12.4 million was primarily due to a \$7.4 million increase in personnel-related costs due to an increase in share-based compensation expense and additional headcount. Additionally, insurance related costs increased \$1.8 million due to becoming a public company, and consulting, legal, and professional fees increased \$1.7 million.

Interest Income

Interest income was \$1.5 million for the year ended December 31, 2022 compared to \$0.5 million for the year ended December 31, 2021. The increase of \$1.0 million was primarily due to an increase in interest rates in 2022 as compared to 2021.

Other Income (Expense), Net

Other income, net was \$1.5 million for the year ended December 31, 2022 compared to other expense, net of \$0.2 million for the year ended December 31, 2021, with the increase being attributed to accretion on investments purchased at a discount.

Provision for Income Taxes

Provision for income taxes was \$0.1 million for the year ended December 31, 2022 compared to \$0.3 million for the year ended December 31, 2021. The income tax provision amount for the period ended December 31, 2022 is primarily attributable to state taxes on interest income earned on marketable securities. The income tax provision amount for the period ended December 31, 2021 is primarily attributable to taxable deferred revenue partially offset by the utilization of federal and state net operating losses and federal and state tax credits.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have generated recurring net losses. We have not yet commercialized any product and we do not expect to generate revenue from sales of any products for several years, if at all. Since our inception, we have funded our operations primarily through proceeds from the issuance of equity in the form of stock and from the proceeds received from our collaboration with Gilead. To date, we have raised an aggregate of approximately \$166.9 million of gross proceeds from the private placement of preferred shares, \$342.1 million of gross proceeds from the Business Combination and PIPE Financing transactions, and \$220.1 million through the collaboration and license agreement with Gilead. As of December 31, 2022, we had cash and cash equivalents and marketable securities of \$366.1 million.

Funding Requirements

We believe that our existing cash, cash equivalents and marketable securities on hand as of December 31, 2022 of \$366.1 million will enable us to fund our operating expenses and capital expenditure requirements at least into 2025. We have based this estimate on assumptions that may prove to be wrong, and we could expend our capital resources sooner than we expect.

Cash Flows

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our cash flows for each of the years presented:

	<u>Year Ended December 31,</u>		<u>Change</u>
	<u>2022</u>	<u>2021</u>	
	(in thousands)		
Net cash used in operating activities	\$ (109,080)	\$ (59,527)	\$ (49,553)
Net cash provided by (used in) investing activities	26,399	(183,434)	209,833
Net cash provided by financing activities	1,615	357,325	(355,710)
Net (decrease) increase in cash, cash equivalents and restricted cash	<u>\$ (81,066)</u>	<u>\$ 114,364</u>	<u>\$ (195,430)</u>

Operating Activities

Net cash used in operating activities was \$109.1 million for the year ended December 31, 2022 compared to net cash used in operating activities of \$59.5 million for the year ended December 31, 2021. The net cash used in operations for the year ended December 31, 2022 was primarily driven by the net loss of \$108.2 million as a direct result of higher operating

expenses related to the advancement of our programs and personnel-related costs. The net cash used in operations for the year ended December 31, 2021 was primarily driven by a net loss of \$58.2 million.

Investing Activities

Net cash provided by investing activities was \$26.4 million for the year ended December 31, 2022 compared to net cash used in investing activities of \$183.4 million for the year ended December 31, 2021. The increase in cash provided by investing activities was primarily due to a decrease in purchases of marketable securities and was partially offset by an increase in sales and maturities of marketable securities.

Financing Activities

Net cash provided by financing activities was \$1.6 million for the year ended December 31, 2022 compared to net cash provided by financing activities of \$357.3 million for the year ended December 31, 2021. The decrease in net cash provided by financing activities was a result of net proceeds of \$326.3 million received upon the closing of the Business Combination and PIPE Financing in August 2021, as well as \$30.0 million in proceeds related to the issuance of shares of redeemable convertible Series B preferred stock in March 2021. The net cash provided by financing activities for the year ended December 31, 2022 was primarily a result of cash provided from the exercises of stock options and ESPP purchases.

On September 1, 2022, we filed a Form S-3 Registration Statement and an accompanying prospectus for an at-the-market, or ATM, offering program and entered into a sales agreement with Jefferies LLC, relating to shares of our common stock. Pursuant to the terms of the sales agreement, we may offer and sell shares of common stock, having an aggregate price of up to \$100.0 million from time to time. During the year ended December 31, 2022, we did not make any sales under the ATM facility.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2022 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments Due by Period				
	Total	Less than 1 Year	1 – 3 Years (in thousands)	3 – 5 Years	More than 5 Years
Operating lease commitments	\$ 61,247	\$ 4,974	\$ 11,151	\$ 11,725	\$ 33,397
Total	\$ 61,247	\$ 4,974	\$ 11,151	\$ 11,725	\$ 33,397

The commitment amounts in the table above primarily reflect the minimum payments due under our amended operating lease for office and laboratory space at our 201 Brookline Avenue, Boston, Massachusetts location. These commitments are also recognized as operating lease liabilities in our balance sheet at December 31, 2022. Refer to Note 8 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional discussion of the lease.

Purchase Obligations

In the normal course of business, we enter into contracts with third parties for preclinical studies, clinical operations, manufacturing, and research and development supplies. These contracts generally do not contain minimum purchase commitments and generally provide for termination on notice, and therefore are cancellable contracts. These payments are not included in the table above as the amount and timing of such payments are not known as of December 31, 2022.

License Agreement Obligations

We have also entered into a license agreement under which we may be obligated to make milestone and royalty payments. We have not included future milestone or royalty payments under the agreement in the table above since the payment obligations are contingent upon future events, such as achieving certain development, regulatory, and commercial milestones or generating product sales. As of December 31, 2022 and December 31, 2021, we were unable to estimate the timing or likelihood of achieving these milestones or generating future product sales. Refer to Note 9 of our audited consolidated financial statements and related notes for the year ended December 31, 2022 included in this Annual Report on Form 10-K for a description of our license agreement.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements have been prepared in accordance with U.S. GAAP. The preparation of these consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues and expenses, and the disclosure of contingent assets and liabilities in our 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 and at the time these estimates are made, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Some of the judgments and estimates we make can be subjective and complex. Our actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts, and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

While our significant accounting policies are described in more detail in Note 2 to our audited consolidated financial statements and related notes included in this Annual Report on Form 10-K for the year ended December 31, 2022, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

The terms of our collaboration agreements may include consideration such as non-refundable up-front payments, license fees, research extension fees, and clinical, regulatory and sales-based milestones and royalties on product sales.

We recognize revenue under ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606, which applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. ASC 606 provides a five-step framework whereby revenue is recognized when control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of the revenue standard, we perform the following five steps: (i) identify the promised goods or services in the contract; (ii) determine whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measure the transaction price, including the constraint on variable consideration; (iv) allocate the transaction price to the performance obligations; and (v) recognize revenue when (or as) we satisfy each performance obligation. We only apply the five-step model to contracts when collectability of the consideration to which we are entitled in exchange for the goods or services we transfer to the customer is determined to be probable. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. We then allocate the transaction price (the amount of consideration we expect to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognize the associated revenue when (or as) each performance obligation is satisfied. Our estimate of the transaction price for each contract includes all variable consideration to which we expect to be entitled.

We recognize the transaction price allocated to license payments as revenue upon delivery of the license to the customer and resulting ability of the customer to use and benefit from the license, if the license is determined to be distinct from the other performance obligations identified in the contract. If the license is considered to not be distinct from other performance obligations, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied (i) at a point in time, but only for licenses determined to be distinct from other performance obligations in the contract, or (ii) over time; and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from license payments. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

We evaluate whether it is probable that the consideration associated with each milestone payment will not be subject to a significant reversal in the cumulative amount of revenue recognized. Amounts that meet this threshold are included in the transaction price using the most likely amount method, whereas amounts that do not meet this threshold are considered constrained and excluded from the transaction price until they meet this threshold. Milestones tied to regulatory approval, and therefore not within our control, are considered constrained until such approval is received. Upfront and ongoing development milestones under our collaboration agreements are not subject to refund if the development activities are not successful. At the end of each subsequent reporting period, we re-evaluate the probability of a significant reversal of the cumulative revenue recognized for the milestones, and, if necessary, adjust the estimate of the overall transaction price. Any

such adjustments are recorded on a cumulative catch-up basis, which would affect revenues from collaborators in the period of adjustment. We exclude sales-based milestone payments and royalties from the transaction price until the sale occurs (or, if later, until the underlying performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied), because the license to our intellectual property is deemed to be the predominant item to which the royalties relate as it is the primary driver of value.

ASC 606 requires us to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined in ASC 606 as the price at which an entity would sell a promised good or service separately to a customer. If other observable transactions in which we have sold the same performance obligation separately are not available, we are required to estimate the standalone selling price of each performance obligation. Key assumptions to determine the standalone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Whenever we determine that multiple promises to a customer are not distinct and comprise a combined performance obligation that includes services, we recognize revenue over time using the cost-to-cost input method, based on the total estimated cost to fulfill the obligation. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we are expected to complete our performance obligations under an arrangement.

Consideration that does not meet the requirements to satisfy the above revenue recognition criteria is a contract liability and is recorded as deferred revenue in the consolidated balance sheets. We have recorded short-term and long-term deferred revenue on our consolidated balance sheets based on our best estimate of when such revenue will be recognized. Short-term deferred revenue consists of amounts that are expected to be recognized as revenue in the next 12 months. Amounts that we expect will not be recognized within the next 12 months are classified as long-term deferred revenue.

In certain instances, the timing of and total costs of satisfying these obligations under our collaboration agreement can be difficult to estimate. Accordingly, our estimates may change in the future. If these estimates and judgments change over the course of these agreements, it may affect the timing and amount of revenue that we will recognize and record in future periods.

Under ASC 606, we will recognize revenue when we fulfill our performance obligations under the agreement with Gilead. As the required performance obligation is satisfied, we will recognize revenue for the portion satisfied and record a receivable for any fees that have not been received. Amounts are recorded as short-term collaboration receivables when our right to consideration is unconditional. A contract liability is recognized when a customer prepays consideration or owes payment to an entity in advance of our performance according to a contract. We do not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less or the amount is immaterial.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves estimating the level of service performed and the associated cost incurred for the service 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, which would be recorded as a prepaid expense in other assets, or if there is the right of offset, offset against our liability balance with the counterparty. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. At each period end, we corroborate the accuracy of these estimates with the service providers and make adjustments, if necessary.

We record the expense and accrual related to research and development activities performed by our vendors based on our estimates of the services received and efforts expended considering a number of factors, including our knowledge of the progress towards completion of the research and development activities; invoicing to date under the contracts; communication from the vendors of any actual costs incurred during the period that have not yet been invoiced; and the costs included in the contracts and purchase orders. 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 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. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We estimate the fair value of our stock option awards using the Black Scholes method utilizing the “simplified method,” for determining the expected life of the award, which is based on the mid-point between the vesting date and the end of the contractual term as all options granted after becoming a public entity will be granted “at-the-money.” We determine the volatility for options granted based on an analysis of reported data for a peer group of companies. The expected volatility of granted options has been determined using a weighted-average of the historical volatility measures of this peer group of companies. We will continue to apply this method until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. The fair value of each share of common stock underlying stock-based awards is based on the closing price of our common stock as reported by Nasdaq on the date of grant. The risk-free interest rate utilized in our calculations is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as we have never paid dividends and do not have current plans to pay any dividends on our common stock.

We measure stock-based awards granted to employees, non-employees and directors based on their fair value on the date of the grant using the Black Scholes option-pricing model for options or the difference between the purchase price per share of the award, if any, and the fair value of our common stock for restricted common stock awards.

Prior to the consummation of the Business Combination, as there was not a public market for our common stock prior to becoming publicly traded in August 2021, the estimated fair value of our common stock was determined by our board of directors as of the date of grant of each option or restricted stock award, considering our most recently available third-party valuations of common stock and our board of directors’ assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants’ Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Our common stock valuations were prepared using either an option pricing method, or OPM, or a hybrid method, both of which used market approaches to estimate our enterprise value. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company’s securities changes. Under this method, the common stock had value only if the funds available for distribution to stockholders exceed the value of the preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. The hybrid method was a probability-weighted expected return method, or PWERM, where the equity value in one or more scenarios is calculated using an OPM. The PWERM is a scenario-based methodology that estimated the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The common stock value was based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome was discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. A discount for lack of marketability of the common stock is then applied to arrive at an indication of value for the common stock. The Black-Scholes option-pricing model also uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected term of our common stock options, the risk-free interest rate for a period that approximates the expected term of our common stock options, and our expected dividend yield.

Compensation expense for awards is recognized over the requisite service period, which is generally the vesting period of the respective award for employees and directors and the period during which services are performed for non-employees. We use the straight-line method to record the expense of awards with service-based vesting conditions.

We believe our methodologies are reasonable based upon our internal peer company analyses. If different assumptions had been made, equity-based compensation expense, consolidated net loss and consolidated net loss per share could have been significantly different.

Recently Adopted Accounting Pronouncements

A description of recently issued and adopted accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 2 to our audited consolidated financial statements and related notes appearing in this this Annual Report on Form 10-K for the year ended December 31, 2022.

Emerging Growth Company and Smaller Reporting Company Status

We are an “emerging growth company,” under the JOBS Act. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as private entities. As an emerging growth company, we may take advantage of certain exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an emerging growth company:

- we may present only two years of audited financial statements and only two years of related Management’s Discussion and Analysis of Financial Condition and Results of Operations in our periodic reports and registration statements, including this Annual Report on Form 10-K;
- we may avail ourselves of the exemption from providing an auditor’s attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act;
- we may provide reduced disclosure about our executive compensation arrangements; and
- we may not require nonbinding advisory votes on executive compensation or stockholder approval of any golden parachute payments.

We will remain an emerging growth company until the earliest of (i) December 31, 2025, (ii) the last day of the fiscal year in which we have total annual gross revenues of \$1.235 billion or more, (iii) the last day of the fiscal year in which we are deemed to be a “large accelerated filer” as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded \$700.0 million as of the last business day of the second fiscal quarter of such year, provided we have been subject to the Exchange Act for at least 12 calendar months and have filed at least one annual report pursuant to the Exchange Act or (iv) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period. We may choose to take advantage of some but not all of these exemptions.

We are also a “smaller reporting company,” meaning that the market value of our stock held by non-affiliates is less than \$700 million and our annual revenue was less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if 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. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to certain market risks in the ordinary course of our business. Market risk represents the risk of loss that may impact our financial position due to adverse changes in financial market prices and rates.

Interest Rate Risk

We had cash, cash equivalents and marketable securities of \$366.1 million and \$485.3 million as of December 31, 2022 and December 31, 2021, respectively, which consisted of cash, money market funds, U.S. Treasury bills and U.S. government agency bonds. Interest income is sensitive to changes in the general level of interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we believe an immediate 1% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We have the ability to

hold our investments until maturity, and therefore, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investment portfolio.

Foreign Currency Exchange Risk

Our reporting and functional currency is the U.S. dollar. We currently do not have significant exposure to foreign currencies as we hold no foreign exchange contracts, option contracts, or other foreign hedging arrangements. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Effects of Inflation

We do not believe that inflation has had a material effect on our business, financial condition or results of operations. Our operations may be subject to inflation in the future. Inflation generally affects us by increasing our cost of labor, clinical trial and manufacturing costs and indirectly increasing interest rates. Inflation rates, particularly in the U.S., have increased recently to levels not seen in years. We have not seen a significant impact from inflation on our business, financial condition or results of operations during the twelve months ended December 31, 2022. However, if inflation remains at current levels for an extended period of time, or increases, our costs are likely to increase, which may negatively impact our cash flows.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the report of the independent registered public accounting firm, are appended to this Annual Report on Form 10-K and an index of those consolidated financial statements can be found beginning on page F-1.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2022. Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2022.

Changes in Internal Controls Over Financial Reporting

There were no changes in the Company's internal control over financial reporting identified in connection with the evaluation required by paragraph (d) of Exchange Act Rules 13a-15 or 15d-15 that occurred during the quarter ended December 31, 2022 that materially affected, or were reasonably likely to materially affect, the Company's internal control over financial reporting.

Management's Report on Internal Control Over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Securities Exchange Act of 1934, as amended. Our management, including our Chief Executive Officer and Chief Financial Officer, conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in *Internal Control-Integrated Framework (2013)* issued by the Committee of Sponsoring Organization of the Treadway Commission. Based on this assessment, management concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

This Annual Report on Form 10-K does not include an attestation report of the independent registered public accounting firm due to an exemption established by the JOBS Act for “emerging growth companies.”

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Except as set forth below, the information required by this Item 10 will be included in our definitive proxy statement to be filed with the Securities and Exchange Commission, or SEC, within 120 days after the end of the fiscal year ended December 31, 2022, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

We have adopted a Code of Conduct that applies to all of our directors, officers and employees, including our principal executive officer and principal financial officer. The Code of Conduct is posted on our website at <https://ir.tangotx.com/corporate-governance/governance-overview>.

We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Code of Conduct by posting such information on our website, at the address and location specified above and, to the extent required by the listing standards of The Nasdaq Global Stock Market, by filing a Current Report on Form 8-K with the SEC, disclosing such information.

Item 11. Executive Compensation

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC, within 120 days after the end of the fiscal year ended December 31, 2022, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC, within 120 days after the end of the fiscal year ended December 31, 2022, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC, within 120 days after the end of the fiscal year ended December 31, 2022, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC, within 120 days after the end of the fiscal year ended December 31, 2022, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) Financial Statements

See the Index to the Consolidated Financial Statements section beginning on page F-1 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

All financial statement schedules have been omitted as they are not required, not applicable, or the required information is included in the financial statements or notes to the financial statements.

(3) Exhibits

The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report on Form 10-K are listed in the Exhibit Index below.

Exhibit Index

Exhibit Number	Description
3.1	<u>Second Amended and Restated Certificate of Incorporation of Tango Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's registration statement on Form S-1 filed with the SEC on September 10, 2021).</u>
3.2	<u>Amended and Restated Bylaws of Tango Therapeutics, Inc. (incorporated by reference to Exhibit 4.2 to the Registrant's registration statement on Form S-8 filed with the SEC on October 14, 2021).</u>
4.1	<u>Specimen Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.5 to the Registration Statement on Form S-4/A filed by the Registrant on July 15, 2021).</u>
4.2*	<u>Description of Securities.</u>
10.1	<u>Amended and Restated Registration and Stockholder Rights Agreement, dated August 10, 2021, by and among Tango Therapeutics, Inc. and the stockholders party thereto (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed by the Registrant on August 13, 2021).</u>
10.2#	<u>Tango Therapeutics, Inc. 2021 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.4 to the Current Report on Form 8-K filed by the Registrant on August 13, 2021).</u>
10.3#	<u>Forms of Award Agreements under the Tango Therapeutics, Inc. 2021 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.5 to the Current Report on Form 8-K filed by the Registrant on August 13, 2021).</u>
10.4#	<u>Tango Therapeutics, Inc. 2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.6 to the Current Report on Form 8-K filed by the Registrant on August 13, 2021).</u>
10.5†	<u>Amended and Restated Research Collaboration and License Agreement between Tango Therapeutics, Inc. and Gilead Sciences, Inc., dated August 17, 2020 (incorporated by reference to Exhibit 10.19 to the Registration Statement on Form S-4/A filed by the Registrant on June 17, 2021).</u>
10.6†	<u>License Agreement between Tango Therapeutics, Inc. and Medivir AB, dated March 12, 2020 (incorporated by reference to Exhibit 10.20 to the Registration Statement on Form S-4/A filed by the Registrant on June 17, 2021).</u>
10.7#	<u>Form of Executive Employment Agreement (incorporated by reference to Exhibit 10.7 to the Current Report on Form 8-K filed by the Registrant on August 13, 2021).</u>
10.8	<u>Form of Indemnification Agreement (Directors) (incorporated by reference to Exhibit 10.9 to the Current Report on Form 8-K filed by the Registrant on August 13, 2021).</u>
10.9#	<u>Form of Indemnification Agreement (Officers) (incorporated by reference to Exhibit 10.10 to the Current Report on Form 8-K filed by the Registrant on August 13, 2021).</u>
10.10#	<u>Senior Executive Cash Annual Incentive Plan (incorporated by reference to Exhibit 10.11 to the Current Report on Form 8-K filed by the Registrant on August 13, 2021).</u>
10.11+	<u>Lease Agreement between the Company and ARE-MA Region No. 87 Tenant, LLC dated as of November 4, 2021 (incorporated by reference to Exhibit 10.14 to Annual Report on Form 10-K filed by the Registrant on March 28, 2022).</u>
10.12#	<u>Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on May 11, 2022).</u>
10.13	<u>Tango Therapeutics, Inc. 2023 Inducement Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 99.1 to the registration statement on Form S-8 filed by the Registrant on February 7, 2023).</u>
16.1	<u>Letter dated August 13, 2021 from Withum to the SEC (incorporated by reference to Exhibit 16.1 to the Current Report on Form 8-K filed by the Registrant on August 13, 2021).</u>
21.1	<u>List of subsidiaries of Tango Therapeutics, Inc.</u>
23.1*	<u>Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm of Tango Therapeutics, Inc.</u>
31.1*	<u>Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
31.2*	<u>Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
32.1**	<u>Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
32.2**	<u>Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>

101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

† Portions of this exhibit (indicated by asterisks) have been omitted in accordance with Item 601(b)(10) of Regulation S-K.

Indicates a management contract or any compensatory plan, contract or arrangement.

+ Portions of this exhibit (indicated by brackets and asterisks) have been omitted because the registrant has determined that the information is both not material and is the type that the registrant treats as private or confidential.

** The certifications furnished in Exhibit 32 hereto are deemed to be furnished with this Annual Report on Form 10-K and will not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the registrant specifically incorporates it by reference.

Item 16. Form 10-K Summary

Not applicable.

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Tango Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Tango Therapeutics, Inc. and its subsidiaries (the “Company”) as of December 31, 2022 and 2021, and the related consolidated statements of operations and comprehensive loss, of redeemable convertible preferred stock and stockholders' equity and of cash flows for the years then ended, including the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s consolidated 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 of these consolidated financial statements 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 consolidated 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 consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 27, 2023

We have served as the Company's auditor since 2017.

TANGO THERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31,	
	2022	2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 59,968	\$ 142,745
Marketable securities	306,165	342,510
Accounts receivable	2,000	2,000
Restricted cash	567	567
Prepaid expenses and other current assets	6,572	4,516
Total current assets	375,272	492,338
Property and equipment, net	10,884	4,832
Operating lease right-of-use assets	46,886	1,254
Restricted cash, net of current portion	3,423	1,712
Other assets	5	19
Total assets	\$ 436,470	\$ 500,155
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 4,453	\$ 3,226
Accrued expenses and other current liabilities	17,495	9,887
Operating lease liabilities	1,770	1,503
Deferred revenue	31,792	26,022
Income tax payable	35	52
Total current liabilities	55,545	40,690
Operating lease liabilities, net of current portion	39,361	—
Deferred revenue, net of current portion	92,088	114,718
Total liabilities	186,994	155,408
Commitments and contingencies (Note 9)		
Preferred stock, \$0.001 par value; 10,000,000 shares authorized; no shares issued and outstanding as of December 31, 2022 and 2021, respectively	—	—
Stockholders' equity:		
Common stock, \$0.001 par value; 200,000,000 shares authorized at December 31, 2022 and December 31, 2021, respectively; 88,179,374 and 87,598,184 shares issued and outstanding as of December 31, 2022 and 2021, respectively	88	88
Additional paid-in capital	522,605	506,760
Accumulated other comprehensive loss	(3,705)	(765)
Accumulated deficit	(269,512)	(161,336)
Total stockholders' equity	249,476	344,747
Total liabilities and stockholders' equity	\$ 436,470	\$ 500,155

The accompanying notes are an integral part of the consolidated financial statements.

TANGO THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2022	2021
Collaboration revenue	\$ 24,860	\$ 26,042
License revenue	—	11,000
Total revenue	<u>24,860</u>	<u>37,042</u>
Operating expenses:		
Research and development	105,906	77,636
General and administrative	30,025	17,596
Total operating expenses	<u>135,931</u>	<u>95,232</u>
Loss from operations	(111,071)	(58,190)
Other income (expense):		
Interest income	1,456	495
Other income (expense), net	1,493	(248)
Total other income, net	<u>2,949</u>	<u>247</u>
Loss before income taxes	(108,122)	(57,943)
Provision for income taxes	(54)	(292)
Net loss	<u>\$ (108,176)</u>	<u>\$ (58,235)</u>
Net loss per common share – basic and diluted	\$ (1.23)	\$ (0.94)
Weighted average number of common shares outstanding – basic and diluted	87,820,037	62,108,032
Net loss	<u>\$ (108,176)</u>	<u>\$ (58,235)</u>
Other comprehensive loss:		
Unrealized loss on marketable securities	(2,940)	(782)
Comprehensive loss	<u>\$ (111,116)</u>	<u>\$ (59,017)</u>

The accompanying notes are an integral part of the consolidated financial statements.

TANGO THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY
(in thousands, except share amounts)

	Series B		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balance at December 31, 2020	—	—	40,372,133	40	141,644	17	(103,101)	38,600
Issuance of Series B redeemable convertible preferred stock, net of issuance costs of \$0.1 million	22,686,025	29,990	—	—	—	—	—	—
Retroactive application of recapitalization	(22,686,025)	(29,990)	7,706,861	8	29,982	—	—	29,990
Shares issued in Business Combination and PIPE Financing, net of issuance costs of \$15.8 million	—	—	38,880,436	39	326,238	—	—	326,277
Exercise of stock options	—	—	638,754	1	1,057	—	—	1,058
Vesting of restricted common stock awards	—	—	—	—	6	—	—	6
Stock based compensation expense	—	—	—	—	7,833	—	—	7,833
Other comprehensive loss	—	—	—	—	—	(782)	—	(782)
Net loss	—	—	—	—	—	—	(58,235)	(58,235)
Balance at December 31, 2021	—	\$ —	87,598,184	\$ 88	\$ 506,760	\$ (765)	\$ (161,336)	\$ 344,747
Issuance of common stock from exercise of options and employee stock purchase plan	—	—	581,190	—	1,623	—	—	1,623
Stock based compensation expense	—	—	—	—	14,230	—	—	14,230
Business combination and PIPE financing, issuance costs	—	—	—	—	(8)	—	—	(8)
Other comprehensive loss	—	—	—	—	—	(2,940)	—	(2,940)
Net loss	—	—	—	—	—	—	(108,176)	(108,176)
Balance at December 31, 2022	—	\$ —	88,179,374	\$ 88	\$ 522,605	\$ (3,705)	\$ (269,512)	\$ 249,476

The accompanying notes are an integral part of the consolidated financial statements.

TANGO THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2022	2021
Cash flows from operating activities		
Net loss	\$ (108,176)	\$ (58,235)
Adjustments to reconcile net loss to net cash from operating activities:		
Depreciation	1,608	897
Noncash operating lease expense	2,420	1,069
Stock-based compensation	14,230	7,833
Other, net	(669)	254
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(2,056)	(3,159)
Right-of-use asset	(10,125)	—
Other long-term assets	122	(139)
Accounts payable	1,097	1,232
Accrued expenses and other liabilities	7,629	3,829
Operating lease liabilities	1,700	(1,066)
Deferred revenue	(16,860)	(12,042)
Net cash used in operating activities	(109,080)	(59,527)
Cash flows from investing activities		
Purchase of property and equipment	(7,692)	(1,837)
Sales and maturities of marketable securities	242,595	190,764
Purchases of marketable securities	(208,504)	(372,361)
Net cash provided by (used in) investing activities	26,399	(183,434)
Cash flows from financing activities		
Proceeds from issuance of preferred stock, net of issuance costs	—	29,990
Proceeds from issuance of common stock upon exercise of stock options and purchase of shares under ESPP	1,623	1,058
Business Combination and PIPE Financing, gross proceeds	—	342,113
Payment of Business Combination and PIPE Financing transaction costs	(8)	(15,836)
Net cash provided by financing activities	1,615	357,325
Net change in cash, cash equivalents and restricted cash	(81,066)	114,364
Cash, cash equivalents and restricted cash, beginning of period	145,024	30,660
Cash, cash equivalents and restricted cash, end of period	\$ 63,958	\$ 145,024
Supplemental disclosure of noncash investing and financing activity:		
Conversion of Preferred Shares to Common Shares	\$ —	\$ 166,534
Revaluation of right-of-use asset and lease liability upon lease modification	\$ 300	\$ 5,315
Purchases of property and equipment included in accounts payable and accrued expenses	\$ 131	\$ 154
Right-of-use asset obtained in exchange for a lease liability	\$ 48,352	\$ —

The accompanying notes are an integral part of the consolidated financial statements.

TANGO THERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of the Business and Basis of Presentation

Tango Therapeutics, Inc. (Tango or the Company) is a precision oncology company committed to the discovery and development of novel drugs in defined patient populations with high unmet medical need.

Tango Therapeutics, Inc. (together with its consolidated subsidiaries, Tango or the Company) formerly known as BCTG Acquisition Corp. (BCTG), was incorporated in Delaware on May 21, 2020. BCTG was a Special Purpose Acquisition Company (SPAC) formed for the purpose of effecting a merger, capital stock exchange, asset acquisition, stock purchase, reorganization or similar business combination.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (U.S. GAAP). The accompanying consolidated financial statements reflect the operations of Tango and its wholly owned subsidiaries. All intercompany accounts and transactions have been eliminated. The functional and reporting currency of the Company and its subsidiaries is the U.S. dollar.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of consolidated financial statements requires that the Company make estimates, judgments and assumptions that may affect the reported amounts of assets, liabilities, equity, revenues and expenses and related disclosure of contingent assets and liabilities. Significant estimates and assumptions made in the consolidated financial statements include, but are not limited to, the revenue recognized from collaboration agreements, the valuation of stock-based awards and the accrual for research and development expenses. On an ongoing basis, the Company evaluates its estimates, judgments and methodologies. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets, liabilities and equity and the amount of revenues and expenses. As of the date of issuance of these consolidated financial statements, the Company is not aware of any specific event or circumstance that would require the Company to update estimates, judgments or revise the carrying value of any assets or liabilities. Actual results may differ from these estimates under different assumptions or conditions. Changes in estimates are reflected in reported results in the period in which they become known.

Segment Information

Operating segments are defined as components of an enterprise for which separate financial information is available for evaluation by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company operates in one operating segment, the business of discovering and developing precision oncology therapies.

Cash Equivalents

All highly liquid marketable securities purchased with an original maturity date of 90 days or less at the date of purchase are considered to be cash equivalents. Cash equivalents consisted of money market funds and U.S. Treasury bills as of December 31, 2022 and 2021.

Investments in Marketable Securities

Marketable debt securities consist of investments with original maturities greater than 90 days. The Company classifies its investments with maturities beyond one year as short-term, based on their highly liquid nature and because such marketable securities represent the investment of cash that is available for current operations. The Company considers its investment portfolio of marketable securities to be available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Unrealized gains are reported as a component of accumulated other comprehensive income in stockholders' equity. Amortization and accretion of premiums and discounts are recorded in

interest income. Realized gains and losses are included as a component of other income, net in the consolidated statements of operations.

The Company evaluates its investments with unrealized losses for impairment. When assessing investments for unrealized declines in value, the Company considers whether the decline in value is related to a credit loss or non-credit loss. For credit losses, the Company reduces the investment to fair value through an allowance for credit losses recorded to the balance sheet and corresponding charge to the statement of operations. The allowance for credit losses and corresponding impairment charge is adjusted each period for changes in fair value. For non-credit losses, the Company reduces the investment to fair value through a charge to the statement of comprehensive loss, reported as a component of accumulated other comprehensive income (loss) in stockholders' equity. No credit losses were recorded during the periods presented.

Fair Value Measurements

The accounting standard for fair value measurements defines fair value, establishes a framework for measuring fair value in accordance with U.S. GAAP, and requires certain disclosures about fair value measurements. Under this standard, fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1 — Fair values are determined utilizing prices (unadjusted) in active markets for identical assets or liabilities that the Company has the ability to access.
- Level 2 — Fair values are determined by utilizing quoted prices for identical or similar assets and liabilities in active markets or other market observable inputs such as interest rates, yield curves, and foreign currency spot rates.
- Level 3 — Prices or valuations that require inputs that are both significant to the fair value measurement and unobservable.

The fair value of the Company's cash equivalents and marketable securities are determined according to the fair value hierarchy described below (see Note 5). The carrying values of the Company's accounts receivable, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities.

Concentration of Credit Risk and Significant Suppliers

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist of cash, cash equivalents and marketable debt securities. The Company's cash, cash equivalent and marketable securities balances are held by major financial institutions that management believes to be creditworthy. The Company uses multiple financial institutions to limit the amount of credit exposure to any one financial institution. Substantially all the Company's cash, cash equivalent and marketable debt securities were invested in money market funds, U.S. Treasury bills, and U.S. government agency bonds at December 31, 2022 and 2021. At times, the Company's cash deposits may exceed the amount of federal insurance provided on such deposits. The Company has not experienced any losses in such accounts and believes it is not exposed to significant credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company relies, and expects to continue to rely, on a small number of vendors to perform research activities and clinical trial activities that continue to progress its product candidates for its development programs. These programs could be adversely affected by a significant interruption in the related processes of these vendors.

Restricted Cash

Cash accounts with any type of restriction are considered restricted cash and are classified on the balance sheet based on the length of the restrictive obligation. As of December 31, 2022 and 2021, the Company recorded restricted cash of \$4.0 million and \$2.3 million, respectively, all of which was related to security deposits associated with the Company's facility leases in Boston, Massachusetts and Cambridge, Massachusetts. The security deposit associated with the Company's facility lease in Boston, Massachusetts is recorded as non-current in its balance sheet as of December 31, 2022 and December 31, 2021 because the deposit is required for the duration of the lease which is greater than a year. The security deposit associated with the Company's previous facility lease in Cambridge, Massachusetts is recorded as current in its balance sheet as of

December 31, 2022 and December 31, 2021 because the deposit associated with the terminated lease was expected to be returned in less than a year from the balance sheet dates. The security deposit was released to the Company in March 2023.

The reconciliation of cash and cash equivalents and restricted cash to amounts presented in the consolidated statements of cash flows are as follows:

	December 31,	
	2022	2021
	(in thousands)	
Cash and cash equivalents	\$ 59,968	\$ 142,745
Restricted cash	3,990	2,279
Cash, cash equivalents and restricted cash	<u>\$ 63,958</u>	<u>\$ 145,024</u>

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation and amortization expense is recognized using the straight-line method over the estimated useful lives of each asset. Estimated useful lives are periodically assessed to determine if changes are appropriate. The estimated useful lives of the Company's property and equipment are as follows:

Asset	Estimated useful life
Computer equipment	3 years
Computer software	5 years
Furniture and fixtures	7 years
Laboratory equipment	7 years
Leasehold improvements	Shorter of remaining lease term or 10 years

The Company reviews long-lived assets, such as property and equipment, for impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. If indicators of impairment are present, the assets are tested for recoverability by comparing the carrying amount of the assets to the related estimated future undiscounted cash flows that the assets are expected to generate. If the expected cash flows are less than the carrying value of the asset group, then the asset group is considered to be impaired and its carrying value is written down to fair value, based on the related estimated discounted future cash flows. To date, no such impairment losses have been recorded.

Costs for assets not yet placed into service are capitalized as construction-in-progress and depreciated or amortized in accordance with the above useful lives once placed into service. Upon retirement or sale, the related cost and accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in the consolidated statements of operations. Repairs and maintenance costs are expensed as incurred.

Operating Leases

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on specific facts and circumstances and the existence of an identified asset(s), if any, and its control over the use of the identified asset(s), if applicable. Upon lease commencement, operating lease liabilities and their corresponding right-of-use assets are recorded on the balance sheet based at the present value of lease payments over the expected lease term. Leases with an initial term of 12 months or less are not recorded on the balance sheet. Lease expense is recognized over the expected term on a straight-line basis.

Lease payments are discounted at the lease commencement date using the interest rate implicit in the lease contract. As this rate is typically not readily determinable, the Company determines an incremental borrowing rate that is used to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Certain prospective adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received.

The Company elected to account for lease and non-lease components as a single lease component, however non-lease components that are variable, such as common area maintenance and utilities, are generally paid separately from rent based on actual costs incurred and therefore are not included in the right-of-use asset and operating lease liability and are reflected as an expense in the period incurred. The Company's lease terms often include renewal options. The amounts determined for

the Company's right-of-use assets and lease liabilities generally do not assume that any renewal options or any early-termination provisions, if any, are exercised, unless it is reasonably certain that the Company will exercise such options.

Revenue Recognition

At contract inception, the Company assesses whether the collaboration arrangements are within the scope of ASC Topic 808, Collaborative Arrangements, or ASC 808, to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed based on the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the arrangement are within the scope of ASC 808 and which elements are within the scope of ASC 606 (as described below). For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. To date, the Company has not entered into any arrangements within the scope of ASC 808.

The Company's revenues are generated through its license and collaboration agreements with Gilead. Refer to Note 4, "Collaboration Agreements" elsewhere in these notes to the Company's consolidated financial statements.

The Company recognizes revenue in accordance with ASC Topic 606, Revenue from Contracts with Customers. ASC 606 provides a five-step framework whereby revenue is recognized when control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) performance obligations are satisfied. The Company only applies this framework to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. The Company then allocates the transaction price (that is, the amount of consideration the Company expects to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognizes the associated revenue when (or as) each performance obligation is satisfied. The Company's estimate of the transaction price for each contract includes all variable consideration to which the Company expects to be entitled, subject to the constraint on variable consideration. Variable consideration is not constrained if the potential reversal of cumulative revenue recognized at the contract level is not significant.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under active agreements, the Company must use its judgment to determine: (a) the number of performance obligations based on the determination under step (ii) above; (b) the transaction price under step (iii) above; (c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above; and (d) the contract term and pattern of satisfaction of the performance obligations under step (v) above. The Company uses judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below. The transaction price is allocated to the identified performance obligations on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. In certain instances, the timing of satisfying these obligations can be difficult to estimate. Accordingly, the Company's estimates may change in the future and those changes could be material. Such changes to estimates would result in a change in amounts of revenue recognized. If these estimates and judgments change over the course of these agreements, it may affect the timing and amount of revenue that the Company recognizes and records in future periods.

Amounts due to the Company for satisfying the revenue recognition criteria or that are contractually due based upon the terms of the collaboration agreements are recorded as accounts receivable in the Company's consolidated balance sheet. Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the Company's consolidated balance sheets. Amounts expected to be recognized as revenue within the one year following the balance sheet date are classified as current deferred revenue. Amounts not expected to be recognized as revenue within the one year following the balance sheet date are classified as deferred revenue, net of current portion. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets.

Exclusive License Rights — If the license to the Company’s intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, which generally include research and development services, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a license is distinct from the other promises, the Company considers relevant facts and circumstances of each arrangement, including the research and development capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining promises, whether the value of the license is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises and whether it is separately identifiable from the remaining promises. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation and whether the license is the predominant promise within the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. If the license is the predominant promise, and it is determined that the license represents functional intellectual property (“IP”), revenue is recognized at the point in time when control of the license is transferred. If it is determined that the license does not represent functional IP, revenue is recognized over time using an appropriate method of measuring progress.

Research and Development Services — The obligations under the Company’s collaboration agreements may include research and development services to be performed by the Company to benefit the collaboration partner. For performance obligations that include research and development services, the Company generally recognizes revenue allocated to such performance obligations based on an appropriate measure of progress. The Company utilizes judgment to determine the appropriate method of measuring progress for purposes of recognizing revenue, which is generally an input measure such as costs incurred. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods of which revenue should be recognized, are subject to estimates by management and may change over the course of the contract. Reimbursements from the partner that are the result of a collaborative relationship with the partner, instead of a customer relationship, such as co-development activities, are recorded as a reduction to research and development expense. No collaborative arrangements existed that would result in such reimbursements for the periods presented.

Customer Options — The Company’s arrangements may provide a collaborator with the right to acquire additional goods or services in the future. Under these agreements, fees may be due to the Company (i) upon the exercise of the customer option or (ii) in equal installment payments over an agreed upon period. If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the additional goods and services underlying the customer options are evaluated in order to determine if these additional goods or services are distinct from those included as a performance obligation at the outset of the arrangement. If the additional services are not determined to be distinct, the variable consideration pertaining to the customer option is added to the initial transaction price at the time in which the option exercise becomes probable, so long as a potential for reversal of cumulative revenue recognized at the contract level is not significant. Any such adjustments to the transaction price are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If the additional services are distinct, the Company evaluates the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the inception of the arrangement. The Company allocates the transaction price to material rights based on the relative stand-alone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires.

Milestone Payments — At the inception of an arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered likely of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue recognized would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If a milestone or other variable consideration relates specifically to the Company’s efforts to satisfy a single performance obligation or to a specific

outcome from satisfying the performance obligation, the Company generally allocates the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur.

Royalties — For arrangements that include sales-based royalties, including milestone payments based on a level of sales, where the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from licensing agreements.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our drug discovery efforts and the development of our product candidates. These expenses include salaries, employee benefits, and stock-based compensation expense for our research and development personnel, materials, supplies, depreciation on and maintenance of research equipment, the cost of services provided by outside CROs and consultants to conduct research and development activities including costs of clinical trials and manufacturing, and the allocable portions of facility costs, such as rent, utilities, and general support services. All costs incurred to fulfill the Company's obligations under the collaboration with Gilead are classified as research and development expenses. All costs associated with research and development are expensed as incurred.

Management estimates the Company's accrued research and development expenses as of each balance sheet date in the Company's financial statements based on facts and circumstances known to the Company at that time. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly. Nonrefundable advance payments for goods and services are deferred and recognized as expense in the period that the related goods are consumed or services are performed.

Patent Costs

All patent-related costs 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.

Stock-Based Compensation

The Company measures the cost of employee services received in exchange for stock-based awards based on the grant-date fair value of the awards. The Company calculates the fair value of restricted stock awards based on the grant date fair value of the underlying common stock. The Company recognizes stock-based compensation expense on a straight-line basis over the requisite service period of the awards for service-based awards, which is generally the vesting period. The Company recognizes stock-based compensation for performance-based awards when the underlying performance conditions are considered probable of occurrence and recognizes the cumulative effect of current and prior period changes in the period of change.

Prior to the consummation of the Business Combination transaction in August 2021, as there was not a public market for the common stock of the Company prior to becoming publicly traded, the fair value of common stock underlying stock-based awards was based on a valuation provided by the board of directors as derived from a recommendation by an unrelated third-party valuation firm. The Company determined the estimated per share fair value of its common stock at various dates considering contemporaneous and retrospective valuations that incorporated objective and subjective factors, including actual and forecasted financial results, market conditions and performance of comparable publicly traded companies, developments and milestones of the Company, the rights and preferences of common and redeemable convertible preferred stock, advice from the third-party valuation specialists, and transactions involving the Company's stock. The estimated per share fair value of the Company's common stock was determined in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*. The fair value of each restricted common stock award was estimated on the date of grant based on the fair value of the Company's common stock on that same date.

Subsequent to becoming a publicly traded Company upon the consummation of the Business Combination transaction, the fair value of common stock underlying stock-based awards is based on an estimate at each grant date using the market price of our common stock and each of the assumptions discussed below.

Expected Term: The expected term of the stock options is estimated using the “simplified method,” as prescribed in SEC’s Staff Accounting Bulletin (SAB) No. 107, as the Company has limited historical information from which to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock option grants. The simplified method is the midpoint between the vesting period and the contractual term of the option.

Expected Volatility: Since there is limited historical data for the Company’s common stock and limited company-specific historical volatility, the Company has determined the share price volatility for options granted based on an analysis of the volatility used by a peer group of publicly traded companies. In evaluating similarity, the Company considers factors such as industry, stage of life cycle and size.

Risk-free Interest Rate: The risk-free rate is based on the U.S. Treasury yield curve commensurate with the expected life of the option.

Dividend Rate: The expected dividend is assumed to be zero as the Company has never paid dividends and has no current plans to do so.

The assumptions used in estimating the fair value of stock-based awards represent management’s estimate and involve inherent uncertainties and the application of management’s judgment. As a result, if factors change and management uses different assumptions, stock-based compensation expense could be materially different for future awards.

Stock-based compensation is classified in the accompanying consolidated statements of operations and comprehensive loss based on the function to which the related services are provided. Forfeitures are accounted for as they occur. Any consideration paid by employees on exercising stock options and the corresponding portion previously credited to additional paid-in capital are credited to share capital.

Deferred Financing Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of an equity financing, these costs are recorded in shareholders’ equity as a reduction of additional paid-in capital generated as a result of the offering.

Income Taxes

The Company accounts for income taxes under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period corresponding to the enactment date. A valuation allowance is established when it is more likely than not that all or some portion of the deferred tax assets will not be realized through generating sufficient future taxable income.

The Company assesses all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. The Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not such tax position will be sustained on examination by the taxing authorities, based solely on the technical merits of the respective tax position. The tax benefits recognized in the financial statements from such a tax position should be measured based on the largest benefit having a more likely than not likelihood of being realized upon ultimate settlement with the tax authority. The recognition and measurement of tax benefits requires significant judgments that are subject to change as new information becomes available.

Penalties and interest expense related to income taxes are included as components of income tax expense and interest expense, respectively, as necessary.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive loss for the years ended December 31, 2022 and 2021 was unrealized losses on investments in marketable securities.

Net Loss Per Share

Basic net loss per share attributable to common stockholders is computed by dividing net loss by the weighted-average number of shares of common shares outstanding during each reporting period. The weighted-average number of shares of common stock outstanding used in the basic net loss per share calculation does not include unvested restricted stock awards as these instruments are considered contingently issuable shares until they vest. Diluted net loss per share attributable to common stockholders includes the effect, if any, from the potential exercise or conversion of securities, such as convertible preferred stock and stock options, which would result in the issuance of incremental shares of common stock. For diluted net loss per share, the weighted-average number of shares of common stock is the same for basic net loss per share due to the fact that when a net loss exists, dilutive securities are not included in the calculation as the impact is anti-dilutive. The Company's unvested restricted stock entitles the holder to participate in dividends and earnings of the Company, and, if the Company were to recognize net income, it would apply the two-class method to calculate earnings per share. The two-class method is not applicable during periods with a net loss, as the holders of the unvested restricted stock have no obligation to fund losses.

The two-class method of computing net loss per share would be applicable in a reporting period that resulted in a net income position, as the Company has issued shares that meet the definition of participating securities. The two-class method determines net loss per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

Commitments and Contingencies

Liabilities for loss contingencies arising from claims, assessments, litigation, fines and penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. Legal costs incurred in connection with loss contingencies are expensed as incurred.

Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but before the financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. Subsequent events have been evaluated as required. The Company has evaluated all subsequent events and determined there are no material recognized or unrecognized subsequent events requiring disclosure.

Emerging Growth Company Status

The Company is an "emerging growth company," 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 other public companies that are not emerging growth companies. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards and as a result of this election, its consolidated financial statements may not be comparable to companies that comply with public company effective dates. The Company may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of an initial public offering or such earlier time that it is no longer an emerging growth company. However, the Company has not yet delayed the adoption of any new accounting standards.

Recently Adopted Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12, *Simplifying the Accounting for Income Taxes*, (ASC 740). The ASU enhances and simplifies various aspects of the income tax accounting guidance in ASC 740, including requirements related to hybrid tax regimes, the tax basis step-up in goodwill obtained in a transaction that is not a business combination,

separate financial statements of entities not subject to tax, the intra-period tax allocation exception to the incremental approach, ownership changes in investments, changes from a subsidiary to an equity method investment, interim-period accounting for enacted changes in tax law, and the year-to-date loss limitation in interim-period tax accounting. This guidance became effective for the Company's fiscal year beginning January 1, 2021. The adoption of this guidance did not have a material impact on the Company's consolidated financial statements.

In August 2020, the FASB issued ASU 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)*. The amendments in this update affect entities that issue convertible instruments and/or contracts indexed to and potentially settled in an entity's own equity. The new ASU eliminates the beneficial conversion and cash conversion accounting models for convertible instruments. It also amends the accounting for certain contracts in an entity's own equity that are currently accounted for as derivatives because of specific settlement provisions. In addition, the new guidance modifies how particular convertible instruments and certain contracts that may be settled in cash or shares impact the diluted EPS computation. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. The Company elected to early adopt this guidance on January 1, 2021. Adoption of the ASU 2020-06 guidance as of January 1, 2021 had no impact on its consolidated financial statements for the year ended December 31, 2020. The Company issued the second tranche of its redeemable convertible Series B preferred stock in March 2021 at an original issue price of \$1.32 per share, which would have resulted in the recognition of a beneficial conversion feature of \$28.4 million prior to the adoption of ASU 2020-06. However, the consummation of the Business Combination and the application of a retroactive adjustment to historical redeemable convertible preferred stock in all periods presented under the reverse recapitalization accounting treatment have resulted in the adoption of this guidance not resulting in a material impact on the Company's financial statements.

Recently Issued Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that recently issued standards that are not yet effective will not have a material impact on the Company's consolidated financial statements.

3. Business Combination

In April 2021, the Company, BCTG Merger Sub Inc., a Delaware corporation, and Tango Therapeutics, Inc. (now known as Tango Therapeutics Sub, Inc. or Old Tango) signed a definitive merger agreement (the Merger Agreement) memorializing the terms of BCTG's acquisition of 100% of Old Tango's issued and outstanding equity securities in exchange for \$550.0 million worth of consideration in the form of BCTG common stock (the Business Combination). The Business Combination was approved in August 2021 by shareholders of BCTG, resulting in BCTG acquiring 100% of Old Tango's issued and outstanding equity securities in August 2021. The Business Combination was accounted for as a "reverse recapitalization" in accordance with U.S. GAAP. As a result of the Business Combination, BCTG was renamed Tango Therapeutics, Inc. The Company's common stock is trading on The Nasdaq Global Market under the ticker symbol TNGX.

Tango received gross proceeds of \$167.1 million upon the closing of the Business Combination. Tango continues to operate under the Old Tango management team. Simultaneous with the closing of the Business Combination, an aggregate of 18,610,000 shares of common stock (the PIPE Financing) were issued, resulting in gross proceeds of an additional \$186.1 million upon the closing of the PIPE Financing. Total transaction costs and redemptions approximated \$26.9 million, resulting in total net proceeds of \$326.3 million.

BCTG Acquisition Corporation IPO

The registration statement for BCTG's initial public offering (IPO) was declared effective on September 2, 2020. On September 8, 2020, the Company consummated its Initial Public Offering of 16,675,000 shares of common stock (the Public Shares), including the 2,175,000 Public Shares as a result of the underwriters' full exercise of their over-allotment option, at an offering price of \$10.00 per Public Share, generating gross proceeds of approximately \$166.8 million, and incurring offering costs of approximately \$9.6 million, inclusive of approximately \$5.8 million in deferred underwriting commissions. Simultaneously with the closing of the Initial Public Offering, the Company consummated the private placement (Private Placement) of 533,500 shares of common stock (the Private Placement shares), at a price of \$10.00 per Private Placement Share to the Sponsor, generating gross proceeds of approximately \$5.3 million. Upon the closing of the Initial Public Offering and the Private Placement, the net proceeds of the Initial Public Offering and certain of the proceeds of the Private

Placement was placed in a trust account (Trust Account) in the United States maintained by Continental Stock Transfer & Trust Company, as trustee, and remained invested only in U.S. government treasury bills, notes and bonds with a maturity of 185 days or less or in money market funds meeting certain conditions under Rule 2a-7 under the Investment Company Act and which invest solely in U.S. Treasuries, until the completion of the Business Combination as described below.

On August 10, 2021 (the Closing Date), BCTG, a Delaware corporation and now predecessor of the Company, consummated the Business Combination, pursuant to the Merger Agreement, by and among BCTG, BCTG Merger Sub Inc., a Delaware corporation (BCTG Merger Sub), and Old Tango. Prior to consummation of the Business Combination, Old Tango changed its name from “Tango Therapeutics, Inc.” to “Tango Therapeutics Sub, Inc.” and in connection with the Business Combination, BCTG changed its name to “Tango Therapeutics, Inc.” (the former name of Old Tango). Pursuant to the Merger Agreement, on the Closing Date, BCTG Merger Sub merged with and into Old Tango, or the Merger, with Old Tango surviving the Merger as a wholly-owned subsidiary of BCTG, and (as noted above) BCTG changed its name to “Tango Therapeutics, Inc.”, or New Tango.

Pursuant to the terms and conditions of the Merger Agreement, the aggregate consideration paid to Old Tango equity holders upon the closing of the Merger was 55,000,000 shares of New Tango common stock. Subsequent to the closing of the Business Combination, New Tango entered into subscription agreements with certain investors (PIPE Investors) pursuant to which the PIPE Investors purchased 18,610,000 shares of New Tango common stock at \$10.00 per share, for aggregate gross proceeds of \$186.1 million, under the PIPE Financing.

The following table summarizes the elements of the net proceeds from the Business Combination and PIPE Financing transaction (in thousands):

	Recapitalization
Cash - BCTG's Trust Account and cash (net of redemptions)	\$ 156,013
Cash - PIPE Financing	186,100
Less transaction costs and advisory fees paid	(15,844)
Net cash proceeds from the Business Combination and PIPE Financing	326,269
Add: non-cash net assets assumed from BCTG	3
Net contributions from Business Combination and PIPE Financing	<u>\$ 326,272</u>

The following table summarizes the number of shares of common stock outstanding immediately following the consummation of the Business Combination and PIPE Financing transaction:

	Number of Shares
BCTG common shares outstanding prior to the Business Combination	21,377,250
Less redemption of BCTG shares	(1,106,814)
Common shares of BCTG outstanding as of the Business Combination	20,270,436
Shares issued pursuant to the PIPE Financing	18,610,000
Business Combination and PIPE Financing shares	38,880,436
Old Tango common shares (after preferred shares were converted 1-for-1 for common shares)	48,593,803
Total shares of Common Stock immediately after Business Combination consummation	<u>87,474,239</u>

The merger consideration of 55,000,000 shares of New Tango common stock issued to Old Tango equity holders consists of 48,593,803 shares issued in exchange for Old Tango common and preferred shares outstanding, included in the table above, as well as 6,406,197 shares issued in exchange for the Old Tango unvested restricted stock awards and unexercised stock options outstanding immediately prior to the effective time of the Business Combination.

Retrospective Application of Recapitalization

As discussed above, the Business Combination with BCTG, which was consummated on August 10, 2021, is accounted for as a reverse recapitalization of equity structure. Under the reverse recapitalization model, the Business Combination was treated as Old Tango issuing equity for the net assets of BCTG, with no goodwill or intangible assets recorded. Under this method of accounting, BCTG was treated as the “acquired” company for financial reporting purposes. This determination was primarily based on the fact that subsequent to the Business Combination, Old Tango’s stockholders possess a majority of the voting power of the combined company, the Company comprises all of the ongoing operations of Old Tango, the

Company comprises a majority of the governing body of Old Tango, and the Company's senior management comprises all of the senior management of Old Tango.

These consolidated financial statements contain recasted stockholders' equity balances resulting from the retroactive application of reverse recapitalization accounting in accordance with U.S. GAAP.

Pursuant to the terms of the Merger Agreement, upon the closing of the Business Combination on August 10, 2021 (the Effective Time), each share of Old Tango's redeemable convertible preferred stock (the Preferred Stock) issued and outstanding immediately prior to the Effective Time was converted into a share of the Company's common stock using the exchange ratio of 0.34 as follows:

Date	Description	Redeemable Convertible Preferred Stock	Preferred to Common Exchange Ratio	Common Stock Shares	8/10/2021 Merger Recapitalization Exchange Ratio	Recapitalization Common Stock
12/31/2019	Series A	55,700,000	1.00	55,700,000	0.34	18,922,317
4/7/2020	Series B (tranche 1)	22,686,025	1.00	22,686,025	0.34	7,706,861
8/17/2020	Series B-1	27,152,255	1.00	27,152,255	0.34	9,224,122
3/18/2021	Series B (tranche 2)	22,686,025	1.00	22,686,025	0.34	7,706,861

All common shares, as well as previously issued share options and restricted stock awards (RSAs), presented in the accompanying recasted consolidated statements of redeemable convertible preferred stock and stockholders' equity and/or in the related notes are presented on an as-converted basis, converted at the ratio of 0.34.

4. Collaboration Agreements

2018 Gilead Agreement

In October 2018, the Company entered into a Research Collaboration and License Agreement (the 2018 Gilead Agreement) with Gilead Sciences, Inc. (Gilead). Pursuant to the 2018 Gilead Agreement, the Company performed target discovery and validation activities in accordance with an agreed-upon multi-year research plan. During the initial three-year research term, Gilead had the option to obtain exclusive, worldwide licenses to develop and commercialize up to five validated programs (Gilead Program License).

In 2018, Gilead paid the Company a \$50.0 million non-refundable upfront payment upon the execution of the 2018 Gilead Agreement. The Company was eligible to receive milestone payments of up to \$1.7 billion across all programs and royalties on future sales of commercialized products, if any. For up to two programs licensed by Gilead, the Company had the option to co-develop and co-promote certain programs licensed by Gilead in the U.S. and was eligible to receive royalties on ex-U.S. sales.

The Company assessed this arrangement in accordance with ASC 606, *Revenue from Contracts with Customers*, and concluded that the contract counterparty, Gilead, was a customer. The Company identified a single performance obligation under the arrangement consisting of the combination of participating on the joint steering committee and the research and development services provided during the research term. The identified promises were determined to not be individually distinct due to the specialized nature of the early-stage research services to be provided by the Company and the interdependent relationship between the promises. The Company determined that the option for Gilead to extend the term of the arrangement was not priced at a discount, and therefore did not provide Gilead with a material right. This option will be excluded from the transaction price until exercised. At the inception of the 2018 Gilead Agreement, the Company also determined that the Gilead program license options provided to Gilead did not include a material right.

The total transaction price, subject to variable consideration constraints, was allocated to the combined single performance obligation. The Company determined that the single combined performance obligation is satisfied over time as the customer is simultaneously receiving and consuming the benefit of the Company's performance. The future milestone payments represent variable consideration that is fully constrained at inception of the arrangement as the achievement of the milestone events are highly uncertain.

Amended Gilead Agreement

In August 2020, Gilead made an equity investment of \$20.0 million into the Company as a participant in the Company's Series B-1 preferred stock offering. At the time of the original investment, as well as of the December 31, 2022 balance sheet date, Gilead maintains an ownership of less than 10% of the Company's common stock and is thus not considered to be a related party to the Company.

In August 2020, the Company and Gilead also entered into an Amended Research Collaboration and License Agreement (the Gilead Agreement), which superseded and replaced the 2018 Gilead Agreement. The Gilead Agreement represents a continuation of the initial target discovery and validation research and development efforts begun under the 2018 Gilead Agreement. Under the Gilead Agreement:

- The Company received upfront, non-refundable consideration of \$125.0 million from Gilead upon execution of the Gilead Agreement in 2020;
- The term of the 2018 Gilead Agreement ended on the date the Gilead Agreement was executed. The Gilead Agreement has a research term of seven years;
- Gilead expanded its option to license up to 15 programs for which Gilead may obtain exclusive, worldwide licenses to develop and commercialize therapies, subject to applicable license fees;
- Prior to exercising its option to license a program, Gilead may "extend" such program, in which case Gilead will pay research option-extension fees and the Company will continue to collaborate with Gilead to discover and develop programs, potentially through early clinical development;
- Gilead has the option to "reserve" a target during which Gilead may: (i) license the target, (ii) "extend" the target, or (iii) decline the target, during the designated reserve target period. If, during the reserve target period Tango elects to work on the reserved target, Tango will retain full rights to the target program and Gilead receives a right of first negotiation in connection with any future partnering or licensing of such target by Tango, if any; and
- For up to five programs licensed by Gilead, the Company has the option to co-develop and co-promote the lead product in the U.S., subject to certain exceptions, and is eligible to receive tiered royalties in the first decile on ex-U.S. sales.

The Company is eligible to receive up to \$410.0 million per program in license, research option-extension, and clinical, regulatory, and commercial milestones and royalties on future sales of commercialized products, if any.

The Gilead Agreement was accounted for as a modification of the 2018 Gilead Agreement under ASC 606 as both the scope and price of the contract were changed under the Gilead Agreement. The additional goods and services to be provided under the Gilead Agreement are not distinct from the combined performance obligation identified under the 2018 Gilead Agreement which was only partially satisfied at the date of contract modification. As such, the Company identified a single combined performance obligation under the Gilead Agreement consisting of the research services and continued participation on the joint steering committee during the research term. As a result, the Company's progress towards completing its research services to Gilead over the seven-year term of the Gilead Agreement was lower than its progress under the three-year term of the 2018 Gilead Agreement and a cumulative catch-up adjustment was recorded during the third quarter of 2020 resulting in a charge of \$11.3 million against revenue previously recognized through the date of the Gilead Agreement.

In December 2020 and in September 2021, Gilead elected to extend two programs for a research extension fee of \$12.0 million each. The Company determined that the additional goods and services relating to the continued research services were not distinct from the early-stage research services already promised to Gilead under the on-going research plan. Consideration pertaining to each of the research option-extensions is paid to the Company in equal quarterly installment payments over an agreed upon payment schedule. Although future research installment payments are not payable in the event of scientific failure, the Company determined that the variable consideration of \$12.0 million for each of the extensions should not be constrained as the potential for a significant reversal of cumulative revenue recognized at the contract level is remote, and therefore the research option-extension consideration was added to the transaction price under the Gilead Agreement.

In April 2021, Gilead licensed a program for an \$11.0 million license fee. The \$11.0 million license fee was received and recognized as revenue in the second quarter of 2021 since Tango has no continued involvement in the advancement of

the program, Gilead can benefit from the license on its own and the license is separately identifiable from the research services.

Gilead Revenue Recognized

The total transaction price allocated to the combined performance obligation under the Gilead Agreement was \$199.0 million at December 31, 2022. The total transaction price was comprised of the \$50.0 million upfront payment pursuant to the 2018 Gilead Agreement, the \$125.0 million upfront payment pursuant to the Gilead Agreement, the \$12.0 million payment pursuant to the research option-extension fee in December 2020, and the \$12.0 million payment pursuant to the research option-extension fee in September 2021. During the years ended December 31, 2022 and 2021, the Company recognized \$24.9 million and \$26.0 million, respectively, of collaboration revenue associated with the Gilead agreements based on performance completed during each period.

The Company reevaluates the transaction price and the total estimated costs expected to be incurred to satisfy the performance obligations at the end of each reporting period and as uncertain events, such as changes to the expected timing and cost of certain research and development activities that the Company is responsible for, are resolved or other changes in circumstances occur. As of December 31, 2022 and 2021, the Company had short-term deferred revenue of \$31.8 million and \$26.0 million, respectively, and long-term deferred revenue of \$92.1 million and \$114.7 million, respectively, related to the Gilead collaboration. The remaining long-term deferred revenue is expected to be recognized proportionally to the completed obligations over an expected remaining contractual term of approximately 4.6 years.

Amounts due to the Company that have not yet been received are recorded as accounts receivable and amounts received that have not yet been recognized as revenue are recorded as deferred revenue on the Company's consolidated balance sheets. As of December 31, 2022, \$10.0 million of the \$12.0 million ongoing research option-extension fee total from September 2021 had been received and the remaining \$2.0 million had been recorded as accounts receivable.

Costs incurred pursuant to the Gilead Agreements are recorded as research and development expense.

5. Fair Value Measurements

The following tables present information about the Company's financial assets measured at fair value on a recurring basis:

	Fair Market Value Measurements as of December 31, 2022			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Cash equivalents:				
Money market funds	\$ 7,577	\$ —	\$ —	\$ 7,577
U.S. Treasury bills	—	16,030	—	16,030
Marketable debt securities:				
U.S. Treasury bills	—	199,245	—	199,245
U.S. government agency bonds	—	106,920	—	106,920
Total assets	\$ 7,577	\$ 322,195	\$ —	\$ 329,772

	Fair Market Value Measurements as of December 31, 2021			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Cash equivalents				
Money market funds	\$ 62,244	\$ —	\$ —	\$ 62,244
U.S. Treasury bills	—	38,433	—	38,433
Marketable debt securities				
U.S. Treasury bills	—	287,123	—	287,123
U.S. government agency bonds	—	55,387	—	55,387
Total assets	\$ 62,244	\$ 380,943	\$ —	\$ 443,187

There were no transfers between fair value levels during the years ended December 31, 2022 and 2021.

6. Marketable Securities

The Company values its marketable securities using independent pricing services which normally derive security prices from recently reported trades for identical or similar securities, making adjustments based on significant observable transactions. At each balance sheet date, observable market inputs may include trade information, broker or dealer quotes, bids, offers or a combination of these data sources.

The following table summarizes the Company's marketable debt securities, classified as available-for-sale:

	Fair Value Measurements as of December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
	(in thousands)			
Marketable debt securities:				
U.S. Treasury bills	\$ 201,834	\$ 21	\$ (2,610)	\$ 199,245
U.S. government agency bonds	108,036	—	(1,116)	106,920
	<u>\$ 309,870</u>	<u>\$ 21</u>	<u>\$ (3,726)</u>	<u>\$ 306,165</u>

	Fair Value Measurements as of December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
	(in thousands)			
Marketable debt securities:				
U.S. Treasury bills	\$ 287,699	\$ 1	\$ (577)	\$ 287,123
U.S. government agency bonds	55,576	—	(189)	55,387
	<u>\$ 343,275</u>	<u>\$ 1</u>	<u>\$ (766)</u>	<u>\$ 342,510</u>

The Company holds marketable debt securities with an aggregate fair value of \$31.2 million as of December 31, 2022 with contractual maturity dates greater than one year.

The following table summarizes the fair value and gross unrealized losses aggregated by category and the length of time that individual securities have been in an unrealized loss position:

	December 31, 2022					
	Less than twelve months		Greater than twelve months		Total	
	Fair value	Unrealized loss	Fair value	Unrealized loss	Fair value	Unrealized loss
	(in thousands)					
U.S. Treasury bills	\$ 44,213	\$ (640)	\$ 84,997	\$ (1,970)	\$ 129,210	\$ (2,610)
U.S. government agency bonds	68,919	(627)	38,000	(489)	106,919	(1,116)
	<u>\$ 113,132</u>	<u>\$ (1,267)</u>	<u>\$ 122,997</u>	<u>\$ (2,459)</u>	<u>\$ 236,129</u>	<u>\$ (3,726)</u>

	December 31, 2021					
	Less than twelve months		Greater than twelve months		Total	
	Fair value	Unrealized loss	Fair value	Unrealized loss	Fair value	Unrealized loss
	(in thousands)					
U.S. Treasury bills	\$ 274,318	\$ (577)	\$ -	\$ -	\$ 274,318	\$ (577)
U.S. government agency bonds	55,387	(189)	-	-	55,387	(189)
	<u>\$ 329,705</u>	<u>\$ (766)</u>	<u>\$ -</u>	<u>\$ -</u>	<u>\$ 329,705</u>	<u>\$ (766)</u>

The Company holds investment grade marketable securities considered to be in an unrealized loss position. Although these marketable securities are held at an unrealized loss position at December 31, 2022, the Company does not intend to sell

the marketable securities prior to the value of the securities being recovered and the Company has concluded that it is more likely than not that the marketable securities cost basis values will be recovered prior to sale of the securities and that there are no conditions or events that might require the Company to sell the securities before recovery of the cost basis occurs. Further, the Company did not record any impairments to marketable securities or reserves for credit losses related to its marketable debt securities during the periods then ended. Marketable securities include \$0.5 million and \$0.2 million in accrued interest at December 31, 2022 and December 31, 2021, respectively.

7. Supplemental Balance Sheet Information

Property and Equipment

Property and equipment, net as of December 31, 2022 and 2021 consists of the following:

	December 31,	
	2022	2021
	(in thousands)	
Laboratory equipment	\$ 7,720	\$ 5,587
Computer equipment	2,235	198
Computer software	125	125
Furniture and fixtures	1,699	467
Leasehold improvements	2,778	246
Construction in progress	8	738
	<u>14,565</u>	<u>7,361</u>
Less: Accumulated depreciation	(3,681)	(2,529)
Property and equipment, net	<u>\$ 10,884</u>	<u>\$ 4,832</u>

Depreciation expense was \$1.6 million and \$0.9 million for the years ended December 31, 2022 and 2021, respectively.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities as of December 31, 2022 and 2021 include the following:

	December 31,	
	2022	2021
	(in thousands)	
Payroll and employee-related costs	\$ 5,738	\$ 3,688
Research and development costs	10,490	5,533
Other	1,267	666
Total accrued expenses and other current liabilities	<u>\$ 17,495</u>	<u>\$ 9,887</u>

8. Leases

Operating Leases

In July 2017, the Company entered into a lease of office and laboratory space at 100 Binney Street in Cambridge, Massachusetts. The lease commenced in March 2018 and lease payments commenced in June 2018. This lease had an original term of eight years with an option to extend for one additional three-year period. The lease agreement required the Company to provide a letter of credit for \$0.6 million that is collateralized with cash that is recorded as long-term restricted cash in the accompanying balance sheets.

In November 2021, the Company entered into a lease termination agreement for the leased office and laboratory space at 100 Binney Street in Cambridge, Massachusetts. The lease termination agreement is a modification of the original lease agreement that provides for, among other things, the acceleration of the expiration of the original term of the lease from June 30, 2026 to an earlier lease termination date of September 30, 2022. The execution of the lease termination agreement resulted in reductions to the associated lease liability and right-of-use asset balances of \$5.3 million and \$5.2 million, respectively, in the fourth quarter of 2021. The \$0.6 million letter of credit associated with the lease and recorded as short-term restricted cash on the balance sheet as of December 31, 2022 was released to the Company in March 2023.

In September 2019, the Company entered into a new lease for office and laboratory space at 201 Brookline Avenue in Boston, Massachusetts. The lease, as amended and restated in November 2021, has a non-cancelable term of ten years with an option to extend for up to two additional five-year periods. The lease commenced in August 2022, when the Company obtained access to the space for its' intended use. The lease agreement provides for initial tenant improvement allowances.

In August 2022, upon commencement of the 201 Brookline Avenue lease, the Company recorded an operating lease liability in the amount of \$37.9 million and related operating lease right-of-use asset in the amount of \$48.0 million. Payments totaling \$10.1 million for tenant improvements, and net of tenant improvement allowance reimbursements, made prior to the lease commencement date were reclassified as an increase to the right-of-use asset upon the commencement of the lease. Additional estimated future tenant improvement allowance reimbursements of \$1.0 million are expected to result in an increase to the lease liability balance in future periods, upon receipt. The fixed annual rent payable under the lease is \$5.1 million, increasing by 3% annually from the rent commencement date. The minimum rent payments to be paid over the 10-year term of the lease total \$61.0 million. The additional rental payments associated with the renewal option were not included in the calculation of the operating lease right-of-use asset and associated operating lease liability as the renewal was not considered probable of occurring. The discount rate applied to the lease payments is 8.0%.

In December 2022, the Company entered into an operating lease agreement to sublease a portion of the 201 Brookline Avenue premise to an unrelated third party. The sublease will expire on December 31, 2024, with a sublessee option to extend the term for six months. Sublease income recognized under the sublease agreement for the years ended December 31, 2022 was approximately \$0.1 million, and was recorded as a reduction of the related lease expense. There was no sublease income recognized during the year ended December 31, 2021.

The Company's rent payments for facility leases during the years ended December 31, 2022 and 2021 are classified as operating lease costs in the chart below. The leases are both considered net leases and therefore the non-lease components, such as common area maintenance, are paid separately from rent based on actual costs incurred; therefore, the non-lease components are not included in the right-of-use asset and lease liability and are reflected as an expense in the period incurred. The non-lease components are classified as variable costs in the chart below. As of December 31, 2022 and 2021, right-of-use assets under operating leases totaled \$46.9 million and \$1.3 million, respectively. The elements of lease cost were as follows (in thousands, unless otherwise noted):

Operating leases	Year Ended December 31,	
	2022	2021
Operating lease cost	\$ 4,079	\$ 1,889
Short-term lease cost	-	133
Variable lease cost	476	673
Sublease Income	(101)	-
Total operating lease costs	\$ 4,454	\$ 2,695

Other information	December 31, 2022	December 31, 2021
Operating cash flows used for operating leases	\$ (82)	\$ 1,835
Weighted average remaining lease term in years	10.0	0.9
Weighted average discount rate	8%	12%

Future minimum lease payments due under operating leases are as follows (in thousands):

Year Ending December 31,	Future minimum lease payments
2023	\$ 4,974
2024	\$ 5,543
2025	\$ 5,608
2026	\$ 5,776
2027	\$ 5,949
Thereafter	\$ 33,397
Total lease payments	61,247
Less: imputed interest	(20,116)
Total operating lease liabilities	\$ 41,131

The future minimum lease payments have not been reduced by minimum net sublease receivables of \$2.5 million due in the future under the Company's non-cancelable subleases for office and laboratory space located at 201 Brookline Ave in Boston, Massachusetts.

9. Commitments and Contingencies

License Agreement

In March 2020, the Company entered into a License Agreement (the Medivir Agreement) with Medivir AB (Medivir), pursuant to which the Company obtained an exclusive license to all patents, know-how and other intellectual property associated with a preclinical-stage research program. Pursuant to the Medivir Agreement, the Company made an upfront payment of \$0.4 million.

Under the terms of the Medivir Agreement, the Company is obligated to pay Medivir in connection with development, regulatory and commercial activities. The Company has agreed to make certain milestone payments of \$1.4 million in the aggregate for the first licensed product that achieves specified clinical milestones, plus \$25.0 million for the first licensed product that achieves specified regulatory approval and sales milestones, in each case, in either of the first two specified genetic contexts and \$0.7 million in the aggregate if that first licensed product achieves specified clinical milestones, plus \$5.0 million if that first licensed product achieves specified regulatory and sales milestones for a third genetic context or the second licensed product achieves such specified development, regulatory and sales milestones in either of the first two specified genetic contexts. The Company has the right to reduce these milestone payments by a specified amount in the event the licensed product is not covered by Medivir's patents or if payments are due to a third party for a license under such third party's intellectual property rights. The Company is also obligated to pay Medivir a low single-digit royalty on net sales of any product covered by a licensed patent. The Medivir Agreement expires on the date of expiration of all royalty obligations. Either party may terminate the Medivir Agreement earlier upon an uncured material breach of the other party.

Upfront fees paid pursuant to the Medivir License Agreement were recorded to research and development expense. No milestones have been achieved to date.

Other Funding Commitments

As of December 31, 2022, the Company had ongoing preclinical and clinical studies. The Company enters into contracts in the normal course of business with contract research organizations in connection with preparation and operation of clinical trials, professional consultants for expert advice and other vendors for clinical supply manufacturing or other preclinical and clinical services. These contracts are generally cancellable, with notice, at the Company's option and do not have significant cancellation penalties.

Guarantees

The Company enters into certain agreements with other parties in the ordinary course of business that contain indemnification provisions. These typically include agreements with directors and officers, business partners, contractors, landlords, construction companies, contract research organizations, clinical trial sites, and other parties. Under these provisions, the Company generally indemnifies and holds harmless the indemnified party for losses suffered or incurred by the indemnified party under the terms of the contract, including as a result of the Company's activities. These indemnification provisions generally survive termination of the underlying agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification provisions is unlimited. However, to date the Company has not incurred material costs to defend lawsuits or settle claims related to these indemnification provisions. As a result, the estimated fair value of these obligations is minimal.

Litigation

The Company, from time to time, may be party to litigation arising in the ordinary course of business. The Company was not subject to any material legal proceedings as of December 31, 2022, and no material legal proceedings are currently pending or threatened. Because of uncertainties related to claims, proceedings and litigation, assessments of potential liabilities are based on the Company's best estimates based on information available at the time of the assessment. On a periodic basis, as additional information becomes available, or based on specific events such as the outcome of litigation, court decisions or settlement of claims (and offers of settlement), the Company may reassess the potential liability related to these matters and may revise these estimates, which could result in a material adverse effect on the operating results of the Company. Costs associated with involvement in legal proceedings are expensed as incurred. The outcome of any such

proceedings, regardless of the merits, is inherently uncertain. If the Company were to be unable to prevail in any such proceedings, the consolidated financial position, results of operations, and future cash flows of the Company may be materially impacted.

10. Redeemable Convertible Preferred Stock

In March 2021, Old Tango sold 22,686,025 additional shares of Series B stock at a price of \$1.32 per share upon the achievement of specified development milestones in connection with the second tranche of the Series B stock purchase agreement. Proceeds from this issuance totaled \$30.0 million. Total issuance costs associated with the March 2021 issuance of Series B preferred stock was less than \$0.1 million.

Conversion of Redeemable Convertible Preferred Stock

Pursuant to the terms of the Merger Agreement, upon the Effective Time, each share of Old Tango's Preferred Stock issued and outstanding immediately prior to the Effective Time was converted into a share of Old Tango's common stock and subsequently converted into shares of New Tango common stock using an exchange ratio of 0.34. A retroactive adjustment has been applied to all periods presented to reflect the Business Combination and reverse recapitalization, therefore, resulting in no outstanding Preferred Stock as of December 31, 2022 and 2021. Refer to Note 3 for additional discussion.

Undesignated Preferred Stock

The Company's Certificate of Incorporation, as amended and restated, authorizes the Company to issue shares of preferred stock with a par value of \$0.001 per share. The number of shares of preferred stock authorized to be issued is 10,000,000 shares as of December 31, 2022. The shares of preferred stock are currently undesignated and no shares are issued or outstanding.

11. Common Stock

The Company's Certificate of Incorporation, as amended and restated, authorizes the Company to issue shares of common stock with a par value of \$0.001 per share. The holder of each share of common stock is entitled to one vote in respect of each share of stock held. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, the funds and assets available for distribution to the stockholders of the Company will be distributed among the holders of shares of common stock, pro rata based on the number of shares of common stock held by each such holder. The holders of Common Stock are also entitled to receive dividends whenever funds and assets are legally available and when declared by the Board of Directors. No dividends have been declared as of December 31, 2022.

The Company increased the number of shares of common stock authorized to be issued to 200,000,000 shares in August 2021, at the time in which the Certificate of Incorporation was amended and restated. As of December 31, 2022 and 2021, there were 88,179,374 and 87,598,184 shares of common stock issued and outstanding, respectively, as adjusted to reflect the Business Combination and reverse recapitalization through the application of a retroactive adjustment.

12. Equity Incentive Plans

Pursuant to the terms of the Business Combination, upon the Closing Date, each option to purchase Old Tango's common stock became an option to purchase shares of common stock of the surviving entity and was subsequently adjusted using an exchange ratio of 0.34. A retroactive adjustment has been applied to all periods presented to reflect the Business Combination and reverse recapitalization as discussed further in Note 3.

Founder and Advisor Awards

During 2017, the Company issued 4,690,000 shares of restricted common stock outside of the Company's 2017 Stock Option and Grant Plan to nonemployee founders and advisors (the Founders and Advisors). The shares were issued under the terms of the respective restricted common stock agreements and were subject to repurchase by the Company at the original purchase price per share upon the termination of the grantee's service relationship with the Company. As the restrictions were released and the awards vested, the value was recorded as common stock and excess of par value was recorded as additional paid in capital on the accompanying balance sheet. As of December 31, 2021, all founder and advisor restricted stock awards (RSAs) had vested.

2017 Stock Option and Grant Plan

In March 2017, the Company's stockholders approved the 2017 Stock Option and Grant Plan (the 2017 Plan), under which stock options and RSAs were granted to eligible employees, officers, directors, consultants, or other key persons who provide services to the Company. Such issuances under the 2017 Plan were subject to vesting, forfeiture and other restrictions as deemed appropriate by the board of directors (Board of Directors) at the time of issuance.

Upon effectiveness of the 2021 Stock Option and Incentive Plan (the 2021 Plan) in August 2021, the remaining shares available under the 2017 Plan ceased to be available for issuance and no future issuances will be made under the 2017 Plan. The shares of common stock underlying outstanding awards under the 2017 Plan that are forfeited, cancelled, reacquired by the Company prior to vesting, expire or are otherwise terminated (other than by exercise) will be added to the shares of common stock available for issuance under the 2021 Plan.

2021 Stock Option and Incentive Plan

Upon the closing of the Business Combination in August 2021, the Company's stockholders approved the 2021 Plan under which stock options, RSAs, unrestricted stock awards, restricted stock units, or any combination of the forgoing may be granted to eligible employees, officers, directors, consultants, or other key persons who provide services to the Company. Such issuances are subject to vesting, forfeiture and other restrictions as deemed appropriate by the Board of Directors at the time of issuance.

Upon approval, the maximum number of shares of stock reserved and available for issuance under the 2021 Plan was 9,498,725 shares. The number of shares available for future grant will automatically increase on the first day of each fiscal year by an amount equal to the least of: (i) five percent of the number of shares of Stock issued and outstanding on the immediately preceding December 31 or (ii) such lesser number of shares as determined by the 2021 Plan Administrator, as appointed by the Board of Directors. Awards that are returned to the Company's equity plan as a result of forfeiture, cancellation, are reacquired by the Company prior to vesting, expiration, or any other form of termination (other than by exercise) are automatically made available for issuance under the 2021 Plan. As of December 31, 2022, there were 6,336,537 shares available for future grant under the 2021 Plan and on January 1, 2023, the number of shares available for future grant under the 2021 Plan increased by 4,408,969 shares.

2021 Employee Stock Purchase Plan

The 2021 Employee Stock Purchase Plan (the 2021 ESPP) was adopted and approved by the Company's board of directors and by the Company's stockholders and became effective upon the closing of the Business Combination in August 2021. An aggregate of 949,873 shares were reserved for issuance. The 2021 ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2022 and each January 1 thereafter, by the least of (i) 1% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31, (ii) 949,873 shares or (iii) such number of shares as determined by the administrator. The 2021 ESPP was increased by 881,793 shares on January 1, 2023. During the year ended December 31, 2022, the Company issued 116,077 shares of common stock under the 2021 ESPP.

2023 Inducement Plan

In February 2023, the Company's Board of Directors approved the 2023 Inducement Plan (the Inducement Plan), under which the Company reserved 3,000,000 shares of Common Stock, to be used exclusively for grants of equity-based awards to individuals who were not previously employees or directors of the Company.

Restricted Stock Awards

The following table summarizes the RSA activity of the Company's plans as of and for the year ended December 31, 2021:

	Number of shares	Weighted Average Grant-Date Fair Value
Unvested restricted common stock outstanding as of December 31, 2020	256,811	\$ 1.22
Vested	(256,598)	\$ 1.22
Forfeited	(213)	\$ 1.35
Unvested restricted common stock outstanding as of December 31, 2021	—	\$ —

RSAs represent an unsecured promise to grant at no cost a set number of shares of common stock upon vesting. RSA recipients are not entitled to cash dividends and have no voting rights during the vesting period. The RSAs are issued under the terms of the respective RSA agreements and are subject to repurchase upon the holder's termination of their service relationship with the Company. The award restrictions are released as the awards vest. Upon vesting, the value is recorded as common stock and excess of par value as is recorded as additional paid in capital on the accompanying balance sheets. The common stock is subject to the Company's right to repurchase at the original purchase price per share.

As of December 31, 2022, no unvested RSAs are outstanding.

Stock Options

The following table summarizes the stock option activity of the Company's plans as of and for the years ended December 31, 2022 and 2021:

	Number of shares	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value
Options outstanding as of December 31, 2021	9,372,993	\$ 5.59	8.55	\$ 51,415,394
Granted	5,065,100	\$ 8.38		
Exercised	(465,113)	\$ 1.92		
Cancelled	(1,048,894)	\$ 9.41		
Options outstanding as of December 31, 2022	12,924,086	\$ 6.50	8.13	\$ 24,267,448
Options exercisable as of December 31, 2022	4,678,164	\$ 4.58	7.04	\$ 15,676,954

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the options and the fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock.

The total intrinsic value of options exercised totaled \$3.1 million and \$4.8 million for the years ended December 31, 2022 and 2021, respectively. The weighted-average grant date fair value per share of stock options granted was \$5.48 and \$5.40 for the years ended December 31, 2022 and 2021, respectively.

As of December 31, 2022, total unrecognized compensation expense related to stock options was \$37.0 million, which the Company expects to recognize over a remaining weighted-average period of 2.6 years. Substantially all options outstanding as of December 31, 2022 are expected to vest.

Stock Option Valuation

The weighted average assumptions used to estimate the grant date fair value of the stock options using the Black-Scholes option pricing model were as follows:

	2022	2021
Expected option life (in years)	6.2	6.2
Expected volatility	72%	72%
Risk-free interest rate	2.2%	0.5%
Expected dividend yield	— %	— %

Stock-Based Compensation Expense

The Company measures stock-based awards at their grant-date fair value and records compensation expense on a straight-line basis over the vesting period of the awards. The Company recorded stock-based compensation expense in the following expense categories in its accompanying statements of operations:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Research and development	\$ 6,812	\$ 4,616
General and administrative	7,418	3,217
Total	\$ 14,230	\$ 7,833

13. Income Taxes

During the year ended December 31, 2022, the Company recorded a total tax provision of \$0.1 million. During the year ended December 31, 2021, the Company recorded a total tax provision of \$0.3 million. All of the Company's operating losses since inception have been generated in the United States.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2022	2021
Income taxes at U.S. federal statutory rate	21.0%	21.0%
State income taxes, net of federal benefit	5.8	6.1
Federal and state research and development tax credits	3.5	5.4
Stock-based compensation expense	(1.5)	(1.1)
Nondeductible/nontaxable permanent items	(0.1)	0.6
Other	0.3	(0.3)
Change in valuation allowance	(29.1)	(32.1)
Effective tax rate	(0.1)%	(0.4)%

The tax effects of temporary differences that give rise to significant components of the deferred tax assets and liabilities are as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Deferred tax assets		
Net operating loss carryforwards	\$ 7,601	\$ 4,403
Research and development credit carryforwards	10,893	7,084
Operating lease liability	13,454	411
Deferred revenue	31,628	34,625
Accruals and reserves	1,498	958
Capitalized research costs	28,173	2,193
Other	2,830	1,008
Total gross deferred tax assets	96,077	50,682
Valuation allowance	(81,044)	(49,568)
Net deferred tax assets	\$ 15,033	\$ 1,114
Deferred tax liabilities		
Depreciation	\$ (2,310)	\$ (771)
Right-of-use asset	(12,723)	(343)
Total gross deferred tax liabilities	(15,033)	(1,114)
Net deferred taxes	\$ —	\$ —

As of December 31, 2022, the Company had U.S. federal and state net operating loss (NOL) carryforwards of \$33.1 million and \$22.2 million, respectively, which may be available to offset future taxable income. The federal NOLs include

\$2.8 million which expire at various dates beginning in 2036 and \$30.3 million which carry forward indefinitely. The state NOLs expire at various dates beginning in 2036. As of December 31, 2022, the Company also had U.S. federal and state research and development tax credit carryforwards of \$8.7 million and \$3.0 million, respectively, which may be available to offset future taxable income.

Utilization of the U.S. federal and state net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code, and corresponding provisions of state law, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income or tax liabilities. In general, an ownership change results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has performed an analysis of ownership changes through December 31, 2021 and determined that on February 6, 2017 and August 17, 2020, ownership changes had occurred. Based on this analysis, the Company's ability to use its pre-change tax attributes to offset federal and state taxable income are subject to annual limitations and a portion of the attributes generated prior to February 6, 2017 will expire unutilized, which could potentially result in an increased future tax liability. The Company has adjusted its deferred tax assets and valuation allowance balance for the affected tax attribute carryforwards to reflect the expiration of the attributes.

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported, if based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2022 and 2021. Management reevaluates the positive and negative evidence at each reporting period. The Company recorded an increase to the valuation allowance of \$31.5 million during 2022 related primarily to the increase in net operating loss carryforwards, research and development tax credit carryforwards, and capitalized research costs.

Beginning in 2022, the Tax Cuts and Jobs Act of 2017 eliminates the option to deduct research and development expenditures currently and requires taxpayers to amortize them over five years for domestically incurred expenditures and over fifteen years for foreign incurred expenditures, pursuant to Internal Revenue Code Section 174. As of December 31, 2022, the Company has recorded a gross deferred tax asset of \$96.3 million related to the capitalized IRC Section 174 expenditures.

As of December 31, 2022 and 2021, the Company had not recorded any amounts for unrecognized tax benefits. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision. As of December 31, 2022 and 2021, the Company had no accrued interest or penalties related to uncertain tax positions in the consolidated statements of operations and comprehensive loss.

The Company files income tax returns in the U.S. federal, Massachusetts and California jurisdictions, as prescribed by tax laws. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. The statute of limitations for federal and state tax authorities is generally closed for years prior to December 31, 2019, although carryforward attributes that were generated prior to 2019 may still be subject to change upon examination if they are utilized to offset taxable income in subsequent tax years. There are currently no federal or state income tax audits in progress.

14. 401(K) Savings Plan

The Company maintains a 401(k) retirement savings plan for employees who satisfy certain eligibility requirements. The savings plan is intended to qualify for favorable tax treatment under Section 401(a) of the Code and contains a cash or deferred feature that is intended to meet the requirements of Section 401(k) of the Code. Participants may make pre-tax and certain after-tax (Roth) salary deferral contributions to the plan from their eligible earnings up to the statutorily prescribed annual limit under the Code. Participants who are 50 years of age or older may contribute additional amounts based on the statutory limits for catch-up contributions. Participant contributions are held in trust as required by law. The Company made matching contributions to participants in the 401(k) plan of \$0.7 million during the year ended December 31, 2022. The Company did not make any matching contributions to participants during the year ended December 31, 2021.

15. Net Loss Per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows:

	Year Ended December 31,	
	(in thousands, except share and per share data)	
	2022	2021
Numerator:		
Net loss	\$ (108,176)	\$ (58,235)
Denominator:		
Weighted-average common stock outstanding – basic and diluted	\$ 87,820,037	62,108,032
Net loss per common share – basic and diluted	\$ (1.23)	\$ (0.94)

The Company's potential dilutive securities, which include common stock options, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2022	2021
Stock options to purchase common stock	12,924,086	9,372,993
Total	12,924,086	9,372,993

**DESCRIPTION OF REGISTRANT'S SECURITIES
REGISTERED PURSUANT TO SECTION 12 OF THE
SECURITIES EXCHANGE ACT OF 1934**

The following summary of certain provisions of Tango Therapeutics, Inc.'s ("Tango", "we", "our") securities does not purport to be complete and is subject to the Second Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation" or "Charter"), the Amended and Restated Bylaws (the "Bylaws") and the provisions of applicable law. The Certificate of Incorporation and the Bylaws are incorporated by reference to our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission.

Authorized and Outstanding Stock

The Charter authorizes the issuance of 210,000,000 shares, consisting of 200,000,000 shares of common stock, \$0.001 par value per share, and 10,000,000 shares of preferred stock, \$0.001 par value, all of which shares of preferred stock are undesignated.

Common Stock

The Charter provides the following with respect to the rights, powers, preferences and privileges of the common stock.

- *Voting Power.* Except as otherwise required by law or as otherwise provided in any certificate of designation for any series of preferred stock, the holders of common stock possess all voting power for the election of Tango's directors and all other matters requiring stockholder action. Holders of common stock are entitled to one vote per share on matters to be voted on by stockholders.
- *Dividends.* Holders of common stock will be entitled to receive such dividends, if any, as may be declared from time to time by our board of directors in its discretion out of funds legally available therefor. In no event will any stock dividends or stock splits or combinations of stock be declared or made on common stock unless the shares of common stock at the time outstanding are treated equally and identically.
- *Liquidation, Dissolution and Winding Up.* In the event of Tango's voluntary or involuntary liquidation, dissolution, distribution of assets or winding-up, the holders of the common stock will be entitled to receive an equal amount per share of all of Tango's assets of whatever kind available for distribution to stockholders, after the rights of the holders of the preferred stock have been satisfied.
- *Preemptive or Other Rights.* Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

Listing of Securities

Our common stock is listed on the Nasdaq Capital Market under the symbol "TNGX".

Transfer Agent

The transfer agent for our common stock is Computershare Trust Company, N.A.

Preferred stock

Our board of directors will have the authority, without further action by our stockholders, to issue up to 10,000,000 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 upon our liquidation. 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. No shares of convertible preferred stock are outstanding, and we have no present plan to issue any shares of convertible preferred stock

Registration Rights

Certain of our stockholders (“Holders”) hold registration rights pursuant to an amended and restated registration and stockholder rights agreement (the “Amended and Restated Registration and Stockholder Rights Agreement”). Stockholders holding a majority-in-interest of such registrable securities are entitled to make a written demand for registration under the Securities Act of 1933, as amended (the “Securities Act”), of all or part of their registrable securities.

In particular, the Amended and Restated Registration and Stockholder Rights Agreement provides for the following registration rights:

- *Shelf registration/demand registration rights.* At any time and from time to time when an effective shelf registration statement is on file with the SEC, a Holder may request to sell all or any portion of such Holder’s registrable securities by means of an underwritten takedown off of the shelf registration statement, except that we are only obligated to effect such underwritten shelf takedown if such offering will include registrable securities proposed to be sold by the requesting Holder, either individually or together with other requesting Holders, with a total offering price reasonably expected to exceed, in the aggregate, \$20.0 million. Additionally, we are not required to effect more than one underwritten shelf takedown in any six-month period.
- *Piggyback registration rights.* Subject to exceptions for certain offerings and registration statements, if at any time, we propose to file a registration statement under the Securities Act, in connection with an offering of our equity securities or securities or other obligations exercisable or exchangeable for, or convertible into, our equity securities, either for our own account or for the account of other stockholders, the Holders are entitled to include their registrable securities in such registration statement.
- *Indemnification.* The Amended and Restated Registration and Stockholder Rights Agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify Holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and Holders of registrable securities are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The registration rights granted under the Amended and Restated Registration and Stockholder Rights Agreement will terminate on the earlier of (i) the 10th anniversary of the date of the agreement and (ii) with respect to any Holder, on the date that such Holder no longer holds any Registrable Securities.

Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law

Charter and Bylaws

Our Charter 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:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate, including the right to approve an acquisition or other change of control;

- provide that the authorized number of directors may be changed only by resolution of our board of directors;
- provide that, subject to the rights of any series of preferred stock to elect directors, directors may be removed only with cause by the holders of at least two thirds (2/3) of all of our then-outstanding shares of the capital stock entitled to vote generally at an election of directors;
- provide that, subject to the rights of any series of preferred stock to fill director vacancies, all director vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice;
- provide that special meetings of our stockholders may be called by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors;
- provide that our board of directors will be divided into three classes of directors, with the classes to be as nearly equal as possible, and with the directors serving three-year terms, therefore making it more difficult for stockholders to change the composition of our board of directors;
- provide that any amendment of our Charter 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, limitation of liability and certificate of incorporation 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; and
- not provide for cumulative voting rights, therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose.

Delaware Anti-Takeover Law

Tango has opted out of Section 203 of the Delaware General Corporation Law (the "DGCL"). Section 203 of the DGCL prohibits a Delaware corporation from engaging in a "business combination" with an "interested stockholder" (i.e. a stockholder owning 15% or more of company's voting stock) for three years following the time that the "interested stockholder" becomes such, subject to certain exceptions.

Exclusive Jurisdiction of Certain Actions

The Bylaws require, to the fullest extent permitted by law, unless we consent in writing to the selection of an alternative forum, that derivative actions brought in the name of Tango, actions against any current or former directors, officers and employees for breach of fiduciary duty, actions asserting a claim arising pursuant to any provision of the DGCL or the Certificate of Incorporation or the Bylaws, actions to interpret, apply, enforce or determine the validity of the Certificate of Incorporation or the Bylaws and actions asserting a claim governed by the internal affairs doctrine may be brought only in the Court of Chancery in the State of Delaware (the "Delaware Forum Provision"). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act and the Securities Exchange Act of 1934. Any person or entity purchasing or otherwise acquiring any

interest in shares of capital stock of Tango shall be deemed to have notice of and consented to this choice of forum provision.

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List of Subsidiaries

Tango Therapeutics Sub, Inc., a Delaware corporation

Tango Securities Corporation, a Massachusetts corporation

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 333-259448 and 333-267224) and Form S-8 (Nos. 333-269620, 333-263893 and 333-260258) of Tango Therapeutics, Inc. of our report dated March 27, 2023 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 27, 2023

**CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO RULE 13a-14(a) / RULE 15d-14(a) OF THE
SECURITIES EXCHANGE ACT OF 1934, AS AMENDED**

I, Barbara Weber, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Tango Therapeutics, Inc.;
 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
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5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 27, 2023

/s/ Barbara Weber, M.D.

Barbara Weber, M.D.
Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO RULE 13a-14(a) / RULE 15d-14(a) OF THE
SECURITIES EXCHANGE ACT OF 1934, AS AMENDED**

I, Daniella Beckman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Tango Therapeutics, Inc.;
 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
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5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 27, 2023

/s/ Daniella Beckman

Daniella Beckman
Chief Financial Officer
(Principal Financial Officer)

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Tango Therapeutics, Inc. (the “Company”) for the fiscal year ended December 31, 2022 as filed with the Securities and Exchange Commission (the “Report”), I, Barbara Weber, M.D., Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, to my knowledge, that:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 27, 2023

/s/ Barbara Weber, M.D.

Barbara Weber, M.D.
Chief Executive Officer
(Principal Executive Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Tango Therapeutics, Inc. (the “Company”) for the fiscal year ended December 31, 2022 as filed with the Securities and Exchange Commission (the “Report”), I, Daniella Beckman, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, to my knowledge, that:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 27, 2023

/s/ Daniella Beckman

Daniella Beckman
Chief Financial Officer
(Principal Financial Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.
