Third Harmonic Bio

2022 Annual Report

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 001-41498

THIRD HARMONIC BIO, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**83-4553503**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
1700 Montgomery Street, Suite 210 San Francisco, California	**94111**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (209) 727-2457

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 $0.0001 per share	**THRD**	**The Nasdaq Stock Market LLC**

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	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 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 ☒

The aggregate market value of the common stock held by non-affiliates of the Registrant, based on the closing price of $17.00 for the shares of common stock on September 19, 2022 as reported by the Nasdaq Stock Market LLC on such date was approximately $388.0 million. The Registrant has elected to use September 19, 2022, which was the closing date of its initial public offering of common stock, as the calculation date because on June 30, 2022 (the last business day of the Registrant's most recently completed second fiscal quarter) the Registrant was a privately-held company. This calculation does not reflect a determination that certain persons are affiliates of the Registrant for any other purpose.

The number of shares of Registrant's Common Stock outstanding as of March 24, 2023 was 40,324,215.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to the 2023 Annual Meeting of Shareholders are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein. The Definitive Proxy Statement will be filed within 120 days of the Registrant's fiscal year ended December 31, 2022. Except with respect to information specifically incorporated by reference in this Form 10-K, the Definitive Proxy Statement is not deemed to be filed as part of this Annual Report on Form 10-K.

Auditor Firm Id: 34 Auditor Name: Deloitte & Touche LLP Auditor Location: Morristown, New Jersey

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Annual Report, contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and section 27A of the Securities Act of 1933, as amended, or the Securities Act. All statements contained in this Annual Report other than statements of historical fact, including but not limited to statements regarding our future results of operations and financial position, business strategy, market size, potential growth opportunities, nonclinical and clinical development activities, efficacy and safety profile of THB001 and any other product candidates, potential therapeutic benefits and economic value of our product candidates, use of net proceeds from our initial public offering, our ability to maintain and recognize the benefits of certain designations received by product candidates, the timing and results of nonclinical studies and clinical trials, commercial collaboration with third parties, the expected impact of the ongoing COVID-19 pandemic on our operations, and the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates, are forward-looking statements. The words "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "predict," "target," "intend," "could," "would," "should," "project," "plan," "expect," and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in Part I, Item 1A, "Risk Factors," and elsewhere in this Annual Report. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Annual Report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this report to conform these statements to actual results or to changes in our expectations, except as required by law. You should read this Annual Report with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

Unless the context indicates otherwise, as used in this Annual Report, the terms "the Company," "we," "us," and "our" refer to Third Harmonic Bio, Inc., a Delaware corporation, and its consolidated subsidiaries taken as a whole, unless otherwise noted. The mark "Third Harmonic Bio" is our registered common law trademark. This Annual Report contains additional trade names, trademarks and service marks of other companies, which are the property of their respective owners. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

RISK FACTOR SUMMARY

Our business is subject to a number of risks and uncertainties, including, those described in Part I, Item 1A. "Risk Factors" in this Annual Report. The principal risks and uncertainties affecting our business includes, among others, the following:

- We have a limited operating history, have not completed any clinical trials beyond Phase 1, and have not had any product candidates approved for commercial sale. We have a history of significant net losses since our inception and expect to continue to incur significant losses for the foreseeable future.
- We have announced the discontinuation of our Phase 1b clinical trial of our product candidate THB001 in chronic inducible urticaria following observation of asymptomatic liver transaminitis in two patients enrolled in the first dose cohort.
- We will need substantial additional funds to pursue our business objectives, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development programs, commercialization efforts or other operations.
- Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults or nonperformance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations, financial condition and results of operations.
- We have identified a material weakness in our internal control over financial reporting. If we do not remediate the material weakness in our internal control over financial reporting, or if we fail to establish and maintain effective internal control, we may not be able to accurately report our financial results or file our periodic reports in a timely manner, which may cause investors to lose confidence in our reported financial information and may lead to a decline in the market price of our common stock.
- Our future performance is substantially dependent on our ability to identify and develop future product candidates.
- Drug development is a lengthy and expensive process, and the outcome of clinical testing is inherently uncertain, and results of earlier studies and trials may not be predictive of future trial results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of an oral KIT inhibitor or any future product candidates.
- Our future clinical trials may reveal significant adverse events not seen in our nonclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of any future product candidates.
- The ongoing COVID-19 pandemic could adversely impact our business, including the conduct of our clinical trials.
- We face competition from entities that have made substantial investments into the rapid development of novel treatments for allergic and inflammatory diseases, including large and specialty pharmaceutical and biotechnology companies developing novel treatments and technology platforms. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize, if approved, product candidates may be adversely affected.
- We rely, and intend to continue to rely, on third parties to conduct our clinical trials and perform all of our research and nonclinical studies. If these third parties do not satisfactorily carry out their contractual duties, fail to comply with applicable regulatory requirements or do not meet expected deadlines, our development programs may be delayed or subject to increased costs or we may be unable to obtain regulatory approval, each of which may have an adverse effect on our business, financial condition, results of operations and prospects.
- If we are not able to obtain, maintain and enforce patent protection for our technologies or product candidates, development and commercialization, if approved, of any future oral KIT inhibitor product candidates may be adversely affected.
- The regulatory approval process is highly uncertain, and we may be unable to obtain, or may be delayed in obtaining, U.S. or foreign regulatory approval and, as a result, unable to commercialize any future oral KIT inhibitor product candidates. Even if we believe our development plans are successful, regulatory authorities may not agree that they provide adequate data on safety or efficacy.

PART I

Item 1. Business.

Overview

We are a biopharmaceutical company focused on the development of the next wave of medicine for the treatment of inflammatory diseases, including dermal, respiratory, and gastrointestinal diseases. We are developing next-generation, highly selective, oral small-molecule inhibitors of KIT, a cell surface receptor that serves as the master regulator of mast cell function and survival. Early clinical studies have demonstrated that KIT inhibition has the potential to address the treatment of a broad range of mast-cell-mediated inflammatory diseases, and that a titratable, oral, intracellular small molecule inhibitor may provide an optimal therapeutic profile against this target. Our initial focus is on developing a KIT inhibitor to treat chronic urticaria.

In December 2022, we announced the discontinuation of our Phase 1b clinical trial of our product candidate THB001 in chronic inducible urticaria following observation of asymptomatic liver transaminitis in two patients enrolled in the first dose cohort. We initiated nonclinical studies to elucidate the mechanism for the observed transaminitis, which was not predicted by extensive toxicology studies including those conducted according to Good Laboratory Practices, or GLP, of THB001 nor observed in our Phase 1a clinical trial. In parallel with the early clinical development of THB001, we have conducted an extensive medicinal chemistry effort to identify chemically distinct next-generation oral wild-type KIT inhibitors and have advanced multiple candidate molecules into exploratory toxicology studies. We intend to nominate a development candidate from this program in 2023.

The Phase 1b clinical trial in chronic inducible urticaria was designed to evaluate the safety and tolerability, efficacy and pharmacokinetics of three dose levels of THB001 over 12 weeks of treatment. Five patients were enrolled in the first dose cohort of 200mg twice daily, or BID. The first subject completed the full 12-week dosing period with no signs or symptoms of liver toxicity. The second and third patients presented with elevations in alanine transaminase or ALT, and aspartate transaminase, or AST, at their week eight study visits, and dosing was halted for both patients. No alternate causes for the transaminitis have been identified, and the patients continue to be monitored per study protocol. We stopped dosing of the fourth and fifth patients enrolled at weeks four and two of dosing, respectively, and neither of these patients has shown any signs or symptoms of liver toxicity to-date. Clinical follow-up of the five enrolled patients will continue per protocol, but no additional patients will be enrolled in the trial.

Preliminary analyses showed evidence of pharmacodynamic and clinical activity at the 200mg BID dose. We plan to present the full data set from the five enrolled patients at an upcoming scientific conference, and we intend to provide an update on overall corporate strategy and outlook in early 2023.

Given the preliminary clinical activity observed in the first patients enrolled in the Phase 1b clinical trial, we plan to continue the development of a next generation oral wild-type KIT inhibitor as we believe this to be an important treatment modality for mast cell-driven inflammatory diseases.

Our Strategy

Our goal is to develop the next wave of medicine for the treatment of inflammatory diseases. The key components of our strategy are to:

- **Develop next-generation KIT inhibitors in a broad range of indications across therapeutic areas where mast cell driven inflammation can benefit from a highly selective, oral small molecule, including in the skin, respiratory and gastrointestinal tracts.** We believe that KIT inhibition may find wide therapeutic utility across a range of inflammatory indications, as mast cells are present in numerous tissue types. There are multiple skin, respiratory and gastrointestinal conditions such as atopic dermatitis, prurigo nodularis, chronic rhinusitis, allergic conjunctivitis, eosinophilic esophagitis and irritable bowel syndrome, where we believe mast cells maintain a vital role in driving the pathophysiology of the disease. We believe these potential opportunities represent attractive markets with clinical unmet need and established development and regulatory pathways.
- **Continue to innovate and potentially expand the pipeline through our internal discovery efforts and selectively evaluate strategic collaborations.** Our team brings invaluable experience from all aspects of drug discovery, clinical development, business development and commercialization. We will continue to invest in research and development and evaluate potential selective collaboration opportunities to build upon our deep knowledge base of oral small molecule KIT inhibition to potentially advance next-generation compounds and expand our pipeline in inflammatory diseases.

We are focused on developing a portfolio of highly selective, oral small molecule inhibitors of KIT, a cell surface receptor that acts as the master survival and functional regulator of mast cells. Mast cells are a part of the immune system, and dysfunctional mast cell activity has been implicated in the pathophysiology of a broad range of inflammatory disorders including urticaria, asthma and gastrointestinal disorders, among others. KIT inhibition has shown positive clinical responses in mast cell mediated diseases such as asthma and chronic urticaria.

Mast cells are a primary driver of allergic inflammatory responses. They are present throughout the body in connective and vascularized tissues, most prominently along surface boundaries with exposure to the external environment: in the skin, the respiratory tract and the gastrointestinal tract. For many patients suffering from allergic conditions, inhibition of mast cell derived mediators, including histamines, leukotrienes and prostaglandins, has demonstrated limited therapeutic value to-date given that many mast cell-driven disorders involve multiple pro-inflammatory mediators. As a result, we believe that targeting mast cells directly through highly selective inhibition of KIT is key to achieving the clinical efficacy needed for broad symptomatic relief across a range of inflammatory disorders.

Since KIT is a cell surface receptor that acts as the master regulator of mast cell function and survival, our approach impacts mast cells directly and provides what we believe to be a favorable point of intervention. Furthermore, significant clinical and nonclinical data has been generated internally and by third parties that demonstrate that KIT is a potential target for broad and potentially clinically differentiated inhibition of mast cells. For example, an anti-KIT antibody demonstrated positive clinical responses in chronic inducible urticaria patients in a third-party Phase 1 trial. In nonclinical studies, THB001 demonstrated what we believe to be evidence of highly selective KIT inhibition and mast cell depletion in skin, respiratory and gastrointestinal tissues with a potent therapeutic profile. We believe that chronic urticaria represents an attractive initial clinical indication for an oral KIT inhibitor. Our goal is to be a leader in the oral KIT inhibitor space, and we continue to invest in formulation and discovery for next generation molecules.

There remains a large unmet need in chronic urticaria. Epidemiological studies indicate that up to 25% of the population suffers from urticaria at some point in their lifetime, with 0.5-1% of the population suffering from the disease at any point in time, suggesting a point prevalence of over 1.5 million patients in the United States. Approximately 70% to 80% of patients with urticaria are women. Many patients are first provided H1 antihistamine therapy when diagnosed with urticaria; however, there remains a large unmet need. Approximately 50% of chronic spontaneous urticaria patients continue to experience itch and hives despite H1 antihistamine treatment at FDA-approved doses. There have been no new approved therapies to treat chronic urticaria in eight years, and the most recently approved treatment, the injectable biologic Xolair, provided complete hive and itch symptom relief to approximately 36% of patients in clinical trials. We believe Xolair is currently addressing less than 20% of eligible patients whose symptoms have failed to be controlled by H1 antihistamine therapy. There is a clear unmet need for chronic urticaria treatments that provide higher levels of complete hive and itch symptom relief, while also providing improved patient comfort and convenience via an oral route of administration. We believe an oral therapy offers clear advantages over an injectable therapy, and an oral therapy with the potential to improve upon the results of the existing standard of care offers a significant opportunity to address a large unmet need. While the potential market opportunity within urticaria alone is vast, dysfunctional mast cell activity has also been implicated in the pathophysiology of a broad range of inflammatory disorders, including respiratory and gastrointestinal disorders. Furthermore, in nonclinical studies, THB001 has demonstrated the ability to deplete mast cells across different tissue types, which we believe supports the ability for an oral small molecule KIT inhibitor to potentially treat a range of mast cell mediated skin, respiratory and gastrointestinal conditions.

Our Team

Founded in 2019, we are led by a strong management team with diverse backgrounds and significant experience in drug discovery, development and company building, as well as a demonstrated track record of delivering breakthrough therapeutic approaches for patients. Our management team are industry veterans with extensive experience at biopharmaceutical companies such as Audentes Therapeutics, Inc., Cadent Therapeutics, Genentech/Roche, Gilead Sciences, Inc., Morphic Holding, Inc. and Pfizer Inc. Together, our team has a proven track record in the discovery, development and commercialization of numerous approved therapeutics.

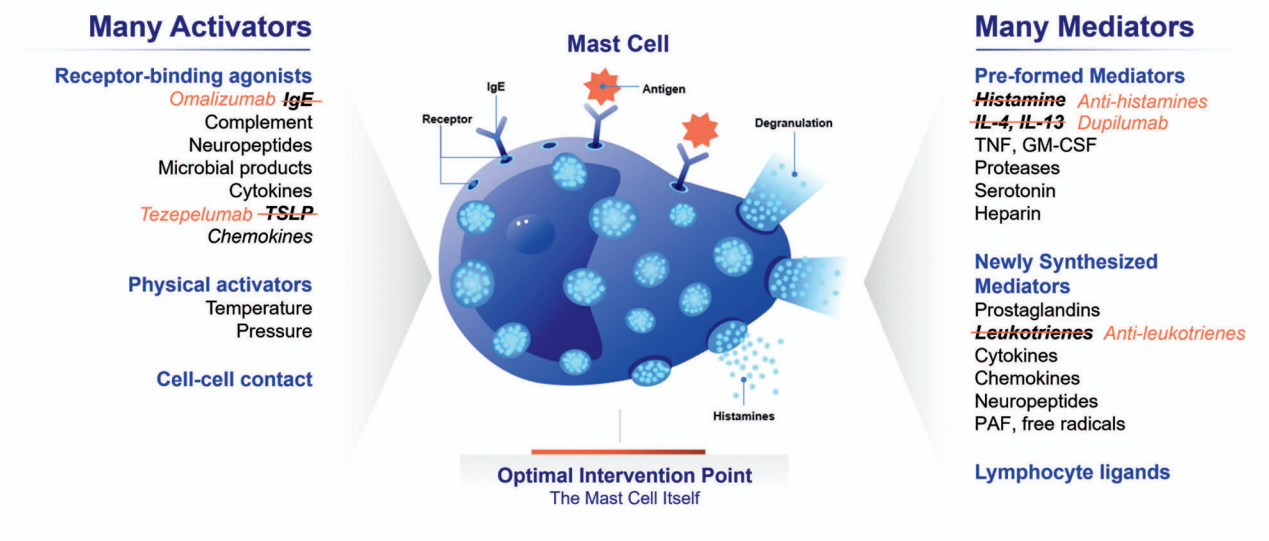
Overview of Mast Cells and KIT

Mast Cells and Their Role in Immunity

Mast cells derive from KIT-positive hematopoietic progenitors in the bone marrow and are present throughout the body in connective and vascularized tissues, most prominently along surface boundaries with exposure to the external environment such as the skin, the respiratory tract and the gastrointestinal tract. Their numerous physiological functions include regulation of inflammation, vasodilation, vascular homeostasis and angiogenesis as well as involvement in the control of other elements of the immune response. Dysfunctional mast cell activity has been implicated in the pathophysiology of a broad range of mast cell driven inflammatory disorders, including urticaria, asthma and gastrointestinal disorders, among others.

The cytoplasm of mast cells stores inflammatory mediators including histamine, the proteolytic enzyme tryptase, and various cytokines including interleukins IL-4, IL-5 and IL-13, and Tumor Necrosis Factor-α, or TNF-α. Mast cells express multiple cell-surface receptors, one of which is FcεR that has particularly high affinity for immunoglobin E, or IgE, antibodies. As shown in the figure below, upon the stimulation of IgE, change of temperature, or pressure, a signaling cascade leads to activation of the mast cell and its degranulation resulting in the release of tryptase, histamine and other inflammatory mediators. In addition to IgE dependent activation, other IgE independent stimuli can also trigger mast cell activation. The release of inflammatory mediators can manifest into a broad range of allergic or inflammatory diseases. Moreover, mast cell activation and degranulation lead to the recruitment of other progenitor cells to the specific tissue site and the propagation of the inflammatory response.

Mast cells mediate multiple pro-inflammatory activities



In the skin, antigens activate mast cells in the deep layers of connective tissue triggering the release of histamine and other vasoactive molecules, and causing allergic reactions, including urticaria. In chronic urticaria, patients will develop wheals, together with the sensations of pain and itch. If antigens activate mast cells deeper in the tissue this can lead to angioedema. Another chronic skin disorder involving mast cells is atopic dermatitis, or eczema.

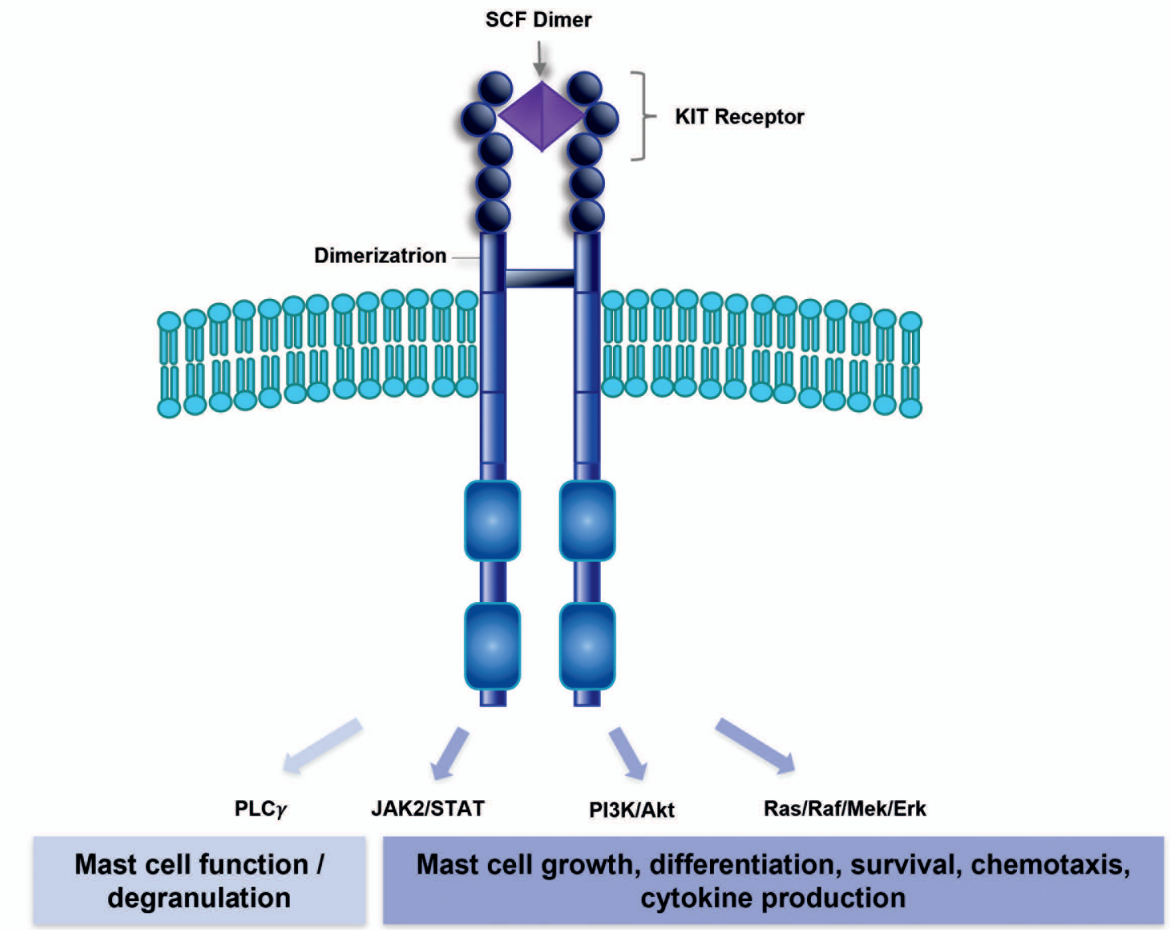
In the respiratory tract, mucosal mast cells in the nasal epithelium are activated by inhaled antigens, eliciting an immune response and resulting in airway constriction, increased mucous production and cough. Mast cells also play a role in the pathophysiology of asthma which is caused by an inflammatory response in the airways due to inhaled antigens that get into the lower respiratory tract and cause mast cell degranulation and local inflammation. This leads to symptoms characteristic of asthma including increased vascular permeability, fluid accumulation, edema, bronchial constriction and obstruction of airways.

In the gastrointestinal tract, dietary proteins can act as antigens and activate the immune system in affected individuals. Antigens permeate the epithelial layer of the mucosa of the gut and bind to IgE antibodies on mucosal mast cells. Elevated numbers of activated mast cells have been observed in allergic eosinophilic gastrointestinal disorders, including eosinophilic esophagitis, gastritis and duodenitis. Mast cells are also involved in the pathophysiology of irritable bowel syndrome and, inflammatory bowel disease, including driving symptomology via their close interaction with nerves.

KIT Signaling in Mast Cells is a Central Node for Therapeutic Intervention

The receptor tyrosine kinase KIT, also known as CD117, is recognized as a master regulator of mast cell activity. Under normal physiological conditions, mast cell progenitors circulate in an immature form and only fully develop into mature mast cells upon migration to a specific tissue type. Mature mast cells remain localized to a designated destination. The figure below shows the KIT structure on the mast cell membrane. As shown below, stem cell factor, or SCF, which is also referred as the c-kit ligand, binds to KIT on the surface of the mast cell, enables signal transduction into the mast cell and activates the KIT-mediated signaling cascade critical to mast cell survival, propagation and differentiation via pathways such as PLCγ, JAK2/STAT, PI3K/AKT and RAS/RAF/MEK/ERK.

KIT (CD117) is the master regulator of mast cell function and survival



As the master regulator of mast cell function and survival, we believe that the KIT-SCF signaling axis is the optimal intervention point to treat many mast cell mediated diseases. Inhibition of KIT drives both mast cell inactivation and depletion, independent of mast cell activation status.

Consistent with our nonclinical findings, significant clinical and nonclinical data that have been generated by us and by third-party organizations support KIT as an attractive therapeutic target for mast cell regulation. The multi-tyrosine kinase inhibitor imatinib, which is sold under the brand name Gleevec, has been approved by the FDA to treat chronic myelogenous leukemia, acute lymphoblastic leukemia and myelodysplastic syndrome, among other indications. In clinical results by a third party published in *The New England Journal of Medicine*, daily imatinib, which has demonstrated KIT inhibitory activity, achieved a 43% reduction in plasma levels of serum tryptase, a biomarker used to assess mast cell activation, for patients with severe refractory asthma, which resulted in statistically significant improvement in airway hyperresponsiveness at 24 weeks. We believe these results provide compelling clinical proof-of-concept that mast cell reduction may drive meaningful symptomatic relief. Furthermore, a third party reported that an anti-KIT antibody demonstrated compelling clinical responses in patients with chronic inducible urticaria in a Phase 1 clinical trial conducted by a third party.

Therapeutic Modulation of the Allergic Response

There are several approved therapeutics used to treat allergy and related inflammatory conditions by targeting specific mediators released by mast cells upon degranulation, including histamines, leukotrienes, cytokines, such as IL-4, IL-5, IL-13, and TNF-α. However, we believe targeting the mast cell directly provides a broader approach to addressing mast cell mediated diseases over only targeting an individual mediator. Due to the involvement of multiple pro-inflammatory mediators, mast cell mediator inhibitors often require use in combination with another treatment modality. As a result, single agent inhibition of individual mast cell mediators, such as the H1 antihistamine, do not provide adequate symptomatic relief to a large proportion of the patient population.

Under current standard of care, patients whose disease does not respond to mediator inhibition, are often candidates for anti-IgE monoclonal antibodies, or mAbs, designed to inhibit IgE-driven mast cell activation. While IgE blockade has demonstrated some clinical benefit in the treatment of a range of mast cell mediated inflammatory disorders, anti-IgE therapy does not fully remedy symptoms for most patients, potentially in part because it does not address IgE-independent pathways of mast cell activation. Omalizumab, the anti-IgE mAb sold under the brand name Xolair, is approved for the treatment of persistent allergic asthma, nasal polyps and chronic spontaneous urticaria. Omalizumab generated an estimated $3.5 billion in 2021 sales worldwide.

Despite current treatment options, there remains a significant unmet need. The targeting of the mast cell directly represents a novel therapeutic approach to address inflammatory diseases. While this approach benefits from clinical validation, advancing the development of therapeutics designed to directly reduce mast cell activity has been thwarted by the potential risk of off-target adverse effects.

Overview of Urticaria

Urticaria, which is also referred to as “hives”, is a common inflammatory disorder that has a lifetime prevalence of up to 25% with females twice as likely to experience the condition as men. Onset peaks between the ages of 20 and 40 years old. It is not a single disease but a reaction pattern that represents cutaneous mast cell degranulation. Mast cell degranulation and the release of vasoactive mediators, primarily histamine, results in extravasation of plasma into the dermis, forming the characteristic hives and edematous pruritic pink wheals of various shape and size.

While the majority of urticaria cases involve acute episodes which are self-limiting and of a short duration, patients with chronic urticaria experience constant or frequently recurring lesions for six or more weeks regularly over months if not years. Chronic urticaria has a negative impact on patients’ quality of life, particularly as the occurrence of angioedema often leads to significant discomfort. Patients have reported an impact on facets of everyday life that include lack of quality sleep, recreation and social interaction, mobility, rest and work. As such, patients with chronic urticaria frequently exhibit psychiatric comorbidities such as anxiety and depression. At any time, 0.5-1% of the population suffers from chronic urticaria, suggesting a point prevalence of over 1.5 million patients in the United States. Approximately 70% to 80% of patients with urticaria are women. The duration of the disease is generally 1-5 years but is likely to be longer in more severe cases.

Chronic urticaria is comprised of two distinct disease types, inducible urticaria and spontaneous urticaria, which was previously referred to as idiopathic urticaria. Chronic inducible urticaria is caused by exposure to specific triggers, which include excessive cold or heat, the application of pressure and exercise. No underlying cause or underlying disease process has been identified in the majority of patients with chronic spontaneous urticaria. In patients with no identified trigger, the rate of spontaneous remission at 1 year is approximately 20% to 50%, while 30% of moderate to severe patients suffer from chronic urticaria for more than 5 years.

Current Treatments for Chronic Urticaria

Current chronic urticaria treatment guidelines recommend first line treatment with second generation H1 antihistamines to provide hive and itch symptom control. For those patients whose symptoms remain uncontrolled following first line therapy, second line treatment is initiated with either elevated doses (up to fourfold) of second generation H1 antihistamines or the addition of another class of agent including first generation H1 antihistamines. For the approximately 50% of chronic spontaneous urticaria patients who remain uncontrolled following second line therapy, Xolair is approved as third line therapy. In clinical trials, Xolair reported complete response rates of approximately 36% in chronic spontaneous urticaria and is estimated to address less than 20% of eligible patients whose symptoms have failed to be controlled by H1 antihistamine therapy. As such, there remains a large population of patients that have unmet need.

Our Solution: Next Generation KIT Inhibitors

Summary

We are developing next-generation, potentially highly potent and selective, small molecule wild-type KIT inhibitors for the treatment of mast cell-mediated inflammatory diseases. Based on nonclinical and available clinical data to date, we believe an oral small molecule may be differentiated from other KIT-targeting therapeutics in the following designed aspects:

- The small molecule modality is anticipated to provide more refined dose titration capabilities than anti-KIT mAbs.
- Oral administration offers improved patient convenience while avoiding mAb-related injection events.
- Potentially higher selectivity for wild-type KIT relative to other commercial KIT inhibitors such as imatinib.
- Our oral small molecule inhibitors of KIT bind intracellularly to an inactive conformation of KIT, avoiding the risk of paradoxical mast cell activation that can result from a KIT mAb binding to the extracellular portion of the KIT receptor.

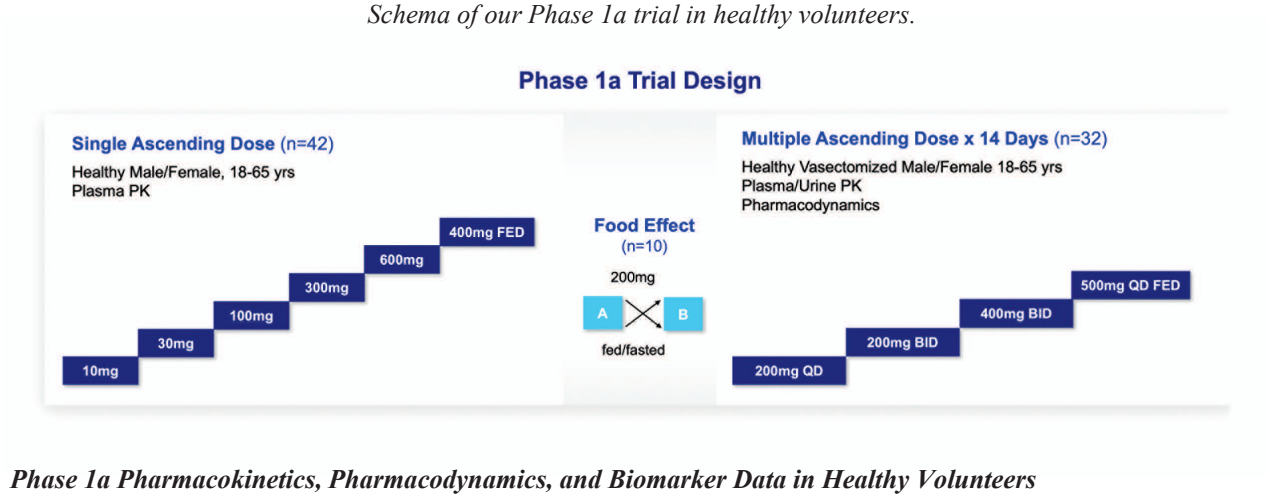
Although we discontinued the Phase 1b clinical trial of THB001 in chronic urticaria, we expect that data generated from the trial, along with data generated from our previously completed Phase 1a clinical trial, will be useful for the development of our next-generation, highly selective, oral KIT inhibitors.

In our Phase 1a clinical trial, THB001 demonstrated dose-dependent reductions of serum tryptase, a key biomarker of mast cell activity which has been shown to correlate with clinical benefit in chronic urticaria patients.

Phase 1a Healthy Volunteer Trial

We conducted a three-part, 84 subject, Phase 1a clinical trial of THB001 in healthy adult volunteers between the ages of 18 and 65. The primary objective is to evaluate safety and tolerability. Secondary objectives include characterizing pharmacokinetics, including in the presence or absence of food to inform further clinical and drug product formulation development and to measure the pharmacodynamic effect by serum tryptase. The first part of this trial was a single-ascending dose, or SAD, involving five cohorts of up to ten participants assigned to receive a single dose of THB001 or placebo in a 3:1 ratio. Doses ranged from 10 mg to 600 mg across the five cohorts. The second part of the trial was designed to evaluate the effect of food on the pharmacokinetics, or PK, profile of 200 mg THB001. A single 200 mg dose was administered to one cohort of ten participants, half of which received THB001 along with a standardized high-fat breakfast, while the other half received THB001 in a fasted state. Following a washout period of at least 7 days, each participant crossed over to receive THB001 in the alternate fed or fasted state. Safety and tolerability of THB001, together with its PK profile was evaluated during this portion of the trial. Upon completion of this second part of the Phase 1a trial, a sixth SAD cohort was added enabling the evaluation of a 400 mg THB001 dose when administered together with food. The third part of the Phase 1a trial was a multiple ascending dose, or MAD, format of four eight-subject cohorts, administered THB001 over 14 consecutive days. The first cohort received 200 mg of THB001 QD, the second cohort received 200 mg of THB001 BID, the third cohort received 400 mg THB001 BID, and the fourth cohort received 500 mg QD administered with a standardized non-high fat breakfast to further characterize the effect of food on the PK of THB001. A schema of our Phase 1a trial is presented below.

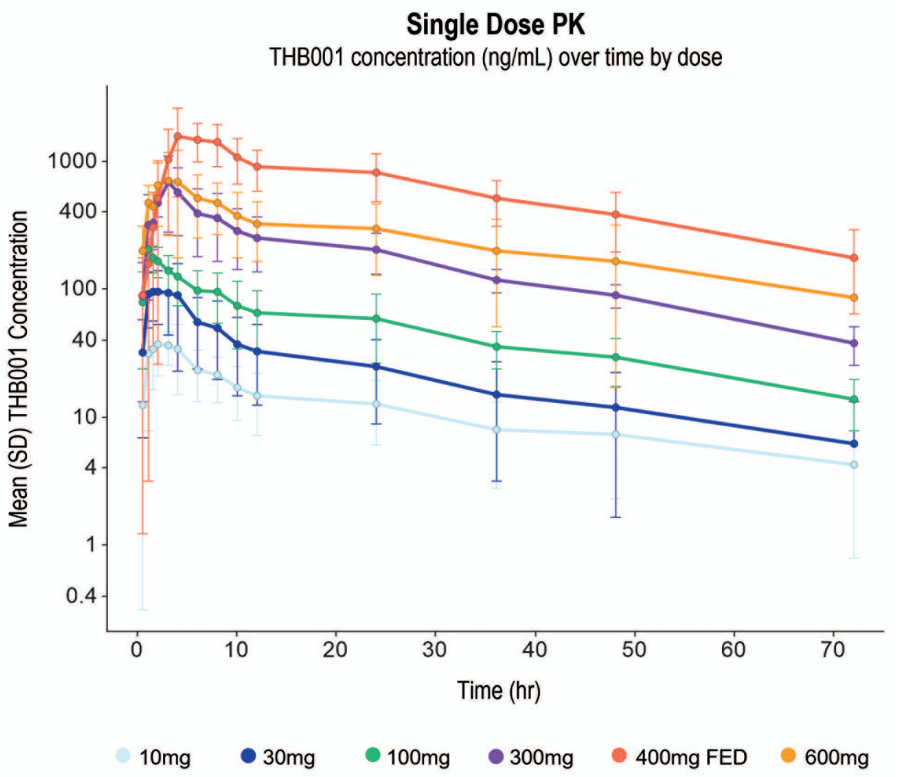
Schema of our Phase 1a trial in healthy volunteers.



Phase 1a Pharmacokinetics, Pharmacodynamics, and Biomarker Data in Healthy Volunteers

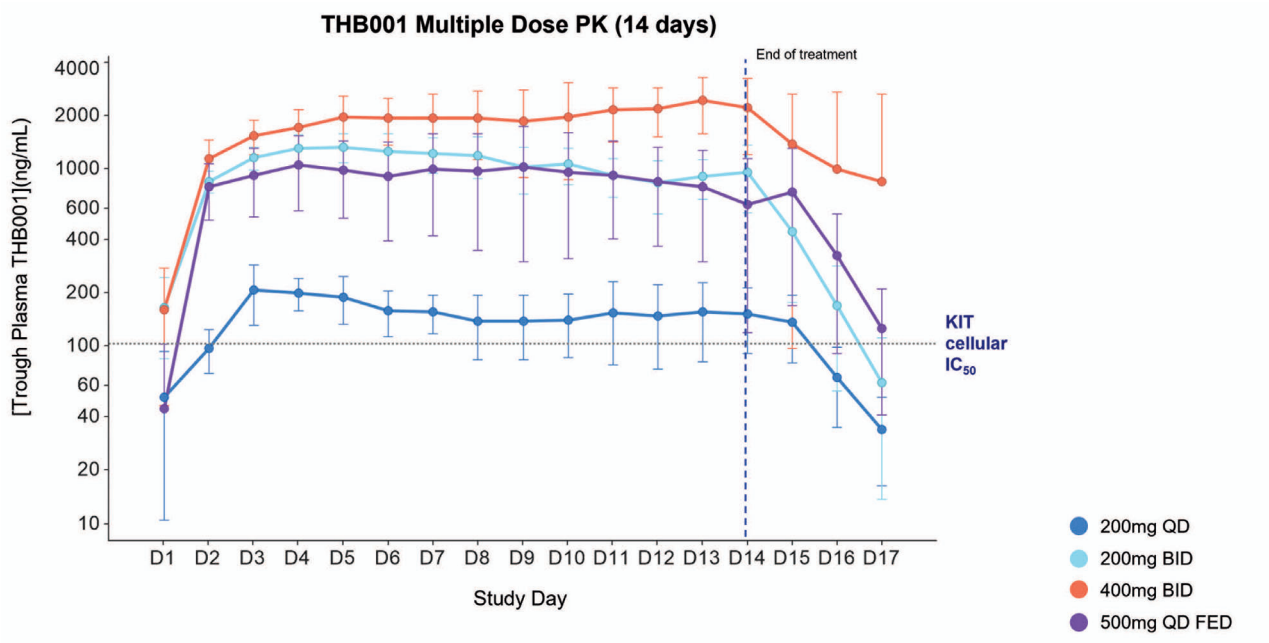
In the SAD portion of the Phase 1a trial, we observed approximately dose proportional increases in serum concentration of THB001 between the 10 mg and 300 mg doses. As reflected in the chart below at 300 mg and higher dosing levels, THB001 concentration exceeded 100 ng/ml through 24 hours, which is the level needed to achieve a KIT half-maximal inhibitory concentration, or IC_{50}, between daily doses. This is consistent with the observed mean half-life of THB001 of approximately 24 hours. Administration of THB001 in combination with food was also noted to enhance exposure approximately three-fold.

SAD pharmacokinetics in doses up to 600 mg



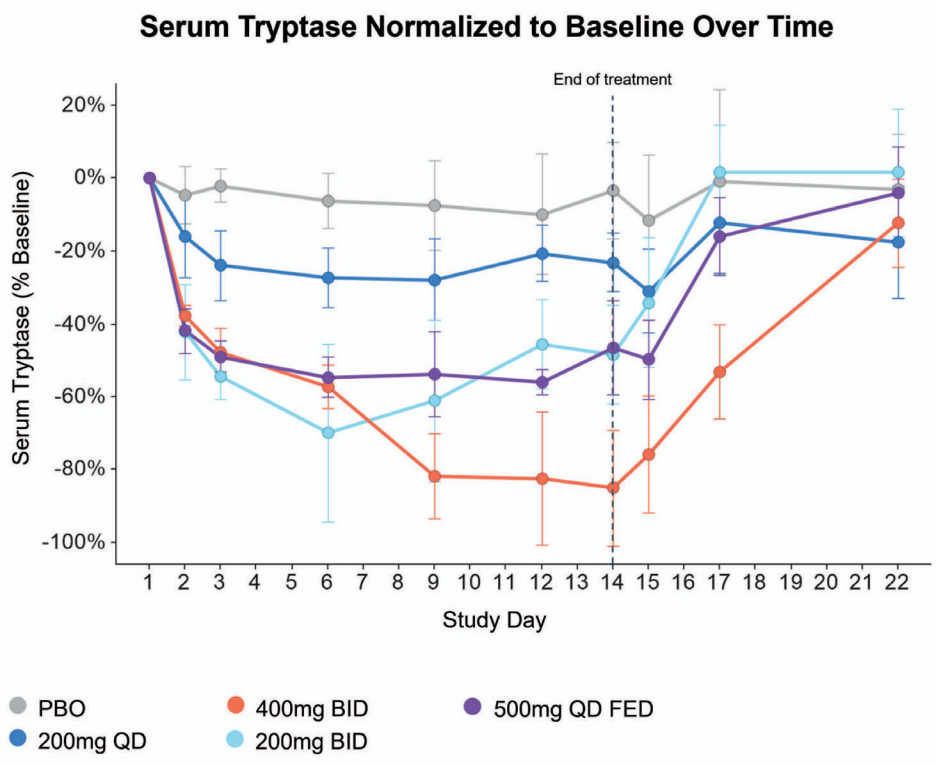
In the MAD portion of the trial, the increase in THB001 dosage from 200 mg BID to 400 mg BID was observed to generate approximately dose proportional increases in THB001 serum concentration levels which provided a trough value difference between THB001 and the protein binding adjusted KIT IC_{50} of approximately 20-fold, which provides evidence of attractive therapeutic exposure. Administration of 500 mg QD with a standardized non-high fat breakfast produced a PK profile that was similar to the 200 mg BID dose administered in the fasted state, confirming the positive effect of food on THB001 exposure.

200/400 mg BID and 500 mg QD dosing of THB001 generated through serum concentrations which exceeded the IC_{50}



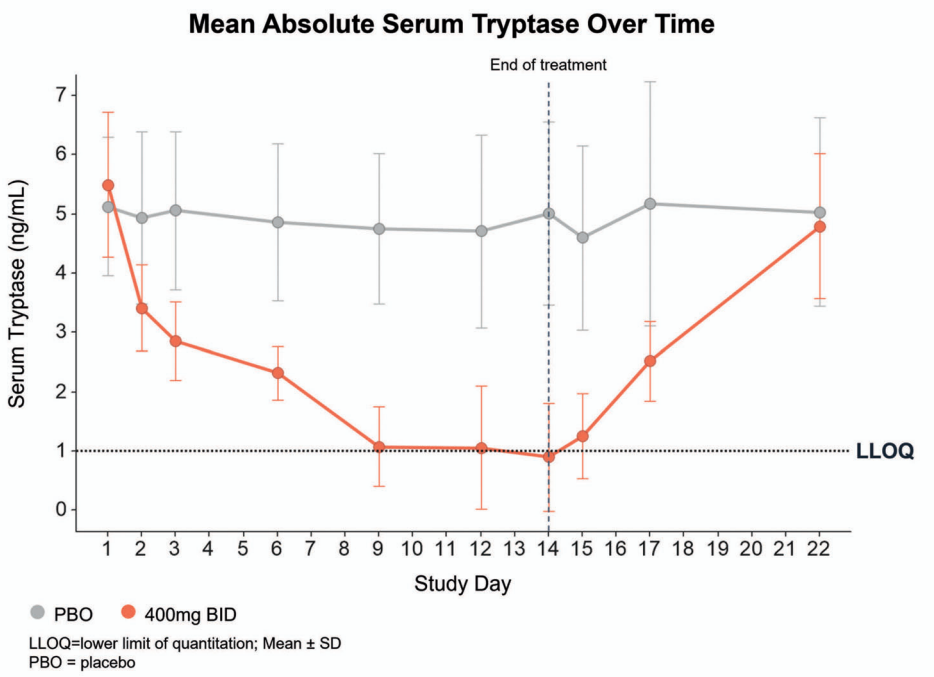
Dose levels of 200 mg per day or greater, given QD or BID, were observed to result in dose dependent declines in serum tryptase concentrations, a key biomarker of mast cell activity which has been demonstrated to correlate with clinical benefit in chronic urticaria, as compared to placebo, or PBO, as reflected in the graph below.

Twice-daily administration of THB001 resulted in a dose-dependent decrease in serum tryptase levels.



As reflected in the chart presented below, which shows absolute serum tryptase levels in patients over time, twice daily dosing of the higher 400 mg level of THB001 resulted in mean serum tryptase which was at the lower limit of quantification.

The higher 400 mg BID dose resulted in a serum tryptase level at the lower limit of quantitation.



Mast Cell-Mediated Diseases Addressable by KIT Inhibition

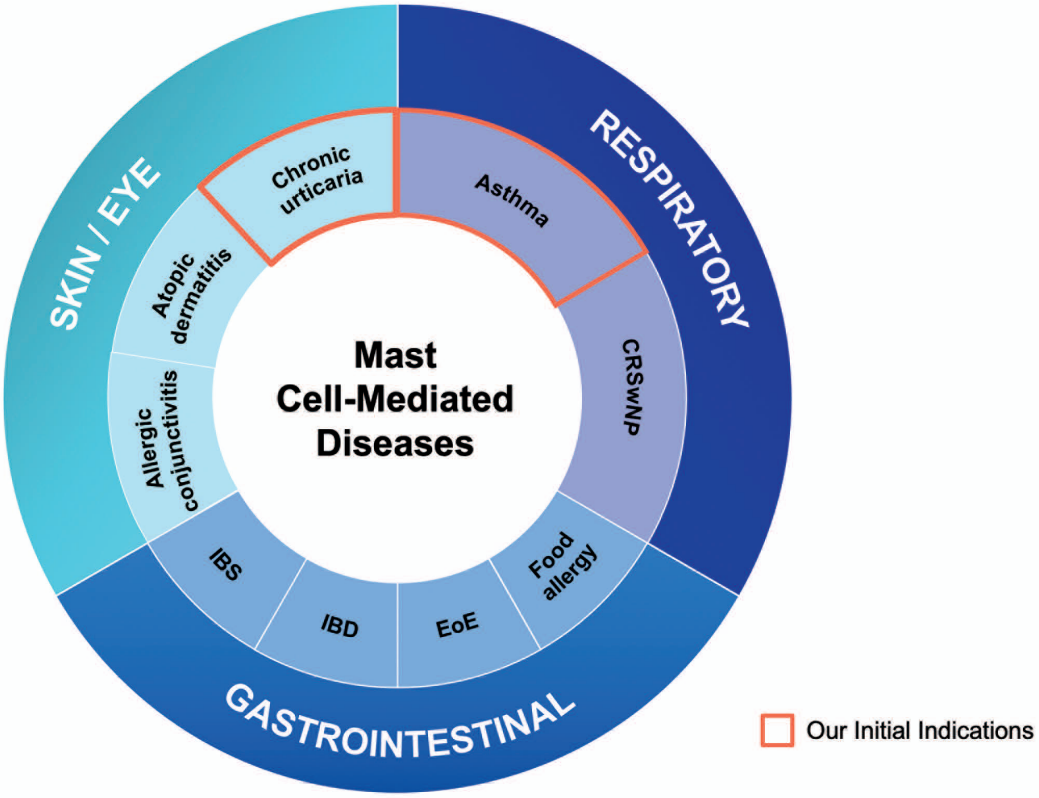
Dysfunctional mast cell activity has been implicated in the pathophysiology of a broad range of inflammatory disorders that impact the skin, eye, respiratory tract and gastrointestinal tract. Given KIT is the master regulator of mast cell function and survival, we believe that KIT inhibition is the optimal approach to treat many of these mast cell mediated diseases.

Related to the skin and eye, potential indications addressable with KIT inhibition include chronic urticaria, systemic sclerosis, atopic dermatitis and allergic conjunctivitis.

In the respiratory tract, potential indications addressable with KIT inhibition include asthma and chronic rhinosinusitis with nasal polyposis, or CRSwNP.

In the gastrointestinal tract, potential indications addressable with KIT inhibition include irritable bowel syndrome, or IBS, inflammatory bowel disease, or IBD, eosinophilic esophagitis and food allergy.

Examples of selected mast cell mediated diseases potentially addressable with KIT inhibition

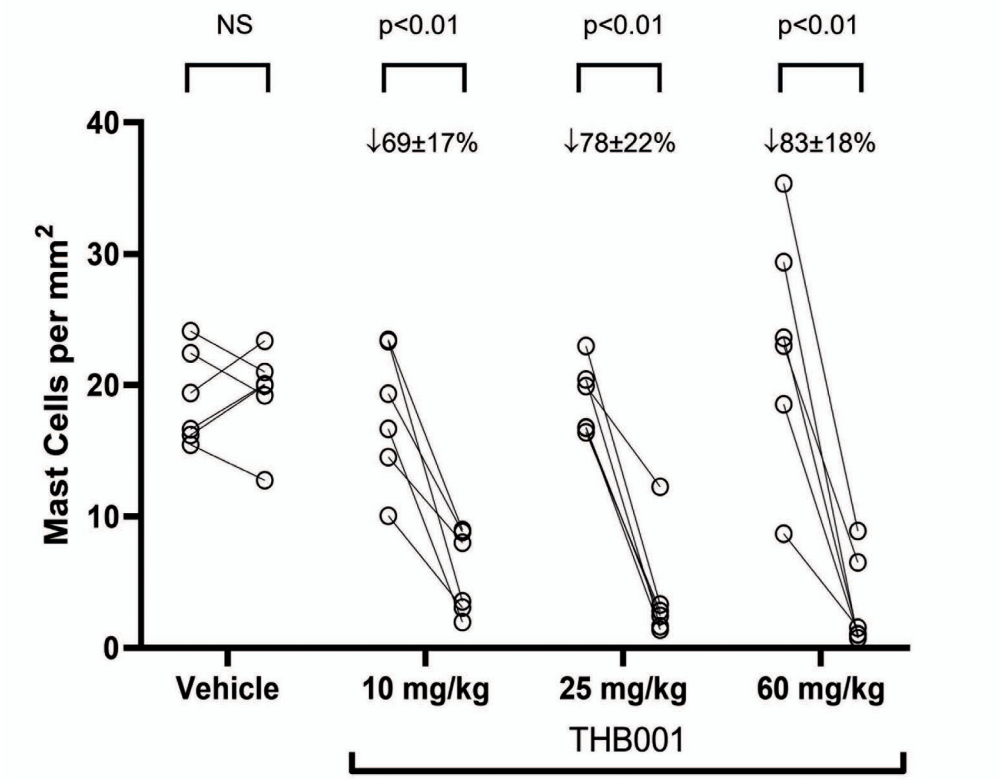


An oral KIT inhibitor's Therapeutic Potential in Other Mast Cell Driven Inflammatory Diseases

Nonclinical studies of THB001 provide evidence of the ability for an oral KIT inhibitor to deplete and inhibit mast cell activity in multiple species and tissue types. Significant therapeutic improvement has also been observed in animal disease models.

In a 14-day repeat dose study of THB001 conducted in dogs, samples were collected from the skin both before and after administration of the drug candidate and evaluated for mast cell counts. As is reflected in the results presented below, we observed a dose-dependent decline in mean skin mast cell count in every treated animal. Statistical significance is important and when used herein is denoted by p-values. The p-value is the probability that the reported result was achieved purely by chance (for example, a p-value < 0.001 means that there is a less than 0.1% chance that the observed change was purely due to chance). Generally, a p-value less than 0.05 is considered to be statistically significant.

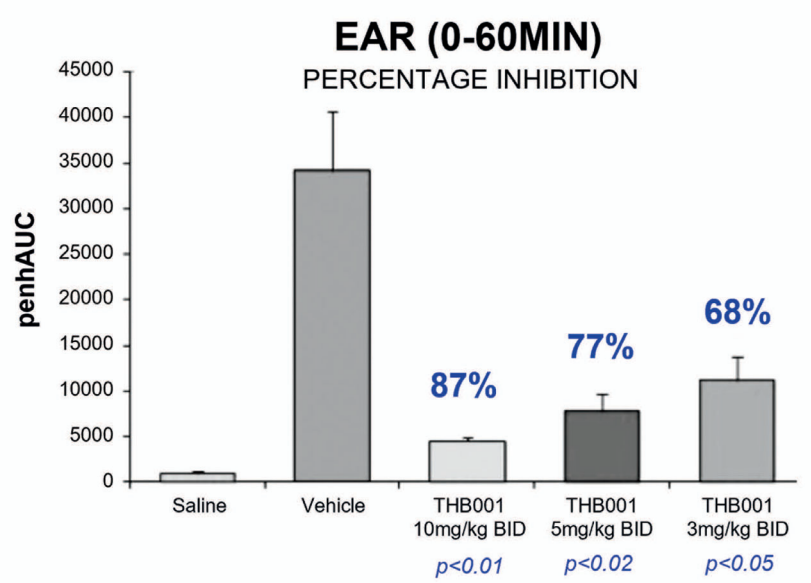
THB001 generated dose-dependent mast cell depletion in a 14-day repeat dose study in dogs.



In a rat model of allergic asthma conducted by Novartis, THB001 also demonstrated robust *in vivo* activity, with improvements in early airway response, or EAR, and reduction in the lung mast cell specific gene signature by approximately 50% or greater. The degranulation of mast cells is the main contributor in the early phase allergic response upon antigen exposure and accordingly, inhibition of mast cell survival and function by prevention of KIT activation is expected to result in the improvement of allergic symptoms.

In this study, animals received OVA antigen to stimulate allergic reaction in the lung with the exception of one cohort receiving saline. The OVA antigen treated animals were administered either a 3 mg/kg, or mpk, 5 mpk or 10 mpk dose of THB001 twice daily for seven days and compared to animals administered vehicle alone. As is reflected in the experimental results presented in the chart below, THB001 produced a dose dependent, statistically significant therapeutic response, with measures of lung function enhanced pause, or Penh, used to assess changes in the shape of airflow pattern entering and leaving the animal, displaying notable improvement with increased KIT inhibition. Moreover, at the lowest level administered to the animals, 3 mg/kg BID, the serum concentration of THB001 exceeded the *in vitro* protein binding adjusted KIT IC_{50} over the dosing period, providing evidence of adequate sustained suppression of KIT-mediated signaling activity.

The use of THB001 produced statistically significant airway improvements in a rat model of allergic asthma.



Gene expression profiles provided further support of THB001's inhibition of mast cell activity. Expression patterns for mast cell associated genes were evaluated after administration of the various dose levels of THB001 relative to expression levels observed after dosing with vehicle. These expression profiles revealed that at approximately one-half the expression levels seen after administration of vehicle, which was achieved at the lower dosing level of 3 mpk, the animals began to benefit from significant airway improvement. These results suggest that modulation to some intermediate inhibitory level that is less than complete inhibition of mast cell activity may provide meaningful clinical benefit. The analysis of the gene expression profiles is outlined in the chart below.

Mast cell-associated gene expression is suppressed in the presence of THB001.

Percentage of Vehicle Response

Treatment	Challenge	Cpa3	Fcε R1α	Mcpt2	Mcpt9
None	Saline	68	80	55	76
Vehicle	OVA	100	100	100	100
3 mg/kg THB001 (BID)	OVA	44	38	46	50
5 mg/kg THB001 (BID)	OVA	41	38	47	54
10 mg/kg THB001 (BID)	OVA	24	21	28	29

Abbreviations: BID=twice daily; Cpa3=carboxypeptidase 3; FceR1a=Fc epsilon receptor 1 alpha chain; Mcpt2=Mast cell tryptase 2; Mcpt9=Mast cell tryptase 9; OVA=ovalbumin.

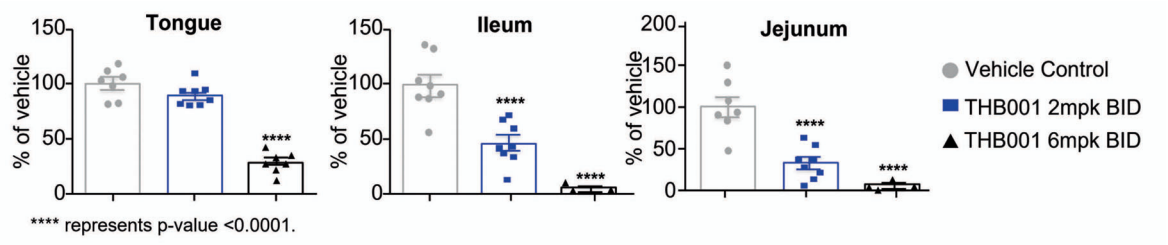
The Therapeutic Benefit of an Oral KIT Inhibitor May Extend to a Range of Tissues

We are exploring development opportunities across a range of other indications where an oral KIT inhibitor may provide benefit to patients suffering from mast cell driven inflammation. We believe that KIT inhibition may provide wide therapeutic utility across other indications as mast cells are present in numerous tissue types with external exposures. In addition to skin, where chronic urticaria represents our initial clinical indication, there are multiple respiratory and gastrointestinal conditions including eosinophilic esophagitis and asthma, where we believe mast cells maintain a vital role in driving the pathophysiology of the disease. We believe these potential additional opportunities represent attractive markets with established development and regulatory pathways, for which there remains a large unmet need.

For example, approximately five to ten percent of asthma patients suffer from severe asthma, or an estimated 750,000 to one million patients in the United States alone.

In a nine-day repeat dose rat pharmacology study, THB001 demonstrated the ability to potently deplete mast cells across all tissues tested. As is noted in the chart below, in tissue taken from the oral cavity (tongue tissue) and the small intestine (ileum and jejunum tissue), there was statistically significant mast cell suppression following administration of THB001.

THB001 demonstrated mass cell depletion across a range of tissue types.



Licenses, Partnerships and Collaborations

License Agreement with Novartis International Pharmaceutical Ltd.

On June 28, 2019, we entered into a license agreement with Novartis International Pharmaceutical Ltd. (which subsequently merged into the company Novartis Pharma AG), or Novartis, as amended, or the Novartis Agreement. Pursuant to the Novartis Agreement, Novartis granted us an exclusive, worldwide, sublicensable (subject to certain requirements therein) license under specified patent rights and know-how related to three licensed compounds to develop, make, use and sell certain products incorporating or comprising a licensed compound, or the Licensed Products. Under the Novartis Agreement, we are solely responsible for all research, development, regulatory and commercialization activities related to the Licensed Products. We are required to use commercially reasonable efforts to develop and seek regulatory approval for, and commercialize, at least one Licensed Product in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan.

Pursuant to the Novartis Agreement, we made a one-time payment of $350,000 to Novartis and agreed to issue shares of preferred stock pursuant to that certain Investment Letter dated as of June 27, 2019, or the Novartis Investment Letter. Pursuant to the Novartis Investment Letter, we have issued Novartis 5,970,000 shares of Series A-1 Preferred Stock (2,642,762 shares of common stock following the conversion of such preferred stock in connection with our initial public offering, or IPO), consisting of shares issued as part of entering into the agreement and shares issued subsequently under the anti-dilution right included within the license agreement. Further, we are obligated to pay Novartis up to an aggregate of (a) $31.7 million upon the achievement of certain specified development milestones for the Licensed Products and (b) $200.0 million upon the achievement of certain specified sales and commercialization milestones with respect to the Licensed Products. We are also required to pay Novartis, on a Licensed Product-by-Licensed Product and country-by-country basis, tiered royalties in the single-digit percentage range on annual net sales of Licensed Products, subject to reduction and offset upon certain specified events. The foregoing royalty payment obligations will expire on the latest to occur of: (i) expiration of the last valid claim of the licensed patent rights that covers such Licensed Product in such country; (ii) the expiration of any regulatory exclusivity for such Licensed Product in such country; and (iii) ten years following the first commercial sale of such Licensed Product in such country. Upon the expiration of such royalty term in a particular country for a particular Licensed Product, the license granted to us with respect to such Licensed Product in such country will become fully paid-up, royalty-free, transferable, perpetual and irrevocable.

The Novartis Agreement will expire (a) on a Licensed Product-by-Licensed Product and country-by-country basis, upon expiration of the royalty term for such Licensed Product in such country and (b) in its entirety upon the expiration of the royalty term with respect to the last Licensed Product being developed, manufactured or commercialized worldwide. Each party may terminate the Novartis Agreement for uncured material breach by the other party or in the case of the other party's insolvency. Additionally, we have the right to terminate the Novartis Agreement for convenience upon 90 days' prior written notice to Novartis. Upon termination of the Novartis Agreement by us for convenience or by Novartis for our uncured material breach or insolvency, the license granted to us by Novartis will terminate and we will be obligated to, (i) grant to Novartis an exclusive, worldwide, reversion license under certain patent rights and know-how with respect to the terminated Licensed Products, (ii) transfer to Novartis certain know-how and regulatory documentation with respect to the terminated Licensed Products and (iii) to the extent applicable, use commercially reasonable efforts to transfer agreements between us and third parties that are solely related to the terminated licensed compounds and Licensed Products.

Manufacturing

We oversee and manage third-party Contract Development and Manufacturing Organizations, or CDMOs, for development and manufacture of future development candidates.

We used two geographically-distributed CDMOs to supply THB001 GMP drug substance. The manufacturing process is robust with readily-sourced commercially available raw materials and straightforward scalability. The drug substance demonstrates excellent room temperature stability, and all batch releases have met all phase-appropriate specifications.

We used three geographically-distributed CDMOs for THB001 drug product manufacturing. The THB001 drug product is a cost-effective and readily scaled solid oral dosage form in standard gelatin capsules. More than 100,000 capsules have been produced to date, which meet all release specifications. Excellent room temperature stability has been established for the THB001 drug product.

As of January 2023, we paused all manufacturing activities on THB001. For our future development candidates, we plan to continue operations with these existing manufacturing CDMOs to support toxicology and clinical studies. Additional manufacturing CDMOs may be on-boarded at later stages of clinical and commercial development.

Competition

We face substantial competition from multiple sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions and governmental agencies and public and private research institutions. Our competitors compete with us on the level of the technologies employed, or on the level of development of product candidates. In addition, many small biotechnology companies have formed collaborations with large, established companies to (i) obtain support for their research, development and commercialization of products or (ii) combine several treatment approaches to develop longer lasting or more efficacious treatments that may potentially directly compete with our future product candidates. We anticipate that we will continue to face increasing competition as new therapies and combinations thereof, technologies, and data emerge within the field of immunology and, furthermore, within the treatment of allergic and inflammatory conditions.

In addition to the current standard of care treatments for patients with mast cell driven inflammatory diseases, numerous commercial and academic nonclinical studies and clinical trials are being undertaken by a large number of parties to assess novel technologies and product candidates. There are numerous other competitive approaches, including inhibitors of activators of mast cells such as IgE antibodies like omalizumab, inhibitors of mediators such as anti-histamines and anti-IL-4 /IL-13 therapies, other small molecule approaches such as Bruton's tyrosine kinase inhibitors, and other small molecule and biologic KIT inhibitors, including Celldex's CDX-0159, a monoclonal antibody KIT inhibitor, among others.

Many of our competitors, either alone or in combination with their respective strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, the regulatory approval process, and marketing than we do. Mergers and acquisition activity in the pharmaceutical, biopharmaceutical and biotechnology sector is likely to result in greater resource concentration among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through sizeable collaborative arrangements with established companies. These competitors also compete with us in recruiting and retain qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if one or more of our competitors develop and commercialize products that are safer, more effective, better tolerated, or of greater convenience or economic benefit than our proposed product offering. Our competitors also may be in a position to obtain FDA or other regulatory approval for their products more rapidly, resulting in a stronger or dominant market position before we are able to enter the market. The key competitive factors affecting the success of all of our programs are likely to be product safety, efficacy, convenience and treatment cost.

Intellectual Property

Intellectual property is of vital importance in our field and in biotechnology generally. We seek to protect and enhance proprietary technology, inventions and improvements that are commercially important to the development of our business by seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. We will also seek to rely on regulatory protection afforded through inclusion in expedited development and review, data exclusivity, market exclusivity and patent term extensions where available.

As with other biotechnology and pharmaceutical companies, our commercial success will depend in part on obtaining and maintaining patent protection of our current and future product candidates and the methods used to develop and manufacture them, as well as successfully defending any such patents against third-party challenges and operating without infringing on the proprietary rights of others. Our ability to stop third parties from making, using, selling, offering to sell or importing our product candidates will depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. 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 patents that may be granted to us in the future will be commercially useful in protecting our product candidates, discovery programs and processes. For this and more comprehensive risks related to our intellectual property, see the section titled "Risk Factors—Risks Related to Our Intellectual Property."

The terms of individual patents depend upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, including the United States, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. In the United States, the term of a patent that covers an FDA-approved drug may also be eligible for extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the subject drug candidate is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to an approved drug may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions to extend the term of a patent that covers an approved drug are available in Europe and other foreign jurisdictions. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We plan to seek patent term extensions to any issued patents we may obtain in any jurisdiction where such patent term extensions are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment that such extensions should be granted, and if granted, the length of such extensions. For more information regarding the risks related to our intellectual property, see the section titled "Risk Factors—Risks Related to Our Intellectual Property."

In some instances, we have submitted and expect to submit patent applications directly to the USPTO as provisional patent applications. Corresponding non-provisional patent applications must be filed not later than 12 months after the provisional application filing date. While we intend to timely file non-provisional patent applications relating to our provisional patent applications, we cannot predict whether any such patent applications will result in the issuance of patents that provide us with any competitive advantage.

We file U.S. non-provisional applications and Patent Cooperation Treaty, or PCT, applications that claim the benefit of the priority date of earlier filed provisional applications, when applicable. The PCT system allows a single application to be filed within 12 months of the original priority date of the patent application, and to designate all of the PCT member states in which national patent applications can later be pursued based on the international patent application filed under the PCT. The PCT searching authority performs a patentability search and issues a non-binding patentability opinion which can be used to evaluate the chances of success for the national applications in foreign countries prior to having to incur the filing fees. Although a PCT application does not issue as a patent, it allows the applicant to seek protection in any of the member states through national-phase applications. At the end of the period of two and a half years from the first priority date of the patent application, separate patent applications can be pursued in any of the PCT member states either by direct national filing or, in some cases by filing through a regional patent organization, such as the European Patent Office. The PCT system delays expenses, allows a limited evaluation of the chances of success for national/regional patent applications and enables substantial savings where applications are abandoned within the first two and a half years of filing.

For all patent applications, we determine claiming strategy on a case-by-case basis. Advice of counsel and our business model and needs are always considered. We seek to file patents containing claims for protection of useful applications of our proprietary technologies and any products, as well as all new applications and/or uses we discover for existing technologies and products, assuming these are strategically valuable. We continuously reassess the number and type of patent applications, as well as the pending and issued patent claims to pursue maximum coverage and value for our processes, and compositions, given existing patent office rules and regulations. Further, claims may be modified during patent prosecution to meet our intellectual property and business needs.

The ability to obtain patent protection and the degree of such protection depends on a number of factors, including the extent of the prior art, the novelty and non-obviousness of the invention, and the ability to satisfy the enablement requirement of the patent laws. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted or further altered even after patent issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our future oral KIT inhibitor product candidates or for our technology platform. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

In addition to patent protection, we also rely on trademark registration, trade secrets, know how, other proprietary information and continuing technological innovation to develop and maintain our competitive position. We seek to protect and maintain the confidentiality of proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Our agreements with employees also provide that all inventions conceived by the employee in the course of employment with us or from the employee's use of our confidential information are our exclusive property. However, such confidentiality agreements and invention assignment agreements can be breached and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting trade secrets, know-how and inventions. For more information regarding the risks related to our intellectual property, see the section titled "Risk Factors—Risks Related to Intellectual Property."

The patent positions of biotechnology companies like ours are generally uncertain and involve complex legal, scientific and factual questions. Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. Third-party patents could require us to alter our development or commercial strategies, or our products or processes, obtain licenses or cease certain activities. Our breach of any license agreements or our failure to obtain a license to proprietary rights required to develop or commercialize our future products may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference or derivation proceedings in the USPTO to determine priority of invention. For more information, see the section titled "Risk Factors—Risks Related to Intellectual Property."

When available to expand market exclusivity, our strategy is to obtain, or license additional intellectual property related to current or contemplated development platforms, core elements of technology and/or clinical candidates.

As of February 9, 2023, our overall patent portfolio contains eleven patent families that collectively contain issued patents, pending provisional and non-provisional U.S. patent applications, PCT international patent applications, and pending patent applications in foreign jurisdictions. The patents and patent applications have claims relating to our prior product candidate THB001, pharmaceutical compositions, methods of use, as well as claims directed to other KIT inhibitor compounds.

THB001

As of February 9, 2023, we exclusively license from Novartis a first patent family to THB001 containing patents and patent applications directed to compositions of matter and methods of use. This first patent family contains one patent in the United States, 67 patents, collectively, in Europe, Japan, Australia, Canada, China, Mexico and other foreign countries, as well as over six patent applications pending, collectively, in India, Thailand and other foreign countries. These U.S. and foreign patents, and any further foreign patents that may issue from these pending foreign patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in 2032, not including any patent term adjustment, patent term extension, or SPC.

As of February 9, 2023, we exclusively license from Novartis one patent family and solely own another patent family, each directed to certain physical forms of THB001 and having patent applications to compositions of matter and methods of use. The patent family that we exclusively license to certain physical forms of THB001 contains 17 patent applications, collectively, in the United States, Europe, Japan, Australia, Canada, China, Mexico and other foreign countries. Any U.S. or foreign patents that issue from these exclusively licensed patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in year 2040, not including any patent term adjustment, patent term extension, or SPC. Our solely owned patent family directed to certain physical forms of THB001 contains one pending U.S. patent application, one pending European patent application, and one pending Japanese patent application. Any U.S. or foreign patents that issue from these solely owned patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in year 2041, not including any patent term adjustment, patent term extension, or SPC.

As of February 9, 2023, we exclusively license from Novartis one patent family and solely own another patent family, each directed to certain pharmaceutical compositions containing THB001 and having patent applications to compositions of matter and methods of use. The patent family that we exclusively license to certain pharmaceutical compositions containing THB001 contains one pending international patent application, one pending U.S. patent application, and one pending patent application in Taiwan, whereby any U.S. or foreign patents that issue based on these exclusively licensed patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in year 2041, not including any patent term adjustment, patent term extension, or SPC. Our solely owned patent family directed to pharmaceutical compositions containing THB001 contains one pending international patent application, one pending U.S. patent application, and one pending patent application in Taiwan, whereby any U.S. or foreign patents that issue based on these solely owned patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in year 2041, not including any patent term adjustment, patent term extension, or SPC.

As of February 9, 2023, we solely own one pending international patent application directed to methods of treatment using THB001 according to particular dosing protocols. Any U.S. or foreign patents that issue from a national phase patent application filed based on this international application, if granted and all appropriate maintenance fees paid, are expected to expire in year 2042, not including any patent term adjustment, patent term extension, or SPC. Additionally, as of February 9, 2023, we solely owned two pending U.S. provisional applications directed to methods of treating certain indications using THB001. Any U.S. or foreign patents that issue from an application claiming priority to these provisional applications, if granted and all appropriate maintenance fees paid, are expected to expire in the year 2043, not including any patent term adjustment, patent term extension, or SPC.

Additional KIT Inhibitor Compounds

As of February 9, 2023, we exclusively license one patent family from Novartis to additional KIT inhibitor compounds containing patents and patent applications directed to compositions of matter and methods of use. This patent family contains three patents in the United States, 22 patents, collectively, in Europe, Japan, Canada, China, Mexico and other foreign countries, as well as two patent applications pending in Brazil. These U.S. and foreign patents, and any further foreign patents that may issue from these pending foreign patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in 2032, not including any patent term adjustment, patent term extension, or SPC. Additionally, as of February 9, 2023, we solely own two pending U.S. provisional applications directed to additional KIT inhibitor compounds. Any U.S. or foreign patents that issue from an application claiming priority to these provisional applications, if granted and all appropriate maintenance fees paid, are expected to expire in the year 2043, not including any patent term adjustment, patent term extension, or SPC.

Government Regulation

Regulation Within the United States

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or FDC Act, and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications, or NDAs, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

Pharmaceutical product development for a new product or certain changes to an approved product in the U.S. typically involves nonclinical laboratory and animal tests, the submission to the FDA of an IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Nonclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the nonclinical tests must comply with federal regulations and requirements, including good laboratory practices. The results of nonclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term nonclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, and ethics committee for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1a, the initial introduction of the drug into healthy human patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence of effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, dosage tolerance and optimum dosage, and to identify common adverse effects and safety risks. If a drug demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial may be sufficient in rare instances, including: (i) where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible; or (ii) when in conjunction with other confirmatory evidence.

The manufacturer of an investigational drug in a Phase 2 or 3 clinical trial for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access to such investigational drug.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all nonclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, and the applicant under an approved NDA is also subject to an annual program fees for each prescription product. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be filed based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is filed, the FDA begins an in-depth review. FDA has agreed to certain performance goals in the review of NDAs to encourage timeliness. Most applications for standard review drug products are reviewed within ten to twelve months of the date of submission of the NDA to the FDA; most applications for priority review drugs are reviewed in six to eight months of the date of submission of the NDA to the FDA. Priority review can be applied to drugs that the FDA determines offer major advances in treatment or provide a treatment where no adequate therapy exists. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an outside advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the product unless compliance with current good manufacturing practices, or cGMPs, is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pediatric Information

Under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. FDA may grant full or partial waivers, or deferrals, for submission of data. With certain exceptions, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month extension of any exclusivity—patent or nonpatent—for a drug if certain conditions are met. Conditions for exclusivity include FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, FDA making a written request for pediatric studies, and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports are required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS and surveillance to monitor the effects of an approved product, or FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the FDA inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

The Hatch-Waxman Amendments

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, nonclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug pursuant to each state's laws on drug substitution.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carve out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Exclusivity

Upon NDA approval of a new chemical entity, or NCE, which is a drug that contains no active moiety that has been approved by FDA in any other NDA, that drug receives five years of marketing exclusivity during which FDA cannot receive any ANDA seeking approval of a generic version of that drug. An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period. Certain changes to a drug, such as the addition of a new indication to the package insert, can be the subject of a three-year period of exclusivity if the application contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to the approval of the application. The FDA cannot approve an ANDA for a generic drug that includes the change during the exclusivity period.

Patent Term Extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension. The allowable patent term extension is calculated as half of the drug's testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval up to a maximum of five years). The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years, and only one patent can be extended. For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the United States Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Regulation Outside of the United States

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing clinical trials, commercial sales, and distribution of our products. Most countries outside of the United States require that clinical trial applications be submitted to and approved by the local regulatory authority for each clinical study. In addition, whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of countries outside the United States before we can commence clinical trials or marketing of the product in those countries. The approval process and requirements vary from country to country, so the number and type of nonclinical, clinical, and manufacturing studies needed may differ, and the time may be longer or shorter than that required for FDA approval.

Non-Clinical Studies and Clinical Trials

Similarly to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements. Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the ICH guidelines on GCP as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products, or ATMPs. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries member states, the sponsor is liable to provide "no fault" compensation to any study subject injured in the clinical trial.

Marketing Authorization

To obtain marketing approval of a product under the EU regulatory system, we are mandated to submit a Marketing Authorization Application, or MAA. The process for doing this depends, among other things, on the nature of the medicinal product. The centralized procedure, which came into operation in 1995, allows applicants to obtain a marketing authorization that is valid throughout the EU. It is compulsory for medicinal products derived from biotechnological processes, designated orphan medicinal products, ATMPs such as gene therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance which was not authorized in the EU before May 20, 2004 (date of entry into force of Regulation (EC) No. 726/2004) and which are intended for the treatment of AIDS, cancer, neurodegenerative disorder, diabetes, auto immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for any other products containing new active substances not authorized in the EU before May 20, 2004 or for products which constitute a significant therapeutic, scientific, or technical innovation or for which the granting of authorization is in the interests of patients at the EU level. The Committee for Advanced Therapies, or CAT, is responsible in conjunction with the Committee for Medicinal Products for Human Use, or CHMP, for the evaluation of ATMPs. The CAT is primarily responsible for the scientific evaluation of ATMPs and prepares a draft opinion on the quality, safety and efficacy of each ATMP for which a MAA is submitted. The CAT's opinion is then taken into account by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT's draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a MAA; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs.

When a company wishes to place on the market a medicinal product that is eligible for the centralized procedure, it sends an application directly to the EMA to be assessed by the CHMP. The CHMP is responsible for conducting the assessment of whether a medicine meets the required quality, safety, and efficacy requirements, and whether the product has a positive risk/benefit profile. The centralized procedure, as described below, culminates with a decision by the European Commission, which is valid in all EU member states. Centrally authorized products may be marketed in all member states.

Full copies of the MAAs are sent to a rapporteur and a co-rapporteur designated by the competent EMA scientific committee. They coordinate the EMA's scientific assessment of the medicinal product and prepare draft reports. Once the draft reports are prepared (other experts might be called upon for this purpose), they are sent to the CHMP, whose comments or objections are communicated to the applicant. The rapporteur is therefore the privileged interlocutor of the applicant and continues to play this role, even after the MAA has been granted.

The rapporteur and co-rapporteur then assess the applicant's replies, submit them for discussion to the CHMP, and taking into account the conclusions of this debate, prepare a final assessment report. Once the evaluation is completed, the CHMP gives a favorable or unfavorable opinion as to whether to grant the authorization. When the opinion is favorable, it will include the draft summary of the product's characteristics, the package leaflet, and the texts proposed for the various packaging materials. The time limit for the evaluation of a MAA by the EMA is 210 days (excluding clock stops). The EMA has fifteen days to forward its opinion to the European Commission. This is the start of the second phase of the procedure: the decision-making process. The EMA sends to the European Commission its opinion and assessment report, together with annexes containing: the SmPC (Annex 1); the particulars of the MAH responsible for batch release, the particulars of the manufacturer of the active substance, and the conditions of the marketing authorization (Annex 2); and the labeling and the package leaflet (Annex 3). The annexes are translated into the 22 other official languages of the EU. During the decision-making process, the European Commission services verify that the marketing authorization complies with EU law. The European Commission has fifteen days to prepare a draft decision. The medicinal product is assigned an EU registration number, which will be placed on its packaging if the marketing authorization is granted. During this period, various European Commission directorates-general are consulted on the draft marketing authorization decision.

The draft decision is then sent to the Standing Committee on Medicinal Products for Human Use, (member states have one representative in the Standing Committees on Medicinal Products for Human Use) for its opinions. The Centralized Procedure provides for the grant of a single marketing authorization that is valid for all EU member states. The Decentralized Procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one-member state, known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to the public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

MAAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance.

Under the Centralized Procedure and in exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops).

Data and Marketing Exclusivity

The EU also provides opportunities for market exclusivity. Upon receiving a MAA, reference product candidates generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MAA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MAA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MAA 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. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

In the EU, there is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

Pediatric Development

A Pediatric Investigation Plan, or PIP, in the EU is aimed at ensuring that the necessary data are obtained to support the authorization of a medicine for children, through studies in children. All MAAs for new medicines have to include the results of studies as described in an agreed PIP, unless the medicine is exempt because of a deferral or waiver. This requirement also applies when a marketing-authorization holder wants to add a new indication, pharmaceutical form, or route of administration for a medicine that is already authorized and covered by intellectual property rights. Several rewards and incentives for the development of pediatric medicines are available in the EU. Medicines authorized across the EU with the results of studies from a PIP included in the product information are eligible for an extension of their supplementary protection certificate by six months (if any is in effect at the time of authorization). This is the case even when the studies' results are negative. For orphan medicines, the incentive is an additional two years of market exclusivity. Scientific advice and protocol assistance at the EMA are free of charge for questions relating to the development of pediatric medicines. Medicines developed specifically for children that are already authorized but are not protected by a patent or supplementary protection certificate are eligible for a pediatric-use marketing authorization, or PUMA. If a PUMA is granted, the product will benefit from ten years of market protection as an incentive.

In March 2016, the EMA launched an initiative, The Priority Medicines (PRIME) scheme, to facilitate development of product candidates that target an unmet medical need and are expected to be of major public health interest. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Post-Approval Requirements

Similar to the United States, both MAA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of a MAA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAA must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk- minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each Member State and can differ from one country to another.

Brexit and the Regulatory Framework in the United Kingdom

The UK left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the UK during the transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement, or TCA, and became effective on the January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law". However, new legislation such as the EU CTR will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an "appropriate authority" to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, is the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain, or GB. Broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a guidance on how various aspects of the UK regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, importing, exporting, and pharmacovigilance and is relevant to any business involved in the research, development, or commercialization of medicines in the UK. The new guidance was given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019, or the Exit Regulations. The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MAA holder chooses to opt-out. In order to use the centralized procedure to obtain a MAA that will be valid throughout the EEA, companies must be established in the EEA. Therefore after Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAAs. In order to obtain a UK MAA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain a MAA to commercialize products in the UK. The MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MAA when determining an application for a GB authorization or use the MHRA's decentralized or mutual recognition procedures which enable MAAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB.

Other Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain general business and marketing practices in the pharmaceutical industry. These laws include anti-kickback, false claims, transparency and health information privacy laws and other healthcare laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. The Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act, or ACA, amended the intent element of the federal Anti-Kickback Statute so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to commit a violation. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers, among others, on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Additionally, the ACA amended the federal Anti-Kickback Statute such that a violation of that statute can serve as a basis for liability under the federal civil False Claims Act.

Federal civil and criminal false claims laws, including the federal civil False Claims Act, prohibit any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. This includes claims made to programs where the federal government reimburses, such as Medicare and Medicaid, as well as programs where the federal government is a direct purchaser, such as when it purchases off the Federal Supply Schedule. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Most states also have statutes or regulations similar to the federal Anti-Kickback Statute and civil False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Other federal statutes pertaining to healthcare fraud and abuse include the Civil Monetary Penalties Law statute, which prohibits, among other things, the offer or payment of remuneration to a Medicaid or Medicare beneficiary that the offeror or payor knows or should know is likely to influence the beneficiary to order or receive a reimbursable item or service from a particular supplier, and the additional federal criminal statutes created by the Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibit, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or obtain by means of false or fraudulent pretenses, representations or promises any money or property owned by or under the control of any healthcare benefit program in connection with the delivery of or payment for healthcare benefits, items or services.

In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, including the Final Omnibus Rule published on January 25, 2013, impose obligations on certain healthcare providers, health plans and healthcare clearinghouses, known as covered entities, as well as their business associates and their subcontractors that perform certain services involving the storage, use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information. HITECH increased the civil and criminal penalties that may be imposed against covered entities, business associates, their covered subcontractors and possibly other persons, 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 attorney's fees and costs associated with pursuing federal civil actions. In addition, many state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, and often are not pre-empted by HIPAA.

Further, pursuant to the ACA, the Centers for Medicare & Medicaid Services, or CMS, issued a final rule that requires certain manufacturers of prescription drugs to collect and annually report information on certain payments or transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals (such as physicians assistants and nurse practitioners) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. The reported data are made available in searchable form on a public website on an annual basis. Failure to submit required information may result in civil monetary penalties.

Analogous state and foreign anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or that apply regardless of payor. In addition, several states now require prescription drug companies to report certain expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual healthcare practitioners in these states. Other states prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals. Further, certain states require the posting of information relating to clinical trials and their outcomes. Some states require the reporting of certain drug pricing information, including information pertaining to and justifying price increases. In addition, certain states require pharmaceutical companies to implement compliance programs and/or marketing codes. Several additional states are considering similar proposals. Certain states and local jurisdictions also require the registration of pharmaceutical sales representatives. Additionally, we may also be subject to state and foreign laws governing the privacy and security of health information in some circumstances, such as California's CCPA or Europe's General Data Protection Regulation, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that business arrangements with third parties comply with applicable state, federal and foreign healthcare laws and regulations involve substantial costs. If a drug company's operations are found to be in violation of any such requirements, it may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of its operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement or other federal or state government healthcare programs, including Medicare and Medicaid, integrity oversight and reporting obligations, imprisonment and reputational harm. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action for an alleged or suspected violation can cause a drug company to incur significant legal expenses and divert management's attention from the operation of the business, even if such action is successfully defended.

Healthcare Reform

Healthcare reforms that have been adopted, and that may be adopted in the future, could result in further reductions in coverage and levels of reimbursement for pharmaceutical products, increases in rebates payable under U.S. government rebate programs and additional downward pressure on pharmaceutical product prices. Healthcare reform initiatives recently culminated in the enactment of the Inflation Reduction Act, or IRA, in August 2022, which will eliminate, beginning in 2025, the coverage gap under Medicare Part D by significantly lowering the enrollee maximum out-of-pocket cost and requiring manufacturers to subsidize, through a newly established manufacturer discount program, 10% of Part D enrollees' prescription costs for brand drugs below the out-of-pocket maximum, and 20% once the out-of-pocket maximum has been reached. The IRA also allow HHS to negotiate the selling price of certain drugs and biologics that CMS reimburses under Medicare Part B and Part D, although only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected, with the negotiated price taking effect two years after the selection year. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price representing a significant discount from average prices to wholesalers and direct purchasers. The law will also, beginning in October 2022 for Medicare Part D and January 2023 for Medicare Part B, penalize drug manufacturers that increase prices of Medicare Part D and Part B drugs at a rate greater than the rate of inflation. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges.

Coverage and Reimbursement

Patients in the U.S. and elsewhere generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Accordingly, market acceptance of any future oral KIT inhibitor product candidates, if approved, will be dependent on the extent to which third-party coverage and reimbursement is available from third-party payors, including government health program administration authorities (including in connection with government healthcare programs, such as Medicare and Medicaid), private healthcare insurers and other healthcare funding organizations. Coverage and reimbursement policies for products can differ significantly from payor to payor, as there is no uniform policy of coverage and reimbursement for products among commercial third-party payors in the United States. There also may be significant delays in obtaining coverage and reimbursement, as the process of determining coverage and reimbursement is often time consuming and can require health care providers to provide clinical support for the use of our products to each payor separately, with no assurance that coverage or adequate reimbursement will be obtained. In addition, the increased emphasis by such third-party payors and government authorities in the United States on managed care and cost containment measures will continue to place pressure on pharmaceutical pricing and coverage. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for any future oral KIT inhibitor product candidates, if approved, less favorable coverage policies and reimbursement rates may be implemented in the future.

Employees and Human Capital Resources

As of December 31, 2022, we had 28 employees, all of whom were full-time and 18 of whom were engaged in research and development activities. Eleven of our employees hold Ph.D. or M.D. degrees. None of our employees are represented by a labor union or covered under a collective bargaining agreement. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Facilities

We currently lease various office space in Cambridge, Massachusetts and in San Francisco, California. Our principal executive office is located at 1700 Montgomery Street, Suite 210, San Francisco, CA, 94111, and our telephone number is (209) 727-2457.

Corporate Information and Trademarks

We were formed as a corporation under the laws of the State of Delaware on April 25, 2019, under the name Project Ige, Inc. We changed our name on June 28, 2019 to Third Harmonic, Bio.

We use various trademarks and trade names in our business, including, without limitation, our corporate name and logo. All other service marks, trademarks and trade names appearing in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names referred to in this Annual Report appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and trade names.

Additional Information

Our Internet website address is https://thirdharmonicbio.com. On our website, we make available, free of charge, our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after the company electronically files such material with, or furnishes such material to, the SEC. The SEC maintains a website at www.sec.gov that contains reports, proxy and information statements and other information regarding us and other companies that file materials with the SEC electronically.

Also available on our website is information relating to our corporate governance and our board of directors, including our corporate governance guidelines; our code of business conduct (for our directors, officers and employees); and our board committee charters. We will provide any of the foregoing information without charge upon written request to our Secretary, Third Harmonic Bio, Inc., 1700 Montgomery Street, Suite 210, San Francisco, CA 94111.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. Before making your decision to invest in shares of our common stock, you should carefully consider the risks described below, together with the other information contained in this Annual Report, including in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and in our consolidated financial statements and the related notes included elsewhere in this Annual Report. We cannot assure you that any of the events discussed below will not occur. These events could have a material and adverse impact on our business, financial condition, results of operations and prospects. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment.

Risks Related to Our Financial Position, Limited Operating History and Need for Additional Capital

We have a limited operating history, have not completed any clinical trials beyond Phase 1, and have not had any product candidates approved for commercial sale. We have a history of significant net losses since our inception and expect to continue to incur significant losses for the foreseeable future.

We are a biopharmaceutical company with a limited operating history on which to base your investment decision. We commenced operations in 2019, and none of our prior or any future oral KIT inhibitor product candidates have completed clinical trials beyond Phase 1 or have been approved for commercial sale. Biopharmaceutical product development is a highly speculative undertaking because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval or become commercially viable.

Since our inception, we have focused substantially all of our efforts and financial resources on the development of our prior product candidate THB001. In December 2022, we announced the discontinuation of our Phase 1b clinical trial of our prior product candidate, THB001, in chronic inducible urticaria following observation of asymptomatic liver transaminitis in two patients enrolled in the first dose cohort. We have not yet demonstrated an ability to successfully complete any late-stage trials, obtain marketing 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 product commercialization. As a result, it may be more difficult for you to accurately evaluate the performance of our business to date or to predict our viability than it would be if we had a longer operating history.

We have incurred significant net losses in each reporting period since our inception, have not generated any revenue to date and have financed our operations principally through private placements of preferred stock prior to the completion of our IPO, as well as the net proceeds from our IPO. Our net losses were $35.2 million and $29.6 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $83.4 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of any future product candidates. The net losses we incur may fluctuate significantly from quarter-to-quarter and year-to-year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We anticipate that our expenses will increase substantially if, and as, we:

- advance any future product candidates through nonclinical studies and clinical development;
- discover and develop new oral KIT inhibitor product candidates;
- obtain, expand, maintain, defend and enforce our intellectual property portfolio;
- manufacture, or have manufactured, nonclinical, clinical and potentially commercial supplies of any future oral KIT inhibitor product candidates;
- seek regulatory approvals for any future oral KIT inhibitor product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize any future oral KIT inhibitor product candidates, if approved;
- identify additional compounds or product candidates and acquire rights from third parties to those compounds or product candidates through licenses;
- hire additional clinical, scientific and management personnel, as well as administrative staff to support the growth of our business;
- add operational, financial and management information systems and personnel;
- incur additional legal, accounting and other costs associated with operating as a public company;
- experience delays related to the ongoing COVID-19 pandemic in the United States and in other countries in which we have planned or have active clinical trial sites and where our third-party contract development and manufacturing organizations, or CDMOs operate; and
- establish licenses, collaborations or strategic partnerships.

Even if we succeed in commercializing one or more product candidates, we may continue to incur substantial research and development expenses and other expenditures to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business, financial condition, results of operations and prospects. The size of our future losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue, if any. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

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

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue, if any, unless and until we, either alone or with a collaborator, are able to obtain regulatory approval for, and successfully commercialize any future oral KIT inhibitor product candidates that we may develop. Successful commercialization will require achievement of many key milestones, including demonstrating safety and efficacy in clinical trials, obtaining regulatory, including marketing, approval for these product candidates, manufacturing, marketing and selling those products for which we, or any future collaborators, may obtain regulatory approval, satisfying any post-marketing requirements and obtaining reimbursement for any future product candidates from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately and precisely predict the timing and amount of revenue, if any, the extent of any further losses or if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenue in an amount sufficient for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Additionally, our expenses could increase if we are required by the FDA, the EMA, or any comparable foreign regulatory authority to perform clinical trials in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any future oral KIT inhibitor product candidates.

Our failure to become and remain profitable would decrease the value of our Company and depress the market price of our common stock and could impair our ability to raise capital, expand our business or continue our operations. If we continue to suffer losses as we have in the past, investors may not receive any return on their investment and may lose their entire investment.

We will need substantial additional funds to pursue our business objectives, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development programs, commercialization efforts or other operations.

Identifying and developing potential product candidates and conducting nonclinical and clinical studies is a time consuming, capital-intensive and uncertain process that takes years to complete. If any future oral KIT inhibitor product candidates enter and advance through nonclinical studies and clinical trials, as applicable, we will need substantial additional funds to expand or create our development, regulatory, manufacturing, marketing and sales capabilities. We have used substantial amounts of cash since inception to develop our prior product candidate, THB001, and will require significant funds to conduct further research and development and nonclinical testing and clinical trials of any future oral KIT inhibitor product candidates, to seek regulatory approvals for any future oral KIT inhibitor product candidates and to manufacture and market products, if any, which are approved for commercial sale. In addition, we expect to incur additional costs associated with operating as a public company. See "*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 and corporate governance practices."* Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations.

Nonclinical studies and clinical trials for any future oral KIT inhibitor product candidates, will require substantial funds to complete. As of December 31, 2022 we had $288.9 million in cash and cash equivalents. Based on our current operating plan, we believe that our existing cash and cash equivalents, will be sufficient to fund our operating expenses and capital expenditure requirements through at least the next twelve months. However, our future capital requirements and the period for which we expect our existing resources to support our operations, fund continued growth of our operations, research and development of product candidates, or otherwise respond to competitive pressures, may vary significantly from what we expect and we may need to seek additional funds sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Our monthly spending levels vary based on new and ongoing research and development and other corporate activities. Because the length of time and activities associated with successful research and development of any future product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any marketing and commercialization activities for approved products. Our future funding requirements for any future product candidates and our ongoing operations, both near and long-term, will depend on many factors, including, but not limited to:

- the timing, cost and progress of nonclinical and clinical development activities;
- the cost of regulatory submissions and timing of regulatory approvals;
- the number and scope of nonclinical and clinical programs we decide to pursue;
- the progress of the development efforts of parties with whom we may in the future enter into collaborations and/or research and development agreements;
- the timing and amount of milestone and other payments we are obligated to make under our Novartis Agreement or any future license agreements;
- the cash requirements of any future acquisitions or discovery of product candidates;
- our ability to establish and maintain collaborations, strategic partnerships or marketing, distribution, licensing or other strategic arrangements with third parties on favorable terms, if at all;
- our ability to achieve sufficient market acceptance, adequate coverage and reimbursement from third-party payors and adequate market share and revenue for any approved product candidates;
- the costs involved in prosecuting and enforcing patent and other intellectual property claims;
- the costs of manufacturing product candidates by third parties;
- the cost of commercialization activities if any future oral KIT inhibitor product candidates are approved for sale, including marketing, sales and distribution costs;

- the availability of capital in the technology and life sciences industries following the closure of Silicon Valley Bank, or SVB, and liquidity concerns at other financial institutions;
- our efforts to enhance operational systems and hire additional personnel, including personnel to support development of product candidates;
- the continued effect of the ongoing COVID-19 pandemic on our business; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems to satisfy our obligations as a public company.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, reduce or terminate our research and development programs and nonclinical studies or clinical trials, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We do not expect to realize revenue from sales of commercial products or royalties from licensed products in the foreseeable future, if at all, and, in no event, before any future oral KIT inhibitor product candidates are clinically tested, approved for commercialization and successfully marketed, if ever.

We will be required to seek additional funding in the future and currently intend to do so through public or private equity offerings or debt financings, credit or loan facilities, additional licensing agreements and/or collaborations, or a combination of one or more of these funding sources. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Our future debt financings, if available, are likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities receive any distribution of our corporate assets. If we raise additional funds through licensing or collaboration arrangements with third parties, we may have to relinquish valuable rights to any future oral KIT inhibitor product candidates, or grant licenses on terms that are not favorable to us. We also could be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. Failure to obtain capital when needed on acceptable terms, or at all, may force us to delay, limit or terminate our product development and commercialization of any future product candidates, which could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults or nonperformance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations, and its financial condition and results of operations.

Adverse developments that affect financial institutions, such as events involving liquidity that are rumored or actual, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, SVB was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation, or FDIC, as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. The Department of the Treasury, the Federal Reserve and the FDIC released a joint statement on March 12, 2023, stating that all depositors of SVB would have access to all of their funds on March 13, 2023, 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. 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. Although we are not a borrower or party to any such instruments with SVB, Signature or any other financial institution currently in receivership, if any of our future lenders or counterparties to any such instruments were to be placed into receivership, we may be unable to access such funds.

We either hold the vast majority of our financial assets in our name and custody them at a third-party financial institution, or we have transferred them out of SVB. Although we have not experienced any adverse impact to our liquidity or to our current and projected business operations, financial condition or results of operations, uncertainty remains over liquidity concerns in the broader financial services industry, and our business, our business partners, or industry as a whole may be adversely impacted in ways that we cannot predict at this time. 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. 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 funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that us, the financial institutions with which we have credit agreements or arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions or financial services industry companies with which we have financial or business relationships, but could also include factors involving financial markets or the financial services industry generally.

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, 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;
- Potential or actual breach of contractual obligations that require us to maintain letters or credit or other credit support arrangements; or
- Termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, widespread 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, financial condition and results of operations.

We have identified a material weakness in our internal control over financial reporting. If we do not remediate the material weakness in our internal control over financial reporting, or if we fail to establish and maintain effective internal control, we may not be able to accurately report our financial results or file our periodic reports in a timely manner, which may cause investors to lose confidence in our reported financial information and may lead to a decline in the market price of our common stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports in a timely manner. During the preparation of our consolidated financial statements for the year ended December 31, 2021, we identified a material weakness in our internal control over financial reporting. The material weakness has not yet been fully remediated and the same weakness remained at the time of the preparation of our financial statements for the year ended December 31, 2022. A material weakness is a significant deficiency, or a combination of significant deficiencies, in internal control over financial reporting such that it is reasonably possible that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis. The material weakness that we identified related to the lack of segregation of duties, certain system limitations in our accounting software and the overall control environment as we had insufficient internal resources with appropriate accounting and finance knowledge and expertise to design, implement, document and operate effective internal controls around our financial reporting process.

During the year ended December 31, 2022, our management team implemented measures designed to improve our internal control over financial reporting to remediate this material weakness, including formalizing our processes and internal control documentation and strengthening supervisory reviews by our financial management; hiring additional qualified accounting and finance personnel and engaging financial consultants to enable the implementation of internal control over financial reporting and segregating duties amongst accounting and finance personnel. In addition, we have implemented an accounting software system with the design and functionality to segregate incompatible accounting duties, which we currently expect will be fully implemented in our 2023 fiscal year.

While we are implementing these measures, we cannot assure you that these efforts will remediate our material weaknesses and significant deficiencies in a timely manner, or at all, or prevent restatements of our financial statements in the future. If we are unable to successfully remediate our material weaknesses, or identify any future significant deficiencies or material weaknesses, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports, and the market price of our common stock may decline as a result.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. We expect to incur additional costs to remediate these control deficiencies, though there can be no assurance that our efforts will be successful or avoid potential future material weaknesses. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or if we identify any additional material weaknesses, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting, and our stock price may decline as a result. We also could become subject to investigations by Nasdaq, the Securities and Exchange Commission, or SEC, or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and make it more difficult for us to effectively market and sell our products to new and existing customers.

Risks Related to Discovery, Development and Commercialization

Our future performance is substantially dependent on our ability to identify and develop future product candidates.

Our future performance is substantially dependent on our ability to timely identify and develop future oral KIT inhibitor product candidates, obtain regulatory approval for, and then successfully commercialize future oral KIT inhibitor product candidates. We are early in our development efforts and we announced in December 2022 the discontinuation of our Phase 1b trial of our prior product candidate, THB001, in chronic inducible urticaria. While we are devoting significant resources to research and development activities, we have not yet identified additional oral KIT inhibitor product candidates. We currently have no products that are approved for sale in any jurisdiction. There can be no assurance that any future oral KIT inhibitor product candidates we develop will achieve success in their clinical trials or obtain regulatory approval.

We plan to seek regulatory approval to commercialize future oral KIT inhibitor product candidates in the United States, the European Union and in selected foreign countries, including the United Kingdom and Japan. In order to obtain separate regulatory approvals in other countries, we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy. Other countries also have their own regulations governing, among other things, clinical trials and commercial sales, as well as pricing and distribution of any future oral KIT inhibitor product candidates, and we will be required to expend significant resources to obtain regulatory approval, which may not be successful, and to comply with ongoing regulations in these jurisdictions.

Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and commercialization of future product candidates. The success of future product candidates will depend on several factors, including the following:

- successful completion of necessary nonclinical studies to enable the initiation of clinical trials;
- acceptance of INDs by the FDA or other similar clinical trial applications from foreign regulatory authorities for our future clinical trials for our pipeline product candidates;
- enrollment of patients in, and the completion of, our clinical trials;
- completion of successful clinical trials with positive risk/benefit profiles;
- receiving required regulatory authorizations for the development and obtaining approvals for the commercialization of any future oral KIT inhibitor product candidates;
- establishing and maintaining arrangements with third-party manufacturers;
- ability to perform drug manufacturing and maintain consistent supply of drugs which meets specifications across various jurisdictions;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for THB001 or any future product candidates and their components and related filings;
- enforcing and defending our intellectual property rights and claims;
- achieving desirable therapeutic properties for any future oral KIT inhibitor product candidates' intended indications;
- launching commercial sales of any future oral KIT inhibitor product candidates, if approved, whether alone or in collaboration with third parties;
- acceptance of any future oral KIT inhibitor product candidates, if approved, by patients, the medical community and third-party payors;
- addressing any delays in our clinical trials resulting from factors related to the ongoing COVID-19 pandemic or other major natural disaster or significant political event;
- effectively competing with other therapies; and
- maintaining an acceptable safety profile of any future oral KIT inhibitor product candidates through clinical trials and following regulatory approval.

Many of these factors are beyond our control, and it is possible that none of our prior or future oral KIT inhibitor product candidates will ever obtain regulatory approval, even if we expend substantial time and resources seeking such approval. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any product candidates, which would materially harm our business.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of any future product candidates may be delayed and, as a result, our stock price may decline and you may lose all or part of your investment.

From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, or at all, the commercialization of any future oral KIT inhibitor product candidates may be delayed or never achieved and, as a result, our stock price may decline. A decline in our stock price and in the value of our Company could cause you to lose all or part of your investment.

Drug development is a lengthy and expensive process, and the outcome of clinical testing is inherently uncertain, and results of earlier studies and trials may not be predictive of future trial results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of an oral KIT inhibitor or any future product candidates.

We currently do not have any product candidates in clinical development. In December 2022, we announced the discontinuation of our Phase 1b clinical trial of our prior product candidate, THB001, in chronic inducible urticaria following observation of asymptomatic liver transaminitis in two patients enrolled in the first dose cohort. It is impossible to predict when or if any future oral KIT inhibitor product candidate will prove effective and safe in humans or will receive regulatory approval. To obtain the requisite regulatory approvals to commercialize any product candidate, we must demonstrate through extensive nonclinical studies and lengthy, complex and expensive clinical trials that our product candidate is safe and effective in humans. Clinical testing can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of nonclinical studies and early clinical trials of any future oral KIT inhibitor product candidates may not be predictive of the results of later-stage clinical trials. We may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, and a clinical trial can fail at any stage of testing. Differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials for product candidates due to lack of efficacy or to unfavorable safety profiles, notwithstanding promising results in earlier trials. There is typically a high rate of failure of product candidates proceeding through clinical trials. Most product candidates that commence clinical trials are never approved as products and there can be no assurance that any of our future clinical trials will ultimately be successful or support clinical development of any future oral KIT inhibitor product candidates.

We or any future collaborators may experience delays in initiating or completing clinical trials. We or any future collaborators also may experience numerous unforeseen events during, or as a result of, any future clinical trials that we could conduct that could delay or prevent our ability to receive marketing approval or commercialize any future oral KIT inhibitor product candidates, including:

- regulators or institutional review boards, or IRBs, the FDA or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site, or may halt or suspend an ongoing clinical trial;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- clinical trials of any product candidates may fail to show safety or efficacy, produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional nonclinical studies or clinical trials or we may decide to abandon product development programs;
- the number of patients required for clinical trials of any product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or patients may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;

- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs, or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our trials are being exposed to unacceptable health risks;
- the cost of clinical trials of any future oral KIT inhibitor product candidates may be greater than we anticipate;
- the quality of any future oral KIT inhibitor product candidates or other materials necessary to conduct clinical trials of any future product candidates may be inadequate to initiate or complete a given clinical trial;
- our inability to manufacture sufficient quantities of any future oral KIT inhibitor product candidates for use in clinical trials;
- our inability to meet drug specifications suitable for use in clinical trials and commercial applications;
- reports from clinical testing of other therapies may raise safety or efficacy concerns about any future oral KIT inhibitor product candidates;
- our failure to establish an appropriate safety profile for a product candidate based on clinical or nonclinical data for such product candidate as well as data emerging from other molecules in the same class as any future oral KIT inhibitor product candidate; and
- the FDA, EMA or other regulatory authorities may require us to submit additional data such as long-term toxicology studies or impose other requirements before permitting us to initiate a clinical trial.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the number and location of clinical sites we enroll, the proximity of patients to clinical sites, the eligibility and exclusion criteria for the trial, the design of the clinical trial, the inability to obtain and maintain patient consents, the risk that enrolled participants will drop out before completion, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs or therapeutic biologics that may be approved for the indications being investigated by us. Furthermore, we may in the future rely on collaborators, CROs and clinical trial sites to ensure the proper and timely conduct of our future clinical trials, including the patient enrollment process, and we have limited influence over their performance. Additionally, we could encounter delays if treating physicians encounter unresolved ethical issues associated with enrolling patients in future clinical trials of any future oral KIT inhibitor product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, or the FDA, EMA or other regulatory authorities, or if a clinical trial is recommended for suspension or termination by the Data Safety Monitoring Board, or the DSMB, for such trial. A suspension or termination may be imposed due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Clinical studies may also be delayed or terminated as a result of ambiguous or negative interim results. 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 any future oral KIT inhibitor product candidates. Further, the FDA, EMA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

Our product development costs will increase if we experience delays in clinical testing or marketing approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize any future oral KIT inhibitor product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize any future oral KIT inhibitor product candidates and harming our business and results of operations. Any delays in our clinical development programs may harm our business, financial condition, results of operations and prospects significantly.

Results of nonclinical studies and early clinical trials may not be predictive of results of future clinical trials.

The outcome of nonclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we have faced and could in the future face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval for future oral KIT inhibitor product candidates. In addition, nonclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in nonclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of clinical trials for any future oral KIT inhibitor product candidates warrant marketing approval, the FDA, EMA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of any future oral KIT inhibitor 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 dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial patients. If we fail to receive positive results in clinical trials of any future oral KIT inhibitor product candidates, the development timeline and regulatory approval and commercialization prospects for such product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

Preliminary, topline or interim 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 audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish preliminary or topline data or data from planned interim analyses of our clinical trials. Preliminary or topline data remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary or topline data that we previously published. Data from planned interim analyses of our 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. As a result, preliminary data and interim analyses should be viewed with caution until the final data are available. Adverse differences between preliminary, topline or interim data and final data could significantly harm our reputation and business prospects.

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

If significant adverse events or other side effects are observed in any of our clinical trials for future oral KIT inhibitor product candidates, 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. In particular, in December 2022, we announced the discontinuation of our Phase 1b clinical trial of our prior product candidate, THB001, in chronic inducible urticaria following observation of asymptomatic liver transaminitis in two patients enrolled in the first dose cohort, which was not predicted by our completed nonclinical toxicology studies of THB001 nor observed in our Phase 1a clinical trial. Mechanistic studies are being conducted to understand the likely cause of hepatotoxicity observed with THB001. KIT inhibition is known to produce certain on-target side effects, including inhibition of spermatogenesis, effects on hematopoietic progenitor cells resulting in reductions in neutrophils, reticulocytes, red blood cells and white blood cells, changes in taste and reduced hair pigmentation. In our Phase 1a trial in healthy volunteers, one moderate adverse effect, or AE, determined to be likely related to THB001 was low neutrophil levels, which resolved after discontinuation in the trial. While we believe that such on-target side effects will be reversible following discontinuation of treatment with an oral KIT inhibitor with sufficient recovery periods, we will need to monitor the severity and duration of side effects in our clinical trials. If such effects are more severe, less reversible than we expect or not reversible at all, we may decide or be required to perform additional nonclinical studies or to halt or delay further clinical development of our future oral KIT inhibitor product candidates, which could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities. We also expect that, similar to other approved oral KIT inhibitor drugs, our future oral KIT inhibitor product candidates may have adverse effects on the fetus and if approved, may require the concomitant use of appropriate birth control measures. AEs and serious adverse events, or SAEs, that emerge during clinical investigation of any of our future oral KIT inhibitor product candidates, or other compounds acting through similar biological pathways, may be deemed to be related to our future oral KIT inhibitor product candidates. This may require longer and more extensive Phase 3 clinical development, or regulatory authorities may increase the amount of data and information required to approve, market, or maintain any of our future oral KIT inhibitor product candidates and could result in warnings and precautions in our product labeling or a restrictive risk evaluation and mitigation strategy, or REMS. This may also result in an inability to obtain approval of any of our future oral KIT inhibitor product candidates. We, the FDA, EMA or other applicable regulatory authorities, or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that patients in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects, including the potential effects on fertility, may inhibit market acceptance of the approved product due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition, results of operations and prospects.

Clinical trials of any future oral KIT inhibitor product candidates may not uncover all possible AEs that patients may experience.

Clinical trials are conducted in representative samples of healthy volunteers and the potential patient population, which may have significant variability. By design, clinical trials are based on a limited number of patients and are of limited duration of exposure to the product, to determine whether the product candidate demonstrates the substantial evidence of efficacy and safety necessary to obtain regulatory approval. As with the results of any statistical sampling, we cannot be sure that all side effects of any future oral KIT inhibitor product candidates may be uncovered. It may be the case that only with a significantly larger number of patients exposed to the product candidate for a longer duration may a more complete safety profile be identified. Further, even larger clinical trials may not identify rare SAEs, and the duration of such studies may not be sufficient to identify when those events may occur. Other products have been approved by the regulatory authorities for which safety concerns have been uncovered following approval. Such safety concerns have led to labeling changes, restrictions on distribution through use of a REMS, or withdrawal of products from the market, and any future oral KIT inhibitor product candidates may be subject to similar risks.

If safety problems occur or are identified after any future oral KIT inhibitor product candidates, if any, reach the market, we may make the decision or be required by regulatory authorities to amend the labeling of our products, recall our products, or even withdraw approval for such products.

The ongoing COVID-19 pandemic could adversely impact our business, including the conduct of our clinical trials.

The ongoing COVID-19 pandemic could cause significant disruptions that could severely impact our business, including:

- delays or difficulties in screening, enrolling and maintaining patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;

- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- inability or unwillingness of patients to travel to the clinical trial sites;
- delays, difficulties or incompleteness in data collection and analysis and other related activities;
- decreased implementation of protocol required clinical trial activities and quality of source data verification at clinical trial sites;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials and our other research and development activities, including because of sickness of employees or their families or mitigation measures such as lock-downs and social distancing;
- delays due to production shortages resulting from any events affecting raw material supply or manufacturing capabilities domestically and abroad;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials;
- interruption in global and domestic shipping that may affect the transport of clinical trial materials, such as investigational drug products used in our clinical trials;
- changes in local regulations as part of a response to the ongoing COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, delays or require us to discontinue the clinical trials altogether;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- refusal of regulatory authorities such as FDA or EMA, to accept data from clinical trials in affected geographies; and
- adverse impacts on global economic conditions which could have an adverse effect on our business and financial condition, including impairing our ability to raise capital when needed.

Such disruptions could impede, delay, limit or prevent completion of our ongoing clinical trials and nonclinical studies or commencement of new clinical trials and ultimately lead to the delay or denial of regulatory approval of any future oral KIT inhibitor product candidates, which would increase our costs and expenses and seriously harm our business, financial condition, results of operations and prospects. Furthermore, if either we or any third party in the supply chain for materials used in the production of any future oral KIT inhibitor product candidate are adversely impacted by restrictions resulting from the ongoing COVID-19 pandemic, our supply chain may be disrupted, limiting our ability to manufacture product candidates for our clinical trials. We are in close contact with our clinical research organizations, or CROs, our CDMOs and clinical sites as we seek to mitigate the impact of the ongoing COVID-19 pandemic on our current timelines. Measures we have taken in response to the ongoing COVID-19 pandemic include, where feasible, conducting remote clinical trial site activations and data monitoring. However, despite these efforts, we have experienced delays in trial site initiations, patient participation and patient enrollment in our clinical trial and we may continue to experience some delays in our clinical trials and nonclinical studies and delays in data collection and analysis.

These delays so far have had a limited impact on our development prospects for our prior product candidate THB001, but the negative impacts could be exacerbated as the ongoing COVID-19 pandemic and the response to it continue to evolve. The ongoing COVID-19 pandemic could also affect the business of the FDA, EMA or other health authorities, which could result in delays in meetings related to planned or completed clinical trials and ultimately of reviews and approvals of any future oral KIT inhibitor product candidate. The extent to which the ongoing COVID-19 pandemic impacts our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the success of mass vaccination efforts globally, travel restrictions and social distancing in the United States and other countries, the impact of new COVID-19 variants, business closures or business disruptions and the effectiveness of actions taken by governmental authorities to contain and address the challenges posed by the ongoing COVID-19 pandemic.

If we experience delays or difficulties in enrolling patients in our ongoing or planned clinical trials, our receipt of necessary regulatory approval could be delayed or prevented.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the number and location of clinical sites we enroll, the proximity of patients to clinical sites, the eligibility and exclusion criteria for the trial, the design of the clinical trial, the inability to obtain and maintain patient consents, the risk that enrolled participants will drop out before completion, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs or therapeutic biologics that may be approved for the indications being investigated by us. The ongoing COVID-19 pandemic may also delay clinical trials if there are inadequate clinical resources for sites to safely conduct clinical research. Furthermore, we expect to rely on our collaborators, CROs, and clinical trial sites to ensure the proper and timely conduct of our future clinical trials, including the patient enrollment process, and we have limited influence over their performance. Additionally, we could encounter delays if treating physicians encounter unresolved ethical issues associated with enrolling patients in future clinical trials of any future oral KIT inhibitor product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles.

If we are unable to enroll a sufficient number of patients for our clinical trials, it would result in significant delays or might require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for any future oral KIT inhibitor product candidates, slow down or halt our product candidate development and approval process and jeopardize our ability to seek and obtain the marketing approval required to commence product sales and to generate revenue, which would cause the value of our Company to decline and limit our ability to obtain additional financing if needed.

We face competition from entities that have made substantial investments into the rapid development of novel treatments for allergic and inflammatory diseases, including large and specialty pharmaceutical and biotechnology companies developing novel treatments and technology platforms. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize, if approved, product candidates may be adversely affected.

The development and commercialization of drugs is highly competitive. An oral KIT inhibitor, if approved, will face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration. Most of our competitors have significantly greater resources than we do and we may not be able to successfully compete. We face substantial competition from multiple sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions and governmental agencies and public and private research institutions. Our competitors compete with us on the level of the technologies employed, or on the level of development of product candidates. In addition, many small biotechnology companies have formed collaborations with large, established companies to (i) obtain support for their research, development and commercialization of products or (ii) combine several treatment approaches to develop longer lasting or more efficacious treatments that may potentially directly compete with any of our future oral KIT inhibitor product candidates. We anticipate that we will continue to face increasing competition as new therapies and combinations thereof, technologies, and data emerge within the field of immunology and, furthermore, within the treatment of allergies and inflammatory conditions.

Our likelihood of success will depend partially on our ability to develop and commercialize therapeutics that are safer and more effective than competing products. Our commercial opportunity and likelihood of success will be reduced or eliminated if competing products are safer, more effective, or less expensive than the therapeutics we are trying, or may try, to develop.

Our competitors have developed, are developing or will develop product candidates and processes competitive with any future oral KIT inhibitor product candidates, and processes. Therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments, including those based on novel technology platforms that enter the market. In addition to the current standard of care treatments for patients with allergies and inflammatory diseases, numerous commercial and academic nonclinical studies and clinical trials are being undertaken by a large number of parties to assess novel technologies and product candidates. There are numerous other competitive approaches, including inhibitors of activators of mast cells such as IgE antibodies like omalizumab, inhibitors of mediators such as anti-histamines and anti-IL-4 /IL-13 therapies, other small molecule approaches such as Bruton's tyrosine kinase inhibitors, and other small molecule and biologic KIT inhibitors such as Celldex's barzolvolimab or monoclonal antibody KIT inhibitor, among others.

Many of these competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we have. If we obtain regulatory approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of future oral KIT inhibitor product candidates, the ease with which any future oral KIT inhibitor product candidates can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing any future oral KIT inhibitor product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

Any future oral KIT inhibitor product candidates may not achieve adequate market acceptance among physicians, patients, healthcare third-party payors and others in the medical community necessary for commercial success, if approved, and we may not generate any future revenue from the sale or licensing of product candidates.

Even if regulatory approval is obtained for a product candidate, we may not generate or sustain revenue from sales of the product due to factors such as whether the product can be sold at a competitive cost and whether it will otherwise be accepted in the market. Market participants with significant influence over acceptance of new treatments, such as physicians and third-party payors, may not adopt any future oral KIT inhibitor product candidates, and we may not be able to convince the medical community and third-party payors to accept and use, or to provide favorable reimbursement for, any product candidates developed by us or future collaborators. Market acceptance of any future product candidates, if approved, will depend on, among other factors:

- the timing of our receipt of any marketing and commercialization approvals;
- the terms of any approvals and the countries in which approvals are obtained;
- the safety and efficacy of any future oral KIT inhibitor product candidates as demonstrated in clinical trials;
- the prevalence and severity of any adverse side effects associated with any future oral KIT inhibitor product candidates;
- limitations or warnings contained in any labeling approved by the FDA, EMA or other regulatory authority;
- relative convenience and ease of administration of any future oral KIT inhibitor product candidates;
- the willingness of patients to accept any new methods of administration;
- unfavorable publicity relating to our current product candidates or any future oral KIT inhibitor product candidates;
- the success of our physician education programs;
- the effectiveness of sales and marketing efforts;
- the availability of coverage and adequate reimbursement from government and third-party payors;
- the pricing of any future oral KIT inhibitor product candidates, particularly as compared to alternative treatments; and
- the availability of alternative effective treatments for the disease indications any future oral KIT inhibitor product candidates are intended to treat and the relative risks, benefits and costs of those treatments.

Sales of medical products also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product, if approved, is safe, therapeutically effective and cost effective as compared with competing treatments. If any product candidate is approved but does not achieve an adequate level of acceptance by such parties, we may not generate or derive sufficient revenue from that product candidate and may not become or remain profitable.

The market opportunities for any of our future oral KIT inhibitor product candidates, if approved, may be limited to certain smaller patient subsets and may be smaller than we estimate them to be.

Our projections of both the number of people who have chronic urticaria as well as other mast cell-mediated allergic and inflammatory diseases we are targeting, and who have the potential to benefit from treatment with any of our future oral KIT inhibitor product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of the indications that we are targeting. The potentially addressable patient population for any of our future oral KIT inhibitor product candidates may be more limited that we currently estimate or may not be amenable to treatment with such product candidates. For example, women are nearly twice as likely as men to experience urticaria, and the expected requirement of concomitant use of appropriate birth control measures may result in a lower addressable patient population than we expect. Consequently, even if any of our future oral KIT inhibitor product candidates are approved, the number of patients that may be eligible for treatment, or willing to be treated, with any future oral KIT inhibitor product candidates may turn out to be much lower than expected. Even if we obtain significant market share for any future oral KIT inhibitor product candidates, if approved, if the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications.

If in the future we are unable to establish U.S. or global sales and marketing capabilities or enter into agreements with third parties to sell and market any future oral KIT inhibitor product candidates, we may not be successful in commercializing our product candidates if they are approved and we may not be able to generate any revenue.

We currently do not have a marketing or sales team for the marketing, sales and distribution of any future oral KIT inhibitor product candidates, if any of them ever obtain regulatory approval. To commercialize any product candidates after approval, we must build on a territory-by-territory basis marketing, sales, distribution, managerial and other non-technical capabilities or arrange with third parties to perform these services, and we may not be successful in doing so. If any future oral KIT inhibitor product candidates receive regulatory approval, we may decide to establish an internal sales or marketing team with technical expertise and supporting distribution capabilities to commercialize any future oral KIT inhibitor product candidates, which will be expensive and time consuming and will require significant attention of our executive officers to manage. For example, some state and local jurisdictions have licensing and continuing education requirements for pharmaceutical sales representatives, which requires time and financial resources. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of any future oral KIT inhibitor product candidates if we obtain approval to market.

With respect to the commercialization of all or certain of any future oral KIT inhibitor product candidates, if approved, we may choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment any future sales force and distribution systems of our own or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements when needed on acceptable terms, or at all, we may not be able to successfully commercialize any future oral KIT inhibitor product candidates if any receive regulatory approval or any such commercialization may experience delays or limitations. If we are not successful in commercializing any future oral KIT inhibitor product candidates, if approved, either on our own or through collaborations with one or more third parties, any future product revenue will suffer and we may incur significant additional losses.

If any future oral KIT inhibitor product candidates receives marketing approval and we or others later identify undesirable side effects caused by the product candidate, our ability to market and derive revenue from the product candidates could be compromised.

Undesirable side effects caused by any future oral KIT inhibitor product candidates could cause regulatory authorities to interrupt, delay or halt clinical trials and could result in more restrictive labeling or the delay or denial of regulatory approval by the FDA, EMA, or other regulatory authorities. Results of future clinical trials could reveal a high and unacceptable severity and prevalence of side effects. In such an event, our future clinical trials could be suspended or terminated and the FDA, EMA, or comparable foreign regulatory authorities could order us to cease further development of or deny approval of any future oral KIT inhibitor product candidates for any or all targeted indications. Such side effects could also affect patient recruitment or the ability of enrolled patients to initiate or complete the clinical trial or result in potential product liability claims. Any of these occurrences may materially and adversely affect our business, financial condition, results of operations and prospects.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of any future oral KIT inhibitor product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate.

In the event that any future oral KIT inhibitor product candidates receive regulatory approval and we or others identify undesirable side effects caused by such product, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we may be required to recall the product or change the way the product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a boxed warning or a contraindication;
- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of these occurrences could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Business and Operations

We expect to significantly expand our development, clinical and regulatory capabilities and operations as we grow our Company, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2022 we had 28 full-time employees. We expect to increase the number of our employees and the scope of our operations, particularly in the areas of clinical development, clinical operations, manufacturing, late-stage regulatory affairs, finance, accounting, business operations, public company compliance, communications and other corporate development functions, and, if any of our future oral KIT inhibitor product candidates receive regulatory and marketing approval, sales, marketing and distribution capabilities. If we acquire additional product candidates or enter into future collaborations, we may have to further expand our employee base beyond our current projections, which may include further nonclinical research and development or later-stage regulatory operations. 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 and the limited experience of our management team in managing a company with such anticipated growth and with developing sales, marketing and distribution infrastructure, we may not be able to effectively manage the 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.

Further, we currently rely, and for the foreseeable future will continue to rely, in substantial part on certain third-party contract organizations, advisors and consultants to provide certain services, including assuming substantial responsibilities for the conduct of our clinical trials and the manufacturing of any future oral KIT inhibitor product candidates. We cannot assure you that the services of such third-party contract organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by our third-party contract organizations, advisors or consultants is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of any future oral KIT inhibitor product candidates or otherwise advance our business. We cannot assure you that we will be able to properly manage our existing third-party contract organizations, advisors or consultants or find other competent outside third-party contract organizations, advisors and consultants on economically reasonable terms, or at all.

If we are not able to effectively manage growth and expand our Company, we may not be able to successfully implement the tasks necessary to further develop and commercialize, if approved, any future oral KIT inhibitor product candidates and, accordingly, we may not achieve our research, development and commercialization goals.

Our future performance depends on our ability to retain key employees and to attract, retain and motivate qualified personnel and manage our human capital.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries largely depends upon our ability to attract, motivate and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on the development and management expertise of our executive officer team. We currently do not maintain key person insurance on these individuals. The loss of one or more members of our management team or other key employees or advisors could delay our research and development programs and have a material and adverse effect on our business, financial condition, results of operations and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel, because of the highly technical nature of any future oral KIT inhibitor product candidates and technologies, and the specialized nature of the regulatory approval process. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty.

We primarily conduct our operations at our facilities in Cambridge, Massachusetts and San Francisco, California. These regions contain the headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in our market, and nationally, is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We also face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations. Our future performance will depend in large part on our continued ability to attract and retain highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation and commercialization. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover and develop product candidates will be limited, which could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future growth may depend, in part, on our ability to develop and commercialize any future oral KIT inhibitor product candidates in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any future oral KIT inhibitor product candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market and may never receive such regulatory approval for any future oral KIT inhibitor product candidates. To obtain separate regulatory approval in many other countries, we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of any future oral KIT inhibitor product candidates, and we cannot predict success in these jurisdictions. If we fail to comply with the regulatory requirements in international markets and receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of any future oral KIT inhibitor product candidates will be harmed and our business will be adversely affected. We may not obtain foreign regulatory approvals on a timely basis, if at all. Our failure to obtain approval of any future oral KIT inhibitor product candidates by regulatory authorities in another country may significantly diminish the commercial prospects of that product candidate and our business, financial condition, results of operations and prospects could be materially and adversely affected. Moreover, even if we obtain approval of any future oral KIT inhibitor product candidates and ultimately commercialize any future oral KIT inhibitor product candidates in foreign markets, we would be subject to the risks and uncertainties, including the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements and reduced protection of intellectual property rights in some foreign countries.

Our business depends on the efficient and uninterrupted operation of our information technology systems and those of our third-party CROs, CDMOs, or other vendors, contractors or consultants, may fail or suffer security breaches, cyber-attacks, loss or leakage of data and other disruptions, which could result in a material disruption of our development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.

Our business success depends on the security and efficient and uninterrupted operation of our information technology systems and we may be unable to adequately protect our information technology systems from cyber-attacks, which could result in the disclosure of confidential information, damage our reputation, and subject us to significant financial and legal exposure. We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to intellectual property, proprietary business information and sensitive personal information). It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We also have outsourced elements of our operations to third parties, and as a result we manage a number of third-party CROs, CDMOs, vendors and other contractors and consultants who have access to our confidential information. System failures or outages, including any potential disruptions due to significantly increased global demand on certain cloud-based systems during the remote work environment resulting from the ongoing COVID-19 pandemic, could compromise our ability to perform these functions in a timely manner, which could harm our ability to conduct business or delay our financial reporting.

Despite the implementation of security measures, given their size and complexity and the increasing amounts of confidential information that they maintain, our internal information technology systems and those of our third-party CROs, CDMOs, vendors and other contractors and consultants are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, accidents by our employees or third party service providers, natural disasters, terrorism, war, global pandemics, and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, third-party CROs, CDMOs, vendors, contractors, consultants, business partners and/or other third parties, or from cyber-attacks or supply chain attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure, or that of our third-party CROs, CDMOs, vendors and other contractors and consultants, or lead to data leakage. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity, and sophistication of attempted attacks and intrusions from around the world have increased. The ongoing COVID-19 pandemic is generally increasing the attack surface available for exploitation, as more companies and individuals work online and remotely, and as such, the risk of a cybersecurity incident occurring, and our investment in risk mitigations against such an incident, are increasing. For example, there has been an increase in phishing and spam email attacks as well as social engineering attempts from "hackers" hoping to use the ongoing COVID-19 pandemic to their advantage. We may not be able to anticipate all types of security threats, nor implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations, or hostile foreign governments or agencies. Any breach, loss or compromise of clinical trial participant personal data may also subject us to civil fines and penalties, including under the Health Insurance Portability and Accountability Act, or HIPAA, and other relevant state and federal privacy laws in the United States. If the information technology systems of our third-party CROs, CDMOs, vendors and other contractors and consultants become subject to disruptions or security breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring.

While we have not experienced any such system failure, accident or security breach to date, we cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, breaches in our systems, or those of our third-party CROs, CDMOs, vendors and other contractors and consultants, or other cyber incidents that could have a material adverse effect upon our reputation, business, operations, or financial condition. For example, if such an event were to occur and cause interruptions in our operations, or those of our third-party CROs, CDMOs, vendors and other contractors and consultants, it could result in a material disruption of our programs and the development of any of our future oral KIT inhibitor product candidates could be delayed. In addition, the loss of clinical trial data for any other future oral KIT inhibitor product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or those of our third-party CROs, CDMOs, vendors and other contractors and consultants, or security breaches could result in the loss, misappropriation and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and sensitive personal information), which could result in financial, legal, business and reputational harm to us.

A security breach could lead to claims by our counterparties that we have failed to comply with such legal or contractual obligations. As a result, we could be subject to legal action or our counterparties could end their relationships with us. There can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages.

In addition, litigation resulting from security breaches may adversely affect our business. Unauthorized access to our platform, systems, networks, or physical facilities could result in litigation with our counterparties. These proceedings could force us to spend money in defense or settlement, divert management's time and attention, increase our costs of doing business, or adversely affect our reputation. We could be required to fundamentally change our business activities and practices or modify our solutions and/or platform capabilities in response to such litigation, which could have an adverse effect on our business. If a security breach were to occur and the confidentiality, integrity or availability of our data or the data of our partners, patients or our counterparties was disrupted, we could incur significant liability, or our platform, systems or networks may be perceived as less desirable, which could negatively affect our business and damage our reputation.

We may not have adequate insurance coverage with respect to security breaches or disruptions. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co-insurance requirements), could have an adverse effect on our business. In addition, we cannot be sure that our existing insurance coverage and coverage for errors and omissions will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim.

Our business entails a significant risk of product liability and our ability to obtain sufficient insurance coverage could have a material and adverse effect on our business, financial condition, results of operations and prospects.

When we conduct clinical trials of our product candidates, we may be exposed to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing products, if approved, such claims could result in an FDA investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs and potentially a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, termination of clinical trial sites or entire trial programs, withdrawal of clinical trial participants, injury to our reputation and significant negative media attention, significant costs to defend the related litigation, a diversion of management's time and our resources from our business operations, substantial monetary awards to trial participants or patients, loss of revenue, the inability to commercialize any products that we may develop, and a decline in our stock price. We currently maintain general liability insurance. We may, however, need to obtain higher levels of product liability insurance for later stages of clinical development or marketing any of our product candidates. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to comply with FDA regulations, provide true, complete and accurate information to the FDA, EMA and other similar foreign regulatory bodies, comply with manufacturing standards we may establish, comply with healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. If we obtain FDA approval of any future oral KIT inhibitor product candidates and begin commercializing those products in the United States, our potential exposure under these laws will increase significantly, and our costs associated with compliance with these laws will likely increase. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, 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. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. It is not always possible to identify and deter employee misconduct, 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 such laws or regulations. 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 material and adverse effect on our business, financial condition, results of operations and prospects, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, EMA, or other foreign regulatory body exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, integrity oversight and reporting obligations, or reputational harm.

If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be affected adversely.

Our research and development activities involve the use of hazardous chemicals and materials, including radioactive materials. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous chemicals and materials. We believe our procedures for storing, handling and disposing these materials in our facilities comply with the relevant guidelines of Middlesex County, Massachusetts. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by applicable regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of animals and biohazardous materials. 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 these materials, this insurance may not provide adequate coverage against potential liabilities. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

We, or the third parties on whom we depend, may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemic, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our CDMOs, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Extreme weather conditions or other natural disasters could further disrupt our operations and have a material and adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our CDMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time, if at all.

Our employees often conduct business outside of any facilities leased by us. These locations may be subject to additional security and other risk factors due to the limited control of our employees. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our CDMOs, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Changes in tax laws or regulations that are applied adversely to us may have a material adverse effect on our business, cash flow, financial condition or results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Cuts and Jobs Act, enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Cuts and Jobs Act may affect us, and certain aspects of the Tax Cuts and Jobs Act could be repealed or modified under proposed legislation. In addition, it is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act, the CARES Act, or any other newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Cuts and Jobs Act, the CARES Act or future reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. Under the Tax Cuts and Jobs Act, as modified by the CARES Act, unused U.S. federal net operating losses generated in tax years beginning after December 31, 2017, will not expire and may be carried forward indefinitely but the deductibility of such federal net operating losses for any year is limited to no more than 80% of the excess, if any, of current year taxable income (without regard to certain deductions) over the amount of federal net operating losses generated in tax years beginning before January 1, 2018 that are deducted in the current year. It is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act or the CARES Act. In addition, both our current and our future unused losses and other tax attributes may be subject to limitation under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, if we undergo, or have undergone, an "ownership change," generally defined as a greater than 50 percentage point change (by value) in our equity ownership by certain stockholders over a three-year period. We have not completed a Section 382 study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since our formation due to the complexity and cost associated with such a study and the fact that there may be additional ownership changes in the future. As a result, if we undergo an ownership change, our ability to use all of our pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset our post-change income or taxes may be limited. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of net operating losses is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, even if we attain profitability, we may be unable to use all or a material portion of our net operating losses and other tax attributes, which could adversely affect our future cash flows.

Risks Related to Our Reliance on Third Parties

We rely, and intend to continue to rely, on third parties to conduct our clinical trials and perform all of our research and nonclinical studies. If these third parties do not satisfactorily carry out their contractual duties, fail to comply with applicable regulatory requirements or do not meet expected deadlines, our development programs may be delayed or subject to increased costs or we may be unable to obtain regulatory approval, each of which may have an adverse effect on our business, financial condition, results of operations and prospects.

We do not have the ability to independently conduct all aspects of our nonclinical testing or clinical trials ourselves. As a result, we are dependent on third parties to conduct our ongoing and planned nonclinical studies and clinical trials of our future product candidates. The timing of the initiation and completion of these trials will therefore be partially controlled by such third parties and may result in delays to our development programs. Specifically, we expect CROs, clinical investigators and consultants to play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these CROs and other third parties are not our employees, and we will not be able to control all aspects of their activities. Nevertheless, we are responsible for ensuring that each clinical trial is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with good clinical practices, or GCP, requirements, which are regulations and guidelines enforced by the FDA for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the data generated in our clinical trials may be deemed unreliable, and the FDA 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 our clinical trials comply with GCPs. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure, or the failure of third parties on whom we rely, to comply with these regulations may require us to stop and/or repeat clinical trials, which would delay the marketing approval process.

There is no guarantee that any such CROs, clinical trial investigators or other third parties on which we rely will devote adequate time and resources to our development activities or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise perform in a substandard manner, or terminate their engagements with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If our clinical trial site terminates for any reason, we may experience the loss of follow-up information on patients enrolled in such clinical trial unless we are able to transfer those patients to another qualified clinical trial site, which may be difficult or impossible.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting clinical trials or other product development activities that could harm our competitive position. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any other future oral KIT inhibitor product candidates and will not be able to, or may be delayed in our efforts to, commercialize our products, if approved.

We may, in the future, enter into collaborations with third parties for the discovery, development and commercialization of product candidates, if approved. If those collaborations are not successful, we may not be able to capitalize on the market potential of any future oral KIT inhibitor product candidates.

We may seek third-party collaborators for the development and commercialization of any future oral KIT inhibitor product candidates, if approved, on a select basis, including potentially in specific foreign jurisdictions. We have not entered into any collaborations to date. Our likely collaborators for any future collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We will face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for a future collaboration will depend, among other things, upon our assessment of the future collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of our business.

If we do enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our future collaborators dedicate to the development or commercialization of any future oral KIT inhibitor product candidates. Our ability to generate revenues from these arrangements will depend on our future collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations with future collaborators involving any future oral KIT inhibitor product candidates would pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may de-emphasize or not pursue development and commercialization of any future oral KIT inhibitor product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, including as a result of a sale or disposition of a business unit or development function, or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with any future oral KIT inhibitor product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product, if approved, relative to other products;
- collaborators may not properly obtain, maintain, defend or enforce our intellectual property rights or may use our proprietary information and intellectual property in such a way as to invite litigation or other intellectual property related proceedings that could jeopardize or invalidate our proprietary information and intellectual property or expose us to potential litigation or other intellectual property related proceedings;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or, if approved, commercialization of any future oral KIT inhibitor product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or, if approved, commercialization of the applicable product candidates;
- collaboration agreements may not lead to development or, if approved, commercialization of product candidates in the most efficient manner or at all; and
- if a future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or, if approved, commercialization program could be delayed, diminished or terminated.

If we establish one or more collaborations, all of the risks relating to product development, regulatory approval and, if approved, commercialization described above would also apply to the activities of any such future collaborators.

We rely on third-party manufacturers and suppliers to supply components of any future oral KIT inhibitor product candidates. The loss of our third-party manufacturers or suppliers, or our or their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, would materially and adversely affect our business.

We do not own or operate facilities for drug manufacturing, storage, distribution or quality testing. We currently rely, and may continue to rely, on CDMOs, including in the United States, China and Europe, to manufacture bulk drug substances, drug products, raw materials, samples, components, or other materials and reports. Reliance on CDMOs may expose us to different risks than if we were to manufacture product candidates ourselves. There can be no assurance that our nonclinical and clinical development product supplies will not be limited, interrupted, terminated or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of our CDMOs could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA, EMA and other foreign regulatory authority review. We, and our suppliers and manufacturers, must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as current Good Manufacturing Practices, or cGMPs. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA, EMA and other foreign regulatory authorities. If our contract manufacturers are unable to maintain a compliance status acceptable to the FDA, EMA and other foreign regulatory authorities, any future oral KIT inhibitor product candidates may not be approved. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or comparable foreign regulatory authorities, we may not be able to rely on their manufacturing facilities for the manufacture of components of any future oral KIT inhibitor product candidates. Moreover, although we do not control the manufacturing process at our contract manufacturers and are completely dependent on them for compliance with current regulatory requirements, we are nonetheless responsible for ensuring that any future oral KIT inhibitor product candidates are manufactured in accordance with applicable laws and regulatory requirements. In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture any future oral KIT inhibitor product candidates may be unique or proprietary to the original contract manufacturer and we may have difficulty transferring the manufacturing of any future oral KIT inhibitor product candidates to another third party. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to enable us, or to have another third party, manufacture any future oral KIT inhibitor product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines, and we may be required to repeat some of the development program. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on CDMOs if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. Any manufacturing facilities used to produce any future oral KIT inhibitor product candidates will be subject to periodic review and inspection by the FDA, EMA and other foreign regulatory authorities, including for continued compliance with cGMP requirements, quality control, quality assurance and corresponding maintenance of records and documents. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize any future oral KIT inhibitor product candidates, if approves. Our or a third party's failure to execute on our manufacturing requirements, to comply with cGMPs or to maintain a compliance status acceptable to the FDA, EMA or other foreign regulatory authorities could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, if any, for product candidates;
- loss of the cooperation of future collaborators;
- subjecting third-party manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of any future oral KIT inhibitor product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

Additionally, our contract manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our contract manufacturers were to encounter any of these difficulties, our ability to provide any future oral KIT inhibitor product candidates to patients in nonclinical and clinical trials, or to provide products for treatment of patients, if approved and commercialized, would be jeopardized.

Risks Related to Intellectual Property

If we are not able to obtain, maintain and enforce patent protection for our technologies or product candidates, development and commercialization, if approved, of any future oral KIT inhibitor product candidates may be adversely affected.

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for any future oral KIT inhibitor product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. Currently, our intellectual property protection includes patent applications owned by us and patents and patent applications that we have in-licensed from Novartis Pharma AG., or Novartis, under the Novartis License Agreement. We may not be able to apply for patents on certain aspects of any future oral KIT inhibitor product candidates in a timely fashion or at all. Further, we may not be able to prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. 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.

There may be circumstances where we may not have the right to control the preparation, filing and prosecution of all patent applications that we license from third parties, or to maintain and/or enforce the rights to patents licensed from third parties, in which case, we will be dependent on our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property. Our licensors may not successfully prosecute the patent applications that are licensed to us and even if patents are issued in respect of these patent applications, our licensors may fail to maintain these patents or may determine not to pursue litigation against other companies that are infringing these patents. In other words, such licensed patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Further, we cannot be certain that such activities related to the preparation, filing, prosecution, maintenance and/or enforcement of the licensed patent rights by licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patent rights. We may have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the licensed patent rights, or defend certain of the licensed patent rights. It is possible that the licensor's infringement proceeding or defense activities with respect to the licensed patent rights may be less vigorous than had we conducted them ourselves. In the event our licensors fail to adequately pursue and maintain patent protection for the licensed patents and patent applications they control, and to timely cede control of such prosecution and/or enforcement to us, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our future issued or granted patents will not later be found to be invalid or unenforceable or that any future issued or granted patents will include claims that are sufficiently broad to cover any future oral KIT inhibitor product candidates or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and biopharmaceutical companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents, or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely affect our position in the market.

Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. 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 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

The U.S. Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a large number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and biopharmaceutical patents. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. The process of obtaining patents is time consuming, expensive and sometimes unpredictable.

Once granted, for a given period after allowance or grant patents may remain open to opposition, interference, re-examination, post-grant review, *inter partes* review, nullification, or derivation action in court or before patent offices or similar proceedings, during which time third parties can raise objections against such initial grant. Such proceedings may continue for a protracted period of time and an adverse determination in any such proceedings could reduce the scope of the allowed or granted claims thus attacked, or could result in our patents being invalidated in whole or in part, or being held unenforceable, which could allow third parties to commercialize any future oral KIT inhibitor product candidates and compete directly with us without payment to us. In addition, there can be no assurance that:

- others will not or may not be able to make, use or sell compounds that are the same as or similar to any future oral KIT inhibitor product candidates but that are not covered by the claims of the patents that we own or license;
- we or our licensors, or our existing or future collaborators are the first to make the inventions covered by each of our issued patents and pending patent applications that we own or license;
- we or our licensors, or our existing or future collaborators are the first to file patent applications covering certain aspects of our inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- a third party may not challenge our patents and, if challenged, a court would hold that our patents are valid, enforceable and infringed;
- any issued patents that we own or have licensed or that we may license in the future will provide us with any competitive advantages, or will not be challenged by third parties;
- we may develop additional proprietary technologies that are patentable;
- the patents of others will not have a material or adverse effect on our business, financial condition, results of operations and prospects; and
- our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

If we or our licensors fail to maintain the patents and patent applications covering any future oral KIT inhibitor product candidates, our competitors might be able to enter the market, which could have a material and adverse effect on our business, financial condition, results of operations and prospects. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection for certain aspects of any future oral KIT inhibitor product candidates, we also consider trade secrets, including confidential and unpatented know-how, important to the maintenance of our competitive position. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed. We seek to protect trade secrets and confidential and unpatented know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants that obligate them to maintain confidentiality and assign their inventions to us. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts in the United States and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed which could have a material and adverse effect on our business, financial condition, results of operations and prospects.

If we breach our license agreements, it could have a material adverse effect on our commercialization efforts for any future oral KIT inhibitor product candidates.

We are party to a license agreement, the Novartis Agreement, that enable us to utilize third-party intellectual property in the development of our prior product candidate, THB001, and we may in the future enter into more such license agreements with third parties under which we license the use, development and commercialization rights to any future oral KIT inhibitor product candidates or technology from third parties.

These intellectual property license agreements may require us to comply with various obligations, including diligence obligations such as development and commercialization obligations, as well as potential royalty and milestone payments and other obligations. If we fail to comply with our obligations under any of these license agreements, use the licensed intellectual property in an unauthorized manner, we are subject to bankruptcy-related proceedings or otherwise materially breach any of these license agreements, the terms of the license granted may be materially modified, such as by rendering currently exclusive licenses non-exclusive, or it may give our licensors the right to terminate the applicable license agreement, in whole or in part. Generally, the loss of or termination of our rights under the Novartis Agreement, or any other licenses we may acquire in the future, could harm our business, financial condition, results of operations and prospects.

We may also, in the future, enter into license agreements with third parties under which we are a sublicensee. If our sublicensor fails to comply with its obligations under its upstream license agreement with its licensor, the licensor may have the right to terminate the upstream license, which may result in termination of our sublicense. If this were to occur, we would no longer have rights to the applicable intellectual property unless we are able to secure our own direct license with the owner of the relevant rights, which we may not be able to do on reasonable terms, or at all, which may impact our ability to continue to develop and commercialize any future oral KIT inhibitor product candidates incorporating the relevant intellectual property.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may 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 on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other intellectual property 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 any future oral KIT inhibitor product candidates, and what activities satisfy those diligence obligations;
- our right to transfer or assign the license;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- whether and the extent to which inventors are able to contest the assignment of their rights to our licensors.

If disputes over intellectual property that we have licensed or license in the future prevent or impair our ability to maintain our current licensing arrangements on acceptable terms or at all, we may be unable to successfully develop and commercialize the affected product candidates, which could have material adverse effect on our business. In addition, if disputes arise as to ownership of licensed intellectual property, our ability to pursue or enforce the licensed patent rights may be jeopardized. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer. Further, certain of our future license agreements with third parties may limit or delay our ability to consummate certain transactions, may impact the value of those transactions or may limit our ability to pursue certain activities (e.g., we may in the future enter into license agreements that are not assignable or transferable, or that require the licensor's express consent in order for an assignment or transfer to take place).

Our intellectual property licensed from various third parties may be subject to retained rights.

Licensors often retain certain rights under license agreements, including the right to use the underlying licensed intellectual property for non-commercial academic and research use, to publish general scientific findings from research related to the licensed intellectual property, and to make customary scientific and scholarly disclosures of information relating to the licensed intellectual property. It is difficult to monitor whether licensors limit their use of the licensed intellectual property to these uses, and we could incur substantial expenses to enforce our rights to our licensed intellectual property in the event of misuse.

In addition, the United States federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act, or the Bayh-Dole Act. The federal government retains a "nonexclusive, nontransferable, irrevocable, paid-up license" for its own benefit. The Bayh Dole Act also provides federal agencies with "march-in rights." March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a "nonexclusive, partially exclusive, or exclusive license" to a "responsible applicant or applicants." If the patent owner refuses to do so, the government may grant the license itself. In the future, we may need to collaborate with academic institutions to accelerate our research or development with respect to any future oral KIT inhibitor product candidates. While we try to avoid engaging our university partners in projects in which there is a risk that federal funds may be commingled, we cannot guarantee that any co-developed intellectual property will be free from government rights pursuant to the Bayh-Dole Act. If, in the future, we co-own or license intellectual property which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh Dole Act, our ability to enforce or otherwise exploit such licensed intellectual property may be adversely affected.

Our strategy of obtaining rights to key technologies through in-licenses may not be successful.

We may seek to expand our product candidate pipeline in part by in-licensing the rights to key technologies. The future growth of our business will depend in part on our ability to in-license or otherwise acquire the rights to additional product candidates or technologies. We cannot assure you that we will be able to in-license or acquire the rights to any product candidates or technologies from third parties on acceptable terms or at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

The in-licensing and acquisition of these technologies is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire product candidates or technologies that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to license rights to us. Furthermore, we may be unable to identify suitable product candidates or technologies within our area of focus. If we are unable to successfully obtain rights to suitable product candidates or technologies, our business, financial condition, results of operations and prospects could suffer.

Other companies or organizations may challenge our or our licensors' patent rights or may assert patent rights that prevent us from developing and commercializing our products.

Oral KIT inhibitor therapies for the treatment of mast cell-mediated mast cell driven inflammatory disease are a relatively new scientific field. In addition to patent applications that we own or in-license to KIT inhibitor therapies, there are pending patent applications by others in the United States and in key markets around the world that claim many different methods, compositions and processes relating to the discovery, development and manufacture of small-molecule KIT inhibitor-based and other therapeutics.

As the field of small-molecule KIT inhibitor-based therapeutics continues to mature, patent applications are being processed by national patent offices around the world. There is uncertainty about which patents will issue and, if they do, as to when, to whom, and with what claims. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material and adverse effect on our business, financial condition, results of operations and prospects or our ability to successfully compete. If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, defending and enforcing patents covering our technology in the United States and in other jurisdictions worldwide would be extremely costly, and our or our licensors' or collaborators' intellectual property rights may not exist in some countries outside the United States or may be less extensive in some countries than in the United States. In jurisdictions where we or our licensors or collaborators have not obtained patent protection, competitors may seek to use our or our licensors' or collaborators' technology to develop competing products and further, may export otherwise infringing products to territories where we have patent protection, but where it is more difficult to enforce a patent as compared to the United States. Competitor products may compete with our future products in jurisdictions where we do not have issued or granted patents or where our or our licensors' or collaborators' issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce patents and such countries may not recognize other types of intellectual property protection, particularly relating to pharmaceuticals or biopharmaceuticals. This could make it difficult for us or our licensors or collaborators to prevent the infringement of our or their patents or marketing of competing products in violation of our or their proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our and our licensors' or collaborators' efforts and attention from other aspects of our business, could put our and our licensors' or collaborators' patents at risk of being invalidated or interpreted narrowly and our and our licensors' or collaborators' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors or collaborators. We or our licensors or collaborators may not prevail in any lawsuits that we or our licensors or collaborators initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful.

When we elect to pursue patent protection on an invention, we generally first file a U.S. provisional patent application (a priority filing) at the USPTO. An international patent application under the Patent Cooperation Treaty, or PCT, is then usually filed within twelve months after the priority filing. Based on the PCT filing, national and regional patent applications may be filed in the United States, the European Patent Office and, depending on the individual case, also in any or all of, *inter alia*, Australia, Brazil, Canada, China, Hong Kong, India, Israel, Japan, Mexico, New Zealand, Eurasia, South Africa, South Korea and other jurisdictions. We have thus far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each national or regional patent office is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant registration authorities, while granted by others. It is also quite common that, depending on the country, various scopes of patent protection may be granted on the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the United States, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we or our licensors or collaborators encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions. 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 a patent. If we or any of our licensors or collaborators are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position in the relevant jurisdiction may be impaired and our business, financial condition, results of operations and prospects may be adversely affected.

We, our licensors or collaborators, or any future strategic partners may need to resort to litigation to protect or enforce our patents, if and when granted, or other proprietary rights, all of which could be costly, time consuming, delay or prevent the development and commercialization of any future oral KIT inhibitor product candidates, or put our patents, if and when granted, and other proprietary rights at risk.

Competitors may infringe our patents, if and when granted, or other intellectual property. If we were to initiate legal proceedings against a third party to enforce a patent covering one of our products or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, lack of adequate written description, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that an individual connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity or unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could have a material and adverse effect on our business, financial condition, results of operations and prospects. Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the inventorship or priority of inventions with respect to our patents or patent applications. An unfavorable outcome 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 or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring any future oral KIT inhibitor product candidates to market. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. Patents and other intellectual property rights will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights.

Intellectual property rights of third parties could adversely affect our ability to commercialize any future oral KIT inhibitor product candidates, and we, our licensors or collaborators, or any future strategic partners may become subject to third party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights. We might be required to litigate or obtain licenses from third parties in order to develop or market any future oral KIT inhibitor product candidates. Such litigation or licenses could be costly or not available on commercially reasonable terms.

We, our licensors or collaborators, or any future strategic partners, may be subject to third-party claims for infringement or misappropriation of patent or other proprietary rights. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries, including patent infringement lawsuits, interferences, derivations, post-grant reviews, oppositions and *inter partes* review proceedings before the USPTO, and corresponding foreign patent offices. There may be issued patents and pending patent applications that claim aspects of our targets or any future oral KIT inhibitor product candidates and modifications that we may need to apply to any future oral KIT inhibitor product candidates. There may be issued patents that claim KIT inhibitors which may be relevant to the products we wish to develop. Thus, it is possible that one or more organizations will hold patent rights to which we will need a license. If those organizations refuse to grant us a license to such patent rights on reasonable terms, we may not be able to market products or perform research and development or other activities covered by these patents, which could have a material and adverse effect on our business, financial condition, results of operations and prospects. If we, our licensors or collaborators, or any future strategic partners are found to infringe a third-party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages and attorneys' fees if we or they are found to have infringed willfully. In addition, we, our licensors or collaborators, or any future strategic partners may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we or our existing or future collaborators may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation could divert our management's attention. 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

Our competitive position may suffer if patents issued to third parties or other third-party intellectual property rights cover our products or product candidates or elements thereof, or our manufacture or uses relevant to our development plans. In such cases, we may not be in a position to develop or commercialize products or product candidates until such patents expire or unless we successfully pursue litigation to nullify or invalidate the third-party intellectual property right concerned, or enter into a license agreement with the intellectual property right holder, if available on commercially reasonable terms. There may be issued patents of which we are not aware, held by third parties that, if found to be valid and enforceable, could be alleged to be infringed by any future oral KIT inhibitor product candidates. There also may be pending patent applications of which we are not aware that may result in issued patents, which could be alleged to be infringed by any future oral KIT inhibitor product candidates. If such an infringement claim should be brought and be successful, we may be required to pay substantial damages, including potentially treble damages and attorneys' fees for willful infringement, and we may be forced to abandon any future oral KIT inhibitor product candidates or seek a license from any patent holders. No assurances can be given that a license will be available on commercially reasonable terms, if at all.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, in certain situations, a U.S. patent application can remain confidential until the patent application issues as a U.S. patent. International patent applications and parallel 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 products could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our products or the use of our products. Third-party intellectual property right holders may also actively bring infringement claims against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or continue costly, unpredictable and time-consuming litigation and may be prevented from or experience substantial delays in marketing our products. Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, financial condition, results of operations and prospects. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing of our future oral KIT inhibitor product candidates that are held to be infringing. We might, if possible, also be forced to redesign product candidates so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business and could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation and other legal proceedings relating to intellectual property claims, with or without merit, are unpredictable and generally expensive and time consuming and are likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments 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. Moreover, such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

We may be subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel.

Many of our employees, including our management, were previously employed at biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Some of these employees executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper our ability to develop and ultimately commercialize, or prevent us from developing and commercializing, any future oral KIT inhibitor product candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Patent terms may be insufficient to protect our competitive position on any future oral KIT inhibitor product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various patent term adjustments or extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering any future oral KIT inhibitor product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. 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, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and/or rely on our outside counsel to pay these fees due to the USPTO and non-U.S. governmental patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop and our technology, our U.S. patent or one or more U.S. patents that may issue in the future based on a patent application that we license or may own may be eligible for limited patent term extension under Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved product, a method for using it or a method for manufacturing it may be extended. The application for the extension must be submitted prior to the expiration of the patent for which extension is sought and within 60 days of FDA approval. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue patent term extension based on a patent that we in-license from a third party, we would need the cooperation of that third party. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in U.S. patent and ex-U.S. patent laws could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of the patent laws in the United States or in other jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. In the United States, numerous recent changes to the patent laws and proposed changes to the rules of the USPTO may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the America Invents Act, involved significant changes in patent legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, some of which cases either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. For example, the decision by the *U.S. Supreme Court in Association for Molecular Pathology v. Myriad Genetics, Inc.* precludes a claim to a nucleic acid having a stated nucleotide sequence that is identical to a sequence found in nature and unmodified. Moreover, in 2012, the USPTO issued a guidance memo to patent examiners indicating that process claims directed to a law of nature, a natural phenomenon or a naturally occurring relation or correlation that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should be rejected as directed to patent-ineligible subject matter. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once granted. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, and similar legislative and regulatory bodies in other countries in which may pursue patent protection, the laws and regulations governing patents could change in unpredictable ways, particularly with respect to pharmaceutical patent protection, that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Risks Related to Government Regulation

The regulatory approval process is highly uncertain, and we may be unable to obtain, or may be delayed in obtaining, U.S. or foreign regulatory approval and, as a result, unable to commercialize any future oral KIT inhibitor product candidates. Even if we believe our development plans are successful, regulatory authorities may not agree that they provide adequate data on safety or efficacy.

Any of our future oral KIT inhibitor product candidates will be subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, post-approval monitoring, marketing and distribution of drugs. Rigorous nonclinical testing and clinical trials and an extensive regulatory approval process are required to be completed successfully in the United States and in many foreign jurisdictions before a new drug can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the product candidates we may develop will obtain the regulatory approvals necessary for us to begin selling them.

We have no prior experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. The time required to obtain FDA and other approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its foreign counterparts use when regulating us require judgment and can change, which makes it difficult to predict with certainty their application. Any analysis we perform of data from nonclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. Further, infections and deaths related to COVID-19 are disrupting certain healthcare and healthcare regulatory systems globally. Such disruptions could divert healthcare resources away from, or materially delay review by, the FDA and comparable foreign regulatory agencies. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of nonclinical studies or clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of THB001 or any future product candidates. It is impossible to predict whether additional legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or the impact of such changes, if any.

Further, the FDA and its foreign counterparts may respond to any NDA that we may submit by defining requirements that we do not anticipate. Such responses could delay clinical development of any future oral KIT inhibitor product candidates.

Any delay or failure in obtaining required approvals could have a material and adverse effect on our ability to generate revenues from the particular product candidate for which we are seeking approval. Furthermore, any regulatory approval to market a product may be subject to limitations on the approved uses for which we may market the product or on the labeling or other restrictions.

We are also subject to or may in the future become subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with the FDA approval process described above, as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. FDA approval does not ensure approval by regulatory authorities outside the United States and vice versa. Any delay or failure to obtain U.S. or foreign regulatory approval for a product candidate could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Even if we receive regulatory approval for any future oral KIT inhibitor product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, any future product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal. We may also be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we obtain for any of our future oral KIT inhibitor product candidates may also be subject to limitations on the approved indicated uses for which a product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing and surveillance to monitor the safety and efficacy of the product candidate.

In addition, if the FDA or a comparable foreign regulatory authority approves any of our future oral KIT inhibitor product candidates, the manufacturing processes, labeling, packaging, distribution, post-approval monitoring and adverse event reporting, storage, import, export, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. The FDA has significant post-market authority, including the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate safety risks related to the use of a product or to require withdrawal of the product from the market. The FDA also has the authority to require a REMS after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. The manufacturing facilities we use to make a future oral KIT inhibitor product, if any, will also be subject to periodic review and inspection by the FDA and other regulatory agencies, including for continued compliance with cGMP requirements. The discovery of any new or previously unknown problems with our CDMOs, manufacturing processes or facilities may result in restrictions on the product, manufacturer or facility, including withdrawal of the product from the market. If we rely on CDMOs, we will not have control over compliance with applicable rules and regulations by such manufacturers. Any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products. If we promote any of our future oral KIT inhibitor product candidates in a manner inconsistent with FDA-approved labeling or otherwise not in compliance with FDA regulations, we may be subject to enforcement action. Moreover, while we believe that any future oral KIT inhibitor product candidates may provide better safety or effectiveness as compared to approved products, if we do not study any future oral KIT inhibitor product candidates in head-to-head trials with those products, we will not be able to make comparative claims for our products, if approved. If we or our, manufacturers or service providers fail to comply with applicable continuing regulatory requirements in the United States or foreign jurisdictions in which we seek to market our products, we or they may be subject to, among other things, fines, warning letters, holds on clinical trials, delay of approval or refusal by the FDA or similar foreign regulatory bodies to approve pending applications or supplements to approved applications, suspension or withdrawal of regulatory approval, product recalls and seizures, administrative detention of products, refusal to permit the import or export of products, operating restrictions, injunction, civil penalties and criminal prosecution.

Subsequent discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our CDMOs 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;
- fines, warning or untitled letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our strategic partners;
- suspension or revocation of product license 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 policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of any of our future oral KIT inhibitor 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 marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. Changes in FDA staffing could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. Similar consequences would also result in the event of another significant shutdown of the federal government such as the one that occurred from December 22, 2018 through January 25, 2019. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If any legislation, executive orders, or lapses in agency funding impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Our operations and relationships with healthcare providers, healthcare organizations, customers and third-party payors will be subject to applicable anti-bribery, anti-kickback, fraud and abuse, transparency and other healthcare and privacy laws and regulations, which could expose us to, among other things, enforcement actions, criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Our current and future arrangements with healthcare providers, healthcare organizations, third-party payors and customers expose us to broadly applicable anti-bribery, fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research as well as market, sell and distribute any of our future oral KIT inhibitor product candidates. In addition, we may be subject to patient data privacy and security regulation by the U.S. federal government and the states and the foreign governments in which we conduct our business. Restrictions under applicable federal and state anti-bribery and healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, individuals and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, 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 under a federal and state healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal criminal and civil false claims and civil monetary penalties laws, including the federal False Claims Act, which can be enforced through civil whistleblower or qui tam actions against individuals or entities, prohibits, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent,. knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Moreover, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act;
- HIPAA, which prohibits, among other things, knowingly and willfully executing, or attempting to execute a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, which impose obligations on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as their business associates and their covered subcontractors that perform certain services involving the storage, use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;

- the federal legislation commonly referred to as 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, and its implementing regulations, which requires certain manufacturers of covered drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with certain exceptions, to report annually to CMS information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members, with the information made publicly available on a searchable website;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and
- certain state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing information, state and local laws that require the registration of pharmaceutical sales representatives, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our current and 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, agency guidance 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 such requirements, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, integrity oversight and reporting obligations, or reputational harm, any of which could adversely affect our financial results.

These risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

We are subject to stringent and changing obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; loss of customers or sales; and other adverse business consequences.

In the ordinary course of business, we process personal data and other sensitive information, including our proprietary and confidential business data, trade secrets, intellectual property, data we collect about trial participants in connection with clinical trials, and other sensitive data. Our data processing activities subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contracts and other obligations that govern the processing of personal data by us and on our behalf.

In the United States, federal, state and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws and consumer protection laws. For example, the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, imposes specific requirements relating to the privacy, security and transmission of individually identifiable health information. At the state level, the California Consumer Privacy Act of 2018, or CCPA, imposes obligations on businesses to which it applies. These obligations include, but are not limited to, providing specific disclosures in privacy notices and affording California residents certain rights related to their personal data. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA could increase compliance costs and potential liability. In addition, it is anticipated that the California Privacy Rights Act of 2020, or CPRA, effective January 1, 2023, will expand the CCPA. Other states have also enacted or proposed data privacy laws, which could further complicate compliance efforts.

Outside the United States, the European Union's General Data Protection Regulation, or EU GDPR, and the United Kingdom's GDPR, or UK GDPR, impose strict requirements for processing the personal data of individuals. For example, under the EU GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines of up to 20 million euros or 4% of annual global revenue, whichever is greater. Further, individuals may initiate litigation related to our processing of their personal data. Certain foreign jurisdictions have enacted data localization laws and cross-border personal data transfer laws, which could make it more difficult to transfer information across jurisdictions (such as transferring or receiving personal data that originates in the EU).

Although we endeavor to comply with all applicable data privacy and security obligations, these obligations are quickly changing, creating some uncertainty as to how to comply. Further, we may at times fail (or be perceived to have failed) to have complied and could face significant consequences. These consequences may include, but are not limited to, government enforcement actions (e.g., investigations, fines, penalties, audits, inspections and similar); litigation (including class-related claims); additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials.

Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including our clinical trials); interruptions or stoppages of data collection needed to train our algorithms; inability to process personal data or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring of our operations.

We may face difficulties from healthcare legislative and regulatory reform measures.

Existing laws and regulatory policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of any of our future oral KIT inhibitor product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, or may face penalties for any approved products, and we may not achieve or sustain profitability.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. Among other things, the ACA, enacted in 2010, increased manufacturers' rebate liability under the Medicaid Drug Rebate Program, imposed a significant annual fee on companies that manufacture or import branded prescription drug products and required manufacturers to provide a discount off the negotiated price of prescriptions filled by beneficiaries in the Medicare Part D coverage gap, referred to as the "donut hole," which is now 70% of the negotiated price.

These initiatives recently culminated in the enactment of the Inflation Reduction Act, or IRA, in August 2022, which, among other things, will allow HHS to negotiate the selling price of certain drugs and biologics that CMS reimburses under Medicare Part B and Part D, although only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected, with the negotiated price taking effect two years after the selection year. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price representing a significant discount from average prices to wholesalers and direct purchasers. Beginning in October 2022 for Medicare Part D and January 2023 for Medicare Part B, the law also penalizes drug manufacturers that increase prices of Medicare Part D and Part B drugs at a rate greater than the rate of inflation. In addition, the law eliminates the "donut hole" under Medicare Part D beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. Thus, it is unclear how the IRA will be implemented but will likely have a significant impact on the pharmaceutical industry.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including restrictions or prohibitions on certain marketing practices, reporting of specified categories of remuneration provided to health care practitioners, and reporting and justification of price increases greater than a specified level. In some cases, states have designed programs to encourage importation from other countries and bulk purchasing, though the federal government has not yet approved any such plans. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for pharmaceuticals and other healthcare products and services, which could result in reduced demand for any future oral KIT inhibitor product candidates or companion diagnostics or additional pricing pressures.

We expect that other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

Even if we are able to commercialize any of our future oral KIT inhibitor product candidates, such product candidate may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.

The regulations that govern regulatory approvals, pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, prescription biopharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any of our future oral KIT inhibitor product candidates obtain regulatory approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors including government authorities, such as Medicare and Medicaid, private health insurers and other organizations. Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Coverage and adequate reimbursement from third-party payors are critical to new product acceptance. Even if we succeed in bringing one or more products to the market, these products may not be considered cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost effectiveness or the likely level or method of coverage and reimbursement. Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for biopharmaceutical products. If the price we are able to charge for any products we develop, or the coverage and reimbursement provided for such products, is inadequate in light of our development and other costs, our return on investment could be affected adversely.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug or therapeutic biologic will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution.

Interim reimbursement levels for new drugs, if applicable, may also be insufficient to cover our costs and may not be made permanent. Reimbursement rates may be based on payments allowed for lower cost drugs that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. As a result, obtaining coverage and reimbursement approval of a product from a third-party payor is a time consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for new drugs that we develop and for which we obtain regulatory approval could have a material and adverse effect on our business, financial condition, results of operations and prospects.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, or FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Export controls and trade sanctions laws and regulations may restrict or prohibit altogether the provision, sale, or supply of any future oral KIT inhibitor product candidates to certain governments, persons, entities, countries and territories, including those that are the target of comprehensive sanctions or an embargo. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents and contractors, from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties to sell our products outside the United States, to conduct clinical trials, and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, or other partners even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenue, if any.

In some countries, particularly member states of the European Union, or EU, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. 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 EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. To obtain coverage and reimbursement or pricing approvals in some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of any future oral KIT inhibitor product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be materially and adversely affected.

Risks Related to Our Common Stock

An active and liquid trading market for our common stock may never be sustained and you may not be able to resell your shares of common stock at or above the purchase price, if at all.

An active trading market for our shares may never develop or be sustained. The market value of our common stock may decrease from the purchase price. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the purchase price, if at all. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair market value of your shares. Furthermore, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies or products by using our shares of common stock as consideration.

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.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expense related to the ongoing development of any future oral KIT inhibitor development programs;
- results of nonclinical and future clinical trials, or the addition or termination of future clinical trials or funding support by us, or existing or future collaborators or licensing partners;
- our execution of any additional collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under existing or future arrangements or the termination or modification of any such existing or future arrangements;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any future oral KIT inhibitor product candidates receives regulatory approval, the terms of such approval and market acceptance and demand for such product candidates;
- the continuing effect of the ongoing COVID-19 pandemic on our business and operations;
- regulatory developments affecting any future oral KIT inhibitor product candidates or those of our competitors; and
- changes in general market and economic conditions.

If our quarterly or annual operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly or annual fluctuations in our operating results may, in turn, cause the price of our common stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

The market price of our common stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely to continue to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control, including without limitation as a result of the ongoing COVID-19 pandemic. As a result of this volatility, investors may not be able to sell their common stock at or above the price initially paid for the stock. The market price for our common stock may be influenced by many factors, including the other risks described in this "Risk Factors" section and the following:

- results of nonclinical studies and future clinical trials of any future oral KIT inhibitor product candidates, or those of our competitors or our existing or future collaborators;
- regulatory or legal developments in the United States or other countries, especially changes in laws or regulations applicable to any future oral KIT inhibitor product candidates;
- the success or failure of competitive products or technologies;
- introductions and announcements of new product candidates by us, any future commercialization partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to any future oral KIT inhibitor product candidates, clinical studies, and, if approved, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional technologies or product candidates;
- developments concerning any future collaborations, including but not limited to those with development and commercialization partners if any future oral KIT inhibitor product candidates are approved;

- market conditions in the pharmaceutical and biotechnology sectors;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for any future oral KIT inhibitor product candidates;
- our ability or inability to raise additional capital and the terms on which we are able to raise it, if at all;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in earnings estimates, development timelines or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;
- fluctuations of trading volume of our common stock;
- sales of our common stock by us, insiders or our stockholders;
- the concentrated ownership of our common stock;
- expiration of market stand-off or lock-up agreements;
- changes in accounting principles;
- actions instituted by activist shareholders or others;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters and other calamities, including global pandemics such as the ongoing COVID-19 pandemic; and
- general economic, industry and market conditions, including rising interest rates and inflation, the government closure of SVB and liquidity concerns at other financial institutions, and the potential for local and/or global economic recessions.

In addition, the stock market in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme price and volume fluctuations that have been often unrelated or disproportionate to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

A sale of a substantial number of shares of our common stock may cause the price of our common stock to decline.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell in the public market, the market price of our stock could decline significantly.

Moreover, the holders of an aggregate of 25,508,705 shares of our outstanding common stock as of December 31, 2022, have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or our stockholders. We also have registered shares of common stock that we may issue under our equity incentive plans. These shares are freely tradeable in the public market.

We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. However, future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of our outstanding options, or the perception that such sales may occur, could adversely affect the market price of our common stock.

We also expect that significant additional capital may be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. To the extent that additional capital is raised through the sale and issuance of shares of common stock or other securities convertible into shares of common stock, our stockholders will be diluted. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares of common stock, could reduce the market price of our common stock.

Our principal stockholders and management own a significant percentage of our common stock and will be able to control matters subject to stockholder approval.

Based on the beneficial ownership of our common stock as of December 31, 2022, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned a substantial portion of our outstanding voting stock. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control of our Company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our Company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

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

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012 or JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (i) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, (ii) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (iii) exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not approved previously.

We could be an "emerging growth company" until December 31, 2027, although circumstances could cause us to lose that status earlier, including if we are deemed to be a "large accelerated filer," which occurs when the market value of our common stock that is held by non-affiliates equals or exceeds $700.0 million as of the prior June 30, or if we have total annual gross revenue of $1.235 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, in which case we would no longer be an emerging growth company immediately.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to take advantage of the benefits of this extended transition period. Our financial statements may therefore not be comparable to those of companies that comply with such new or revised accounting standards. Until the date that we are no longer an "emerging growth company" or affirmatively and irrevocably opt out of the exemption provided by Section 7(a)(2)(B) of the Securities Act, upon issuance of a new or revised accounting standard that applies to our financial statements and that has a different effective date for public and private companies, we will disclose the date on which adoption is required for non-emerging growth companies and the date on which we will adopt the recently issued accounting standard.

We are also a "smaller reporting company," meaning that the market value of our common stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 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 common stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our common stock held by non-affiliates is less than $700.0 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 Reports on Form 10-K, we are not required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

If we fail to maintain proper and effective internal controls over financial reporting our ability to produce accurate and timely financial statements could be impaired.

Pursuant to Section 404 of the Sarbanes-Oxley Act, our management will be required to report upon the effectiveness of our internal control over financial reporting beginning with our Annual Report on Form 10-K for our fiscal year ending December 31, 2023. This assessment will need to include the disclosure of any material weaknesses or significant deficiencies in our internal control over financial reporting identified by our management or our independent registered public accounting firm. When we become an "accelerated filer" or a "large accelerated filer," our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation. 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. This process will be time-consuming, costly and complicated.

In connection with the preparation of our financial statements for the year ended December 31, 2021, we concluded that there was a material weakness in our internal control over financial reporting. See "We have identified a material weakness in our internal control over financial reporting. If we do not remediate the material weakness in our internal control over financial reporting, or if we fail to establish and maintain effective internal control, we may not be able to accurately report our financial results or file our periodic reports in a timely manner, which may cause investors to lose confidence in our reported financial information and may lead to a decline in the market price of our common stock." Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations, or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

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

Our restated certificate of incorporation and our restated bylaws contain provisions that could delay or prevent a change in control of our Company. These provisions could also make it difficult for stockholders to elect directors who are not nominated by current members of our board of directors, or the Board, or take other corporate actions, including effecting changes in our management. These provisions:

- establish a classified Board so that not all members of our Board are elected at one time;
- permit only the Board to establish the number of directors and fill vacancies on the Board;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- require super-majority voting to amend some provisions in our restated certificate of incorporation and restated bylaws;
- authorize the issuance of "blank check" preferred stock that our Board could use to implement a stockholder rights plan;

- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting; and
- establish advance notice requirements for nominations for election to our Board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

In addition, Section 203 of the Delaware General Corporation Law, or DGCL, may discourage, delay or prevent a change in control of our Company. Section 203 imposes certain restrictions on mergers, business combinations and other transactions between us and holders of 15% or more of our common stock.

The exclusive forum provisions in our organizational documents may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or employees, or the underwriters of any offering giving rise to such claim, which may discourage lawsuits with respect to such claims.

Our restated certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware is the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our restated certificate of incorporation, or our restated bylaws; or any action asserting a claim that is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended, or Exchange Act. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, or the underwriters of any offering giving rise to such claims, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, financial condition, results of operations and prospects.

Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all claims brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Our restated bylaws provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision, including for all causes of action asserted against any defendant named in such complaint. For the avoidance of doubt, this provision is intended to benefit and may be enforced by us, our officers and directors, the underwriters to any offering giving rise to such complaint, and any other professional entity whose profession gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying the offering. Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law. While federal or other state courts may not follow the holding of the Delaware Supreme Court or may determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court, and our stockholders cannot waive compliance with the federal securities laws and the rules and regulations thereunder. Section 27 of the Exchange Act creates exclusive federal jurisdiction over all claims brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. In addition, neither the exclusive forum provision nor the Federal Forum Provision applies to suits brought to enforce any duty or liability created by the Exchange Act. Accordingly, actions by our stockholders to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder must be brought in federal court, and our stockholders cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

Any person or entity purchasing or otherwise acquiring or holding any interest in any of our securities shall be deemed to have notice of and consented to our exclusive forum provisions, including the Federal Forum Provision. These provisions may limit a stockholders' ability to bring a claim, and may result in increased costs for a stockholder to bring such a claim, in a judicial forum of their choosing for disputes with us or our directors, officers, other employees or agents, which may discourage lawsuits against us and our directors, officers, other employees or agents.

Because we do not anticipate paying any dividends on our capital stock for the foreseeable future, capital appreciation, if any, will be your sole source of gain and you may never obtain a return on your investment.

We have never declared or paid dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development, operation and expansion of our business and do not anticipate declaring or paying any dividends for the foreseeable future, if at all. In addition, any future debt financings may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future and you may never obtain a return on your investment. As a result, investors seeking cash dividends should not purchase our common stock.

General Risk Factors

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. We do not have any control over the industry or securities analysts, or the content and opinions included in their reports. If no or few securities or industry analysts continue or commence coverage of us, the trading price for our common stock could be impacted negatively. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our nonclinical studies and clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of such analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause a decline in our stock price or trading volume.

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 and corporate governance practices.

As a public company, and particularly after we are no longer an "emerging growth company" or "smaller reporting company," we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq and other applicable securities rules and regulations impose 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, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our Board, our Board committees or as executive officers. The increased costs may require us to reduce costs in other areas of our business. Moreover, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

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. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make any related party transaction disclosures. 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. In addition, we do not have a formal risk management program for identifying and addressing risks to our business in other areas.

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

The market price of our common stock is likely 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.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

As of December 31, 2022, we lease office space at 130 Prospect Street in Cambridge, Massachusetts, which is where our corporate headquarters are located, and which consists of 10,356 rentable square feet. We also lease office space at 1700 Montgomery Street in San Francisco, California, which consists of 4,703 rentable square feet. We believe our current office space is sufficient to meet our office needs until the expiration of the leases in 2028.

Item 3. Legal Proceedings.

From time to time, we may be involved in legal proceedings arising in the ordinary course of business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm.

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.

On September 15, 2022 our common stock began trading on the Nasdaq Stock Market LLC under the symbol "THRD". Prior to such time, there was no public market for our common stock.

Stockholders

As of March 24, 2023, there were 24 stockholders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Recent Sales of Unregistered Securities

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

Use of Proceeds from Public Offering of Common Stock

On September 14, 2022, our Registration Statement on Form S-1, as amended (Registration No. 333-267022) was declared effective by the SEC for our IPO. At the closing of the offering on September 19, 2022, we sold 12,535,000 shares of common stock, including the exercise in full by the underwriters of their option to purchase up to 1,635,000 additional shares of common stock, at a public offering price of $17.00 per share. The aggregate net proceeds to us from the public offering, inclusive of the over-allotment exercise and after underwriting discounts and offering expenses, were approximately $198.2 million. Morgan Stanley & Co. LLC, Jeffries LLC and Cowen and Company, LLC acted as joint book-running managers for the offering. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10% or more of any class of our equity securities or to any other affiliates.

There has been no material change in the planned use of proceeds from our IPO as described in the prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on September 15, 2022.

Dividend Policy

We have never paid or declared any cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors that our board of directors deems relevant.

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item will be included in our Definitive Proxy Statement, or Proxy Statement, for the 2023 Annual Meeting of Stockholders, to be filed within 120 days of the fiscal year ended December 31, 2022, and is incorporated by reference.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Item 6. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our consolidated financial statements and the related notes and other financial information included elsewhere in this Annual Report.

As discussed in the section titled "Special Note Regarding Forward Looking Statements," the following discussion and analysis contains forward-looking statements that involve risks and uncertainties. Our actual results and the timing of selected events could differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those set forth in the section titled "Risk Factors" under Part I, Item 1A.

Overview

We are a biopharmaceutical company focused on the development of the next wave of medicine for the treatment of inflammatory diseases, including dermal, respiratory, and gastrointestinal diseases. We are developing next-generation, highly selective, oral small-molecule inhibitors of KIT, a cell surface receptor that serves as the master regulator of mast cell function and survival. Early clinical studies have demonstrated that KIT inhibition has the potential to address the treatment of a broad range of mast-cell-mediated inflammatory diseases, and that a titratable, oral, intracellular small molecule inhibitor may provide an attractive therapeutic profile against this target. Our initial focus is on developing a KIT inhibitor to treat chronic urticaria.

In December 2022, we announced the discontinuation of our Phase 1b clinical trial of our product candidate THB001 in chronic inducible urticaria following observation of asymptomatic liver transaminitis in two patients enrolled in the first dose cohort. We initiated nonclinical studies to elucidate the mechanism for the observed transaminitis, which was not predicted by extensive toxicology studies including those conducted according to GLP of THB001 nor observed in our Phase 1a clinical trial. In parallel with the early clinical development of THB001, we have conducted an extensive medicinal chemistry effort to identify chemically distinct next-generation oral wild-type KIT inhibitors and have advanced multiple candidate molecules into exploratory toxicology studies. We intend to nominate a development candidate from this program in 2023.

Since our inception in 2019, we have devoted substantially all of our efforts to organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio, acquiring or discovering product candidates, research and development activities for THB001 and other compounds, establishing arrangements with third parties for the manufacture of our product candidates and component materials, and providing general and administrative support for these operations. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have financed our operations primarily with proceeds from sales of shares of our preferred stock and our IPO of our common stock. Our primary uses of capital are, and we expect will continue to be, research and development services, compensation and related expenses, and general overhead costs.

We have incurred significant operating losses since inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of future product candidates. Our net losses were $29.6 million and $35.2 million for the year ended December 31, 2021 and 2022, respectively. As of December 31, 2022, we had an accumulated deficit of $83.4 million. We expect to continue to incur net operating losses for at least the next several years, and we expect our research and development expenses, general and administrative expenses, and capital expenditures will increase substantially in connection with our ongoing activities, particularly if, and as, we:

- advance any future KIT inhibitor product candidates through nonclinical studies and clinical development;
- discover and develop new product candidates;
- obtain, expand, maintain, defend and enforce our intellectual property portfolio;
- manufacture, or have manufactured, nonclinical, clinical and potentially commercial supplies of any future oral KIT inhibitor product candidates;
- seek regulatory approvals for any future oral KIT inhibitor product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize any future oral KIT inhibitor product candidates, if approved;
- identify additional compounds or product candidates and acquire rights from third parties to those compounds or product candidates through licenses;

- hire additional clinical, scientific and management personnel, as well as administrative staff to support the growth of our business;
- add operational, financial and management information systems and personnel;
- incur additional legal, accounting and other costs associated with operating as a public company;
- experience delays related to the ongoing COVID-19 pandemic in the United States and in other countries in which we have planned or have active clinical trial sites and where our third-party CDMOs operate; and
- establish licenses, collaborations or strategic partnerships.

Our net losses may fluctuate significantly from period to period, depending on the timing of expenditures related to our research and development activities.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for a product candidate. In addition, if we obtain regulatory approval for a product candidate 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 such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through equity offerings, debt financings or other capital sources, which could include collaborations, strategic alliances or additional licensing arrangements. We may be unable to raise additional funds or enter into such arrangements when needed, on favorable terms, or at all. Our failure to raise capital or enter into such agreements as, and when, needed, could have a material adverse effect on our business, results of operations and financial condition, including requiring us to have to delay, reduce or eliminate product development or future commercialization efforts. The amount and timing of our future funding requirements will depend on many factors including the successful advancement of any future oral KIT inhibitor product candidates. Our ability to raise additional funds may also be adversely impacted by potential worsening global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide, such as those resulting from the government closure of SVB and liquidity concerns at other financial institutions, from potential recessions, the ongoing COVID-19 pandemic, the hostilities in Ukraine, and increasing interest rates and rates of inflation.

Because of the numerous risks and uncertainties associated with development of treatment of mast cell driven inflammatory diseases, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

We oversee and manage third party Contract Development and Manufacturing Organizations, or CDMOs, to support development and manufacture of any future oral KIT inhibitor product candidates for our clinical trials. The manufacturing process has readily-sourced available raw materials and straightforward scalability. We believe our current manufacturers are able to supply the upcoming clinical trials and additional CDMOs may be on-boarded at later stages of clinical and commercial development.

As of December 31, 2022, we had $288.9 million in cash and cash equivalents. We believe that our existing cash and cash equivalents, will be sufficient to fund our operations and capital expenses through at least the next twelve months. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See the subsection titled “Liquidity and Capital Resources.”

License Agreement with Novartis International Pharmaceutical Ltd.

On June 28, 2019, we entered into a license agreement with Novartis International Pharmaceutical Ltd. (which subsequently merged into the company Novartis Pharma AG), or Novartis, as amended, or the Novartis Agreement. Pursuant to the Novartis Agreement, Novartis granted us an exclusive, worldwide, sublicensable (subject to certain requirements therein) license under specified patent rights and know-how related to three licensed compounds to develop, make, use and sell certain products incorporating or comprising a licensed compound, or the Licensed Products. Under the Novartis Agreement, we are solely responsible for all research, development, regulatory and commercialization activities related to the Licensed Products. We are required to use commercially reasonable efforts to develop and seek regulatory approval for, and commercialize, at least one Licensed Product in the United States, France, Germany, Italy, Spain, the United Kingdom, and Japan.

Pursuant to the Novartis Agreement, we made a one-time payment of $0.4 million to Novartis and agreed to issue shares of preferred stock pursuant to that certain Investment Letter dated as of June 27, 2019, or the Novartis Investment Letter. Pursuant to the Novartis Investment Letter, we have issued Novartis 5,970,000 shares of Series A-1 Preferred Stock (2,642,7621 shares of common stock following the conversion of such preferred stock in connection with our IPO), consisting of shares issued as part of entering into the agreement and shares issued subsequently under the anti-dilution right included within the license agreement. Further, we are obligated to pay Novartis up to an aggregate of: (i) $31.7 million upon the achievement of certain specified development milestones for the Licensed Products and (ii) $200.0 million upon the achievement of certain specified sales and commercialization milestones with respect to the Licensed Products. We are also required to pay Novartis, on a Licensed Product-by-Licensed Product and country-by-country basis, tiered royalties in the single-digit percentage range on annual net sales of Licensed Products, subject to reduction and offset upon certain specified events. The foregoing royalty payment obligations will expire on the latest to occur of: (a) expiration of the last valid claim of the licensed patent rights that covers such Licensed Product in such country; (b) the expiration of any regulatory exclusivity for such Licensed Product in such country; and (c) ten years following the first commercial sale of such Licensed Product in such country. Upon the expiration of such royalty term in a particular country for a particular Licensed Product, the license granted to us with respect to such Licensed Product in such country will become fully paid-up, royalty-free, transferable, perpetual and irrevocable.

For a more detailed description of this agreement, see Note 5 to our audited consolidated financial statements included elsewhere in this Annual Report.

Impact of COVID-19 on Our Business

The impact of COVID-19 on our future results will largely depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, the impact of variants, evolving travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, the ultimate impact on financial markets and the global economy, the effectiveness of vaccines and vaccine distribution efforts and the effectiveness of other actions taken in the United States and other countries to contain and treat the disease. For additional details regarding the ongoing COVID-19 pandemic's impact and potential impact on our business, operations and prospects, see the section titled "Risk Factors—Risks Related to Discovery, Development and Commercialization." The ongoing COVID-19 pandemic could adversely impact our business, including the conduct of our research activities.

Components of Our Results of Operations

Revenue

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products or from other sources in the near future, if at all. If our development efforts for our any product candidates that we may develop in the future are successful and result in marketing approval or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

Operating Expenses

Research and Development

Research and development expenses account for a significant portion of our operating expenses and consist primarily of costs incurred in connection with the discovery, nonclinical development, clinical development and manufacturing of potential future product candidates, and include:

Direct Costs

- expenses incurred under agreements with CROs that are primarily engaged in the oversight and conduct of our clinical trials; CDMOs that are primarily engaged to provide drug substance and product for our clinical trials, research and development programs, as well as investigative sites and consultants that conduct our clinical trials, nonclinical studies and other scientific development services;
- the cost of acquiring and manufacturing nonclinical and clinical trial materials, including manufacturing registration and validation batches;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;

- costs related to compliance with quality and regulatory requirements; and
- payments made under third-party licensing agreements.

Indirect Costs

- personnel-related expenses including, salaries, benefits, stock-based compensation and other related costs for individuals involved in research and development activities; and
- facilities and other expenses not directly tied to a program.

We expense research and development costs as incurred. We recognize direct development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors or our estimate of the level of service that has been performed at each reporting date. Payments for these development activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as prepaid expenses or accrued expenses.

A significant portion of our research and development costs to date have been third-party costs, which we track on an individual product candidate basis after a clinical product candidate has been identified. Our indirect research and development costs are primarily personnel-related costs and facilities and other costs. Employees and infrastructure are not directly tied to any one program and are deployed across our programs. As such, we do not track these costs on a specific program basis. We utilize third party contractors for our research and development activities and CDMOs for our manufacturing activities and we do not have our own laboratory or manufacturing facilities.

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase for the foreseeable future as we continue to discover and develop additional product candidates, expand our headcount and maintain, expand and enforce our intellectual property portfolio. If any future product candidates enter into later stages of clinical development, they will generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. There are numerous factors associated with the successful development and commercialization of any product candidates we may develop in the future, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development program and plans.

Our research and development expenses may vary significantly in the future based on factors, such as:

- the number and scope of nonclinical and IND-enabling studies;
- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the cost and timing of manufacturing our product candidates;
- the phase of development of our product candidates;
- the efficacy and safety profile of our product candidates;
- the extent to which we establish additional collaboration or license agreements; and
- whether we choose to partner any of our product candidates and the terms of such partnership.

Any changes in the outcome of any of these variables with respect to the development of any future product candidates in nonclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA, 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 clinical trials following the applicable regulatory authority's acceptance and clearance, we could be required to expend significant additional financial resources and time to complete clinical development than we currently expect. We may never obtain regulatory approval for any product candidates that we develop.

The successful development of any product candidates we may develop in the future is highly uncertain. Therefore, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development and commercialization of any other product candidates we may develop. We are also unable to predict when, if ever, material net cash inflows will commence from the sale of any future product candidate, if approved. This is due to the numerous risks and uncertainties associated with product development.

General and Administrative

General and administrative expenses consist primarily of personnel-related expenses, including salaries, benefits and stock-based compensation expenses for personnel in executive and other administrative functions. Other significant general and administrative expenses include legal fees relating to patent, intellectual property and corporate matters, and fees paid for accounting, consulting and other professional services, and expenses for rent, insurance and other operating costs.

We expect that our general and administrative expenses will continue to increase in the foreseeable future as our business expands to support our continued research and development activities, including any future clinical trials. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, among other expenses. We also anticipate increased expenses associated with being a public company, including costs for audit, legal, regulatory and tax-related services related to compliance with the rules and regulations of the Securities and Exchange Commission, or SEC, listing standards applicable to companies listed on a national securities exchange, director and officer insurance premiums and investor relations costs. In addition, if we obtain regulatory approval for our current product candidate or any product candidates we may develop in the future and do not enter into a third-party commercialization collaboration, we expect to incur significant expenses related to building a sales and marketing team to support product sales, marketing and distribution activities.

Total Other (Income) Expense, Net

Change in Fair Value of Anti-Dilution Right Liability

We classified the anti-dilution right liability under the Novartis Agreement, as a liability on our consolidated balance sheets as the anti-dilution right liability represented a freestanding financial instrument that required us to transfer equity instruments upon future equity closings. The anti-dilution right liability was initially recorded at fair value upon the date of issuance and was subsequently remeasured to fair value at each reporting date. The issuance date fair value of the derivative liability was recognized as a research and development expense upon entering into the agreement with Novartis. Changes in the fair value of the anti-dilution right liability were recognized as a component of other expense in our consolidated statements of operations. Changes in the fair value of the anti-dilution right liability were recognized until the anti-dilution rights liability was satisfied in the first quarter of 2021.

In February 2021, in connection with our issuance and sale of the second tranche of Series A-2 Preferred Stock, we satisfied our anti-dilution right liability under the Novartis Agreement by issuing 5,970,000 total shares of Series A-1 Preferred Stock to Novartis for a total value of $6.0 million. We remeasured the fair value of the anti-dilution right liability on the date of settlement, and recorded a charge of $0.7 million, in other (income) expense, net.

Change in Fair Value of Preferred Stock Tranche Liability

In connection with the issuance of our Series A Preferred Stock, we granted investors future tranche rights to purchase the Preferred Stock. We classified the preferred stock tranche liability for the future purchase and option to purchase Series A Preferred Stock as a liability on our consolidated balance sheets as the preferred stock tranche liability is a freestanding financial instrument that will require us to transfer equity instruments upon future closings of the Series A Preferred Stock. The preferred stock tranche liability was initially recorded at fair value upon the date of issuance and is subsequently remeasured to fair value at each reporting date. Changes in the fair value of the preferred stock tranche liability are recognized as a component in other (income) expense, net in the consolidated statements of operations. Changes in the fair value of the preferred stock tranche liability were recognized until the tranche liability were fulfilled or otherwise extinguished in the fourth quarter of 2021.

In November 2021, in connection with our issuance and sale of Series A-3 Tranche 2, we satisfied our liability to issue additional shares under the second tranche closing and accordingly reclassified the carrying value of the preferred stock tranche liability associated with the future purchase obligation, equal to the then current value of $16.3 million, to the carrying value of the Series A-3 Preferred Stock.

Other Income

Other income primarily consists of interest income generated from interest bearing money market accounts.

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred in each period or for our earned research and development tax credits, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss carryforwards and tax credits will not be realized. As of December 31, 2022, we had U.S. federal and state net operating loss carryforwards of $38.9 million and $34.1 million, respectively, which may be available to offset future income tax liabilities and expire at various dates beginning in 2039. As of the years ended December 31, 2021 and 2022, we have recorded a full valuation allowance against our deferred tax assets.

Results of Operations

Comparison of the year ended December 31, 2021 and 2022

The following table summarizes our results of operations for each of the periods presented (in thousands, except percentages):

	Year Ended December 31,			
	2021	2022	$ Change	% Change
Operating expenses:				
Research and development	$ 15,748	$ 24,407	$ 8,659	55%
General and administrative	3,256	13,301	10,045	309
Total operating expenses	19,004	37,708	18,704	98
Loss from operations	19,004	37,708	18,704	98
Other (income) expense, net:				
Change in fair value of anti-dilution right liability	682	—	(682)	(100)
Change in fair value of preferred stock tranche liability	9,928	—	(9,928)	(100)
Other income	(5)	(2,553)	(2,548)	*
Total other (income) expense, net	10,605	(2,553)	(13,158)	(124)
Net loss	$ 29,609	$ 35,155	$ 5,546	19%

**Percentage not meaningful.*

Research and Development Expenses

The following table summarizes our research and development expenses for each of the periods presented (in thousands, except percentages):

	Year Ended December 31,			
	2021	2022	$ Change	% Change
Direct costs:				
THB001	$ 11,062	$ 11,130	$ 68	1%
Other discovery and development	2,105	7,129	5,024	239
Indirect costs:				
Personnel-related	2,569	6,023	3,454	134
Facilities and other	12	125	113	942
Total research and development expenses	$ 15,748	$ 24,407	$ 8,659	55%

Research and development expenses increased by $8.7 million from $15.7 million for the year ended December 31, 2021 to $24.4 million for the year ended December 31, 2022. The increase was primarily attributable to the following:

- a $0.1 million increase in costs related to the clinical development of THB001 as part of the Phase1b clinical trial phase which was discontinued in December 2022;
- a $5.0 million increase in other discovery and development costs, relating to the research and nonclinical development of the next generation molecules, discovery compounds and other programs;
- a $3.5 million increase in personnel related costs, including a $1.7 million in stock-based compensation expense, primarily due to an increase in headcount in 2022 to support the advancement of our developmental efforts and the increase in fair value of the awards that were granted in October 2022;
- a $0.1 million increase in facilities and other costs, driven by the increase in office space.

General and Administrative Expenses

General and administrative expenses increased by $10.0 million from $3.3 million for the year ended December 31, 2021 to $13.3 million for the year ended December 31, 2022, primarily driven by the increases in costs associated with personnel-related expenses and the IPO.

Total Other (Income) Expense, Net

Total other (income) expense, net decreased by approximately $13.2 million from $10.6 million of expense for the year ended December 31, 2021 to $2.6 million of income for the year ended December 31, 2022. This increase was primarily attributable to changes in fair value of anti-dilution right liability and preferred stock tranche liability that was recognized during the year ended December 31, 2021 and the increase in interest income received as the Company's cash balance has increased.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant losses in each period and on an aggregate basis. We have not yet commercialized any product candidates, and we do not expect to generate revenue from sales of any product candidates or from other sources for several years, if at all.

On September 19, 2022, we completed our IPO at which time we issued 12,535,000 shares of common stock, including the exercise in full by the underwriters of their option to purchase up to 1,635,000 additional shares of common stock, at a public offering price of $17.00 per share. We received $198.2 million, net of underwriting discounts and commissions, but before deducting offering costs payable by the Company, which were $2.3 million. Prior to our IPO, we funded our operations primarily with gross proceeds from sales of our preferred stock.

As of December 31, 2022, we had $288.9 million in cash and cash equivalents, and we had an accumulated deficit of $83.4 million.

Cash Flows

The following table provides information regarding our cash flows for each of the periods presented (in thousands):

	Year Ended December 31,	
	2021	2022
Net cash used in operating activities	$ (15,746)	$ (34,917)
Net cash used in investing activities	—	(36)
Net cash provided by financing activities	135,749	195,991
Net increase in cash and cash equivalents	$ 120,003	$ 161,038

Net Cash Used in Operating Activities

Net cash used in operating activities for the year ended December 31, 2021 was $15.7 million, and was primarily due to our net loss of $29.6 million, adjusted for non-cash charge of $9.9 million related to the change in fair value of the preferred stock tranche liability, a non-cash charge of $0.7 million related to the change in fair value of the anti-dilution right liability, $0.5 million non-cash stock-based compensation expense and net changes in working capital of $2.8 million.

Net cash used in operating activities for the year ended December 31, 2022 was $34.9 million, and was primarily due to our net loss of $35.2 million, adjusted for $4.8 million non-cash stock-based compensation expense, an increase of $1.0 million in other assets relating to deferred compensation, and net changes in working capital of $3.5 million.

Net Cash Used in Investing Activities

We had no investing activities for the year ended December 31, 2021. Net cash used in investing activities for the year ended December 31, 2022 was $36 thousand, and was related to purchases of property, plant, and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 was $135.7 million, resulting entirely from proceeds received from the issuance and sale of shares of our Series A Preferred Stock, net of issuance costs.

Net cash provided by financing activities for the year ended December 31, 2022 was $196.0 million, and was primarily driven from the proceeds of our IPO, net of issuance costs and underwriting fees of $195.9 million, and $0.1 million related to the exercise of stock options.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, research and development services, compensation and related expenses and general overhead costs. We expect to continue to incur significant expenses and operating losses for the foreseeable future. Following the closing of our IPO, we expect to incur additional costs associated with operating as a public company.

Based on our current operating plan, we believe that our existing cash and cash equivalents, will be sufficient to fund our operations and capital expenses through at least the next twelve months. However, we have based this estimate on assumptions that may prove to be wrong, and we could exhaust our capital resources sooner than we expect.

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

- the timing, cost and progress of nonclinical and clinical development activities;
- the cost of regulatory submissions and timing of regulatory approvals;
- the number and scope of nonclinical and clinical programs we decide to pursue;
- the progress of the development efforts of parties with whom we may in the future enter into collaborations and/or research and development agreements;
- the timing and amount of milestone and other payments we are obligated to make under our Novartis Agreement or any future license agreements;
- the cash requirements of any future acquisitions or discovery of product candidates;
- our ability to establish and maintain collaborations, strategic partnerships or marketing, distribution, licensing or other strategic arrangements with third parties on favorable terms, if at all;
- the costs involved in prosecuting and enforcing patent and other intellectual property claims;
- the costs of manufacturing our product candidates by third parties;
- the cost of commercialization activities if any future oral KIT inhibitor product candidates are approved for sale, including marketing, sales and distribution costs;

- our efforts to enhance operational systems and hire additional personnel, including personnel to support development of our product candidates; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems to satisfy our obligations as a public company.

A change in the outcome of any of these or other variables with respect to the development of any future oral KIT inhibitor product or development candidates we may develop in the future could significantly change the costs and timing associated with our development plans. Further, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings or other capital sources, which could include collaborations, strategic alliances or licensing arrangements. We currently have no credit facility or committed sources of capital. Adequate additional funds may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our existing stockholders may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect the rights of such stockholders. Debt financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research program or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic or otherwise. Because of the numerous risks and uncertainties associated with product development, there is no assurance that we will ever be profitable or generate positive cash flow from operating activities.

Contractual Obligations and Other Commitments

Novartis Agreement

We may incur contingent royalty payments that we are required to make under the Novartis Agreement. Due to the uncertainty of the achievement and timing of the events requiring payment under our license agreement with Novartis, the amounts to be paid by us are not fixed or determinable at this time. We are required to pay Novartis royalties on all sales of licensed products, with such royalty percentages in the mid-single digits of sales. We have not paid any royalties to date as we have no products commercially approved for sale. For additional information regarding the license agreement and royalties payable to Novartis, see Note 6 to our consolidated financial statements included elsewhere in this Annual Report.

Lease Obligations

On October 21, 2022, the Company entered into two separate lease agreements, one for office space located in Cambridge, Massachusetts, or the Cambridge Lease Agreement, and one for office space located in San Francisco, California, or the San Francisco Lease Agreement. The Cambridge Lease Agreement and the San Francisco Lease Agreement each commenced in December 2022, and each have an initial term of 63 months. The aggregate estimated rental payments due over the initial term of the Cambridge Lease Agreement is approximately $4.0 million, and the aggregate estimated rental payments due over the initial term of the San Francisco Lease Agreement is approximately $1.8 million. For additional information regarding the lease accounting policies see Note 2 to our consolidated financial statements included elsewhere in this Annual Report and for additional information regarding the lease obligations see Note 12 to our consolidated financial statements included elsewhere in this Annual Report.

Purchase and Other Obligations

We enter into contracts in the normal course of business with CROs, CDMOs and other third-party vendors for nonclinical research studies and testing, clinical trials and testing and manufacturing services. Most contracts do not contain minimum purchase commitments and are cancellable by us upon written notice. Payments due upon cancellation consist of payments for services provided or expenses incurred, including non-cancellable obligations of our service provided up to one year after the date of cancellation.

Critical Accounting Policies

This management's discussion and analysis is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles or GAAP. The preparation of our consolidated financial statements and related disclosures requires us to make judgments and estimates that affect the reported amounts of assets, liabilities and expenses, as well as related disclosures during the reported periods. We base our estimates on historical experience, known trends and events, and various other factors that we believe are reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. The effects of material revisions in estimates, if any, will be reflected in the financial statements prospectively from the date of change in estimates.

While our accounting policies are described in more detail in the notes to our consolidated financial statements included elsewhere in this Form 10-K, we believe the following accounting policies used in the preparation of our financial statements require the most significant judgments and estimates.

Accrued and Prepaid Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued and prepaid third-party research and development expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued and prepaid expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued and prepaid research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development activities on our behalf. 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 research and development 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 our estimate, we adjust the accrual or prepaid balance accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts incurred.

Stock-Based Compensation

We measure stock-based payment awards granted to employees and non-employees as stock-based compensation expense at fair value, based on the date of the grant, and recognizes compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. Our stock-based payments include stock options and grants of restricted stock awards. For stock-based awards with service-based vesting conditions, we recognize compensation expense using the straight-line method. For awards with both performance and service-based vesting conditions, we record expense using an accelerated attribution method, once the performance conditions are considered probable of being achieved, using our best estimates.

At inception of the 2019 Stock Incentive Plan, we adopted the guidance of Accounting Standards Update, or ASU, No. 2018-07, Compensation— Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting, or ASU No. 2018-07, prior to the issuance of any stock option grants. The measurement date for non-employee awards is the date of grant without changes in the fair value of the award. Stock-based compensation costs for non-employees are recognized as expense over the vesting period on a straight-line basis.

We classify stock-based compensation expense in our statements of operations in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified. The fair value of each stock option is estimated on the grant date using the Black-Scholes option pricing model, which requires inputs based on certain subjective assumptions, including:

- Fair Value of Common Stock—See the subsection titled "—Common Stock Valuations" below.
- Expected Term—The expected term represents the period that the stock-based awards are expected to be outstanding. We use the simplified method to determine the expected term, which is based on the average of the time-to-vesting and the contractual life of the options.
- Expected Volatility—Due to our limited operating history and lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the average volatility for comparable publicly traded biotechnology companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on the similar size, stage in life cycle or area of specialty. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.
- Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the awards.
- Expected Dividend Yield—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

The fair value of each restricted common stock award is estimated on the date of grant based on the fair value of our common stock on that same date. See Note 8 to our consolidated financial statements included elsewhere in this Annual Report for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted in the years ended December 31, 2021 and 2022.

Common Stock Valuations

Historically, for all periods prior to our IPO that was completed on September 19, 2022, as there was no public market for our common stock, the estimated fair value of our common stock has been determined by our board of directors, with input from management, as of the date of each award grant, considering our most recently available independent third-party valuations of common stock and any additional objective and subjective factors that we believed were relevant and which may have changed from the date of the most recent valuation through the date of each award grant. The independent 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. We determined that based on our stage of development and other relevant factors, it was most appropriate to prepare our common stock valuations using the option-pricing method, or OPM, which used a market approach 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 has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. A discount for lack of marketability of the common stock is then applied to arrive at an indication of value for the common stock.

Once a public trading market for our common stock was established in connection with the completion of our IPO, the fair value of our common stock is determined based on the quoted market price of our common stock.

Internal Controls Over Financial Reporting

A company's internal control over financial reporting is a process designed by, or under the supervision of, a company's principal executive and principal financial officers, or persons performing similar functions, and effected by a company's board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. A material weakness is a significant deficiency, or a combination of significant deficiencies, in internal control over financial reporting such that it is reasonably possible that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis.

During the preparation of our consolidated financial statements for the year ended December 31, 2021, we identified a material weakness in our internal control over financial reporting. The material weakness has not yet been fully remediated and the same weakness remained at the time of the preparation of our financial statements for the year ended December 31, 2022. The material weakness we identified related to the lack of segregation of duties, certain system limitations in our accounting software and the overall control environment as we had insufficient internal resources with appropriate accounting and finance knowledge and expertise to design, implement, document and operate effective internal controls around our financial reporting process.

We are implementing measures designed to improve our internal control over financial reporting to remediate this material weakness, including formalizing our processes and internal control documentation and strengthening supervisory reviews by our financial management; hiring additional qualified accounting and finance personnel and engaging financial consultants to enable the implementation of internal control over financial reporting and segregating duties amongst accounting and finance personnel. In addition, we have implemented an accounting software system with the design and functionality to segregate incompatible accounting duties, which we currently expect will be fully implemented in our 2023 fiscal year.

While we are implementing these measures, we cannot assure you that these efforts will remediate our material weakness and significant deficiencies in a timely manner, or at all, or prevent restatements of our financial statements in the future. If we are unable to successfully remediate our material weakness, or identify any future significant deficiencies or material weaknesses, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports, and the market price of our common stock may decline as a result.

Emerging Growth Company and Smaller Reporting Company Status

Under Section 107(b) of the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, an "emerging growth company" can delay the adoption of new or revised accounting standards until such time as those standards would apply to private companies. We have elected this exemption to delay adopting new or revised accounting standards until such time as those standards apply to private companies. Where allowable we have early adopted certain standards as described in Note 2 of our consolidated financial statements included elsewhere in this Annual Report. As a result, our consolidated financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates. We will continue to remain an "emerging growth company" until the earliest of the following: (i) December 31, 2027; (ii) the last day of the fiscal year in which our total annual gross revenue is equal to or more than $1.235 billion; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of our IPO was less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We will continue to be a smaller reporting company until either (i) the market value of our stock held by non-affiliates is more than $250.0 million or (ii) our annual revenue is more than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is more than $700.0 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.

Recent Accounting Pronouncements

We have reviewed all recently issued accounting pronouncements and have determined that, other than as disclosed in Note 2 to our consolidated financial statements included elsewhere in this Annual Report, such standards do not have a material impact on our financial statements or do not otherwise apply to our operations.

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

Interest Rate Risk

Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our cash equivalents are in the form of standard checking accounts and amounts held in money market funds that are invested in U.S. Treasury securities. Interest income is sensitive to changes in the general level of interest rates. However, due to the short-term maturities of our cash equivalents, we believe a hypothetical 100 basis point increase or decrease in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements included elsewhere in this Annual Report.

As of December 31, 2022, we had no debt outstanding and therefore were not exposed to related interest rate risk.

Foreign Currency Exchange Risk

All of our employees and our operations are currently located in the United States and our expenses are generally denominated in U.S. dollars. We therefore are not currently exposed to significant market risk related to changes in foreign currency exchange rates. However, we have contracted with and may continue to contract with non-U.S. vendors who we may pay in local currency. Our operations may be subject to fluctuations in foreign currency exchange rates in the future. To date, foreign currency transaction gains and losses have not been material to our financial statements, and we have not had a formal hedging program with respect to foreign currency. We believe a hypothetical 100 basis point increase or decrease in exchange rates during any of the periods presented would not have a material effect on our consolidated financial statements included elsewhere in this Annual Report.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and clinical trial costs. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, we may experience some effect in the near future (especially if inflation rates continue to rise) due to an impact on the costs to conduct clinical trials, labor costs we incur to attract and retain qualified personnel, and other operational costs. Inflationary costs could adversely affect our business, financial condition and results of operations.

Item 8. Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Audited Consolidated Financial Statements for the Years Ended December 31, 2021 and 2022:

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the shareholders and the Board of Directors of Third Harmonic Bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Third Harmonic Bio, Inc. and subsidiaries (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations, changes in redeemable convertible preferred stock and shareholders' deficit, and cash flows, for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Morristown, NJ

March 29, 2023

We have served as the Company's auditor since 2022.

THIRD HARMONIC BIO, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31, 2021	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 128,280	$ 288,877
Prepaid expenses and other current assets	884	3,958
Total current assets	129,164	292,835
Restricted cash	—	441
Property and equipment, net	—	35
Right of use asset	—	4,327
Other assets	—	1,037
Total assets	$ 129,164	$ 298,675
Liabilities, redeemable convertible preferred stock and stockholders' deficit		
Current liabilities:		
Accounts payable	$ 1,797	$ 2,087
Accrued expenses and other current liabilities	3,889	3,181
Operating lease liability, current	—	385
Total current liabilities	5,686	5,653
Operating lease liability, noncurrent	—	3,954
Preferred stock tranche liability	—	—
Anti-dilution liability	—	—
Total liabilities	5,686	9,607
Commitments and contingencies (Note 13)		
Series A-1 redeemable convertible preferred stock, par value $0.0001. 13,970,000 and - shares authorized as of December 31, 2021 and December 31, 2022, respectively; 13,970,000 and - shares issued and outstanding as of December 31, 2021 and December 31, 2022 respectively; liquidation preference of $13,970 and $- as of December 31, 2021, and December 31, 2022, respectively	12,574	—
Series A-2 redeemable convertible preferred stock, par value $0.0001. 13,750,000 and - shares authorized as of December 31, 2021 and December 31, 2022, respectively; 13,750,000 and - shares issued and outstanding as of December 31, 2021- and December 31, 2022, respectively; liquidation preference of $22,000 and $-, as of December 31, 2021, and December 31, 2022, respectively	19,476	—
Series A-3 redeemable convertible preferred stock, par value $0.0001. 7,812,501 and - shares authorized as of December 31, 2021 and December 31, 2022, respectively; 7,812,501 and - shares issued and outstanding as of December 31, 2021 and December 31, 2022, respectively; liquidation preference of $20,000 and $- as of December 31, 2021 and December 31, 2022, respectively	33,288	—
Series B redeemable convertible preferred stock, par value $0.0001. 14,091,689 and - shares authorized as of December 31, 2021, and December 31, 2022 respectively; 14,091,686 and - shares issued and outstanding as of December 31, 2021, and December 31, 2022, respectively; liquidation preference of $105,000 and $- as of December 31, 2021, and December 31, 2022, respectively	104,846	—
Stockholders' deficit:		
Common stock, $0.0001 par value, 72,731,000 and 500,000,000 shares authorized at December 31, 2021 and December 31, 2022; 4,237,290 and 39,377,222 shares issued and outstanding at December 31, 2021 and December 31, 2022, respectively	1	4
Preferred stock, $0.0001 par value, - and 10,000,000 shares authorized at December 31, 2021 and December 31, 2022; - and - shares issued and outstanding at December 31, 2021 and December 31, 2022, respectively	—	—
Additional paid-in capital	1,534	372,460
Accumulated deficit	(48,241)	(83,396)
Total stockholders' (deficit) equity	(46,706)	289,068
Total liabilities, redeemable convertible preferred stock and stockholders' (deficit) equity	$ 129,164	$ 298,675

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

THIRD HARMONIC BIO, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share amounts)

	Year Ended December 31,	
	2021	2022
Operating expenses:		
Research and development	$ 15,748	$ 24,407
General and administrative	3,256	13,301
Total operating expenses	19,004	37,708
Loss from operations	19,004	37,708
Other (income) expense, net:		
Change in fair value of anti-dilution right liability	682	—
Change in fair value of preferred stock tranche liability	9,928	—
Other (income)	(5)	(2,553)
Total other (income) expense, net	10,605	(2,553)
Net loss	$ 29,609	$ 35,155
Net loss per share of common stock, basic and diluted	$ 7.32	$ 2.62
Weighted-average common stock outstanding, basic and diluted	4,043,416	13,426,066

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

THIRD HARMONIC BIO, INC.
CONSOLIDATED STATEMENTS OF CHANGES IN REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT
(In thousands, except share amounts)

	Redeemable Convertible Preferred Stock												
	Series A-1		Series A-2		Series A-3		Series B		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2020	12,746,961	$ 11,008	6,875,000	$ 7,691	—	$ —	—	$ —	3,866,138	$ 1	$ 274	(18,632)	$ (18,357)
Issuance of Series A-2 redeemable convertible preferred stock under Series A-2 Second Tranche, net of issuance costs of $40	—	—	6,875,000	11,785	—	—	—	—	—	—	—	—	—
Gain on extinguishment of Series A-2 redeemable convertible preferred stock tranche liability	—	—	—	—	—	—	—	—	—	—	750	—	750
Issuance of Series A-1 redeemable convertible preferred stock under anti-dilution liability	1,223,039	1,566	—	—	—	—	—	—	—	—	—	—	—
Issuance of Series A-3 redeemable convertible preferred stock, net of issuance costs of $40	—	—	—	—	7,812,501	33,288	—	—	—	—	—	—	—
Issuance of Series B redeemable convertible preferred stock, net of issuance costs of $154	—	—	—	—	—	—	14,091,686	104,846	—	—	—	—	—
Vesting of restricted stock	—	—	—	—	—	—	—	—	371,152	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	510	—	510
Net loss	—	—	—	—	—	—	—	—	—	—	—	(29,609)	(29,609)
Balance at December 30, 2021	13,970,000	$ 12,574	13,750,000	$ 19,476	7,812,501	$ 33,288	14,091,686	$104,846	4,237,290	$ 1	$ 1,534	(48,241)	$ (46,706)

THIRD HARMONIC BIO, INC.
CONSOLIDATED STATEMENTS OF CHANGES IN REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share amounts)
(continued)

	Redeemable Convertible Preferred Stock												
	Series A-1		Series A-2		Series A-3		Series B		Common Stock		Additional Paid-In	Accumulated	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Deficit	(Deficit)
Balance at December 31, 2021	13,970,000	$ 12,574	13,750,000	$ 19,476	7,812,501	$ 33,288	14,091,686	$ 104,846	4,237,290	$ 1	$ 1,534	$ (48,241)	$ (46,706)
Vesting of restricted stock	—	—	—	—	—	—	—	—	624,334	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—		—	4,751	—	4,751
Exercise of stock options	—	—	—	—	—	—	—	—	13,282	—	107	—	107
Conversion of convertible preferred stock into common stock upon closing of initial public offering	(13,970,000)	(12,574)	(13,750,000)	(19,476)	(7,812,501)	(33,288)	(14,091,686)	(104,846)	21,967,316	2	170,184	—	170,186
Issuance of common stock upon closing of initial public offering, net of issuance costs and underwriting fees of $2.3M	—	—	—	—	—	—	—	—	12,535,000	1	195,884	—	195,885
Net loss	—	—	—	—	—	—	—	—	—	—	—	(35,155)	(35,155)
Balance at December 30, 2022	—	$ —	—	$ —	—	$ —	—	$ —	39,377,222	$ 4	$ 372,460	$ (83,396)	$ 289,068

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

THIRD HARMONIC BIO, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands, except share and per share amounts)

	Year Ended December 31, 2021	2022
Cash flows from operating activities:		
Net loss	$ (29,609)	$ (35,155)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	510	4,751
Depreciation	—	1
Change in fair value of preferred stock tranche liability	9,928	—
Change in fair value of anti-dilution liability	682	—
Noncash operating lease expense	—	37
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(728)	(3,071)
Other assets	—	(1,037)
Accounts payable	1,216	290
Accrued expenses and other current liabilities	2,255	(708)
Changes in operating lease liabilities	—	(25)
Net cash used in operating activities	(15,746)	(34,917)
Cash flows from investing activities:		
Purchase of property and equipment	—	(36)
Net cash used in investing activities	—	(36)
Cash flows from financing activities:		
Proceeds from issuance of preferred stock, net of issuance costs	135,749	—
Proceeds from issuance of common stock in initial public offering, net of issuance costs and underwriting fees	—	198,178
Proceeds from the exercise of stock options	—	107
Payment of offering costs	—	(2,294)
Net cash provided by financing activities	135,749	195,991
Net increase in cash, cash equivalents and restricted cash	120,003	161,038
Cash, cash equivalents and restricted cash at beginning of period	8,277	128,280
Cash, cash equivalents and restricted cash at end of period	$ 128,280	$ 289,318
Supplemental disclosure of cash flows:		
Right of use asset obtained in exchange for operating lease liability	$ —	$ 4,364
Conversion of preferred stock into common stock	$ —	$ 170,184
Preferred stock tranche liability established in connection with the issuance of redeemable convertible preferred stock	$ 2,979	$ —
Issuance of redeemable convertible preferred stock in settlement of preferred stock tranche liability	$ 17,149	$ —
Gain on extinguishment of preferred stock tranche liability record to additional paid in capital	$ 750	$ —
Issuance of redeemable convertible preferred stock in settlement of anti-dilution right liability	$ 1,566	$ —

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

1. Nature of the Business

Third Harmonic Bio, Inc., or the Company, is a biopharmaceutical company focused on advancing the next wave of medicine for the treatment of inflammatory disease, including dermal, respiratory, and gastrointestinal diseases.

The Company was incorporated in 2019 as a Delaware corporation, and we have two offices located in San Francisco, California and Cambridge, Massachusetts. In December 2021, the Company formed THB MS, Inc., a Delaware corporation and wholly-owned subsidiary of the Company, which is classified as a Security Corporation in Massachusetts.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, completion and success of clinical testing, development by competitors of new technological innovations, compliance with governmental regulations, dependence on key personnel and protection of proprietary technology and the ability to secure additional capital to fund operations. Development of a drug candidate requires extensive research and development and clinical testing prior to regulatory approval and commercialization. These efforts require significant amounts of additional capital, adequate personnel, and infrastructure and extensive compliance-reporting capabilities. Even if the Company's drug development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Initial public offering

On September 19, 2022, the Company closed its initial public offering, or the IPO, and issued 12,535,000 shares of common stock, including the exercise in full by the underwriters of their option to purchase up to 1,635,000 additional shares of common stock, at a public offering price of $17.00 per share. The Company received $198.2 million, net of underwriting discounts and commissions, but before deducting offering costs payable by the Company, which were $2.3 million. Immediately prior to the closing of the IPO, all outstanding shares of redeemable convertible preferred stock converted into 21,967,316 shares of common stock (see Note 8). In connection with the closing of its IPO, on September 19, 2022, the Company amended its certificate of incorporation to authorize the issuance of up to 500,000,000 shares of $0.0001 par value common stock and 10,000,000 shares of $0.0001 par value preferred stock.

Reverse stock split

On September 7, 2022, the Company effected a 1-for-2.259 reverse stock split of the Company's outstanding common stock. All common stock, stock options and per share information presented in the consolidated financial statements have been adjusted to reflect the reverse stock split on a retroactive basis for all periods presented. There was no change in the par value of the Company's common stock. The ratio by which shares of preferred stock are convertible into shares of common stock was adjusted to reflect the effects of the reverse stock split.

Liquidity

In accordance with Accounting Standards Codification, or ASC, 205-40, *Going Concern*, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date the accompanying consolidated financial statements were issued.

As an emerging growth entity, the Company has devoted substantially all of its resources since inception to organizing and staffing the Company, business planning, raising capital, establishing its intellectual property portfolio, acquiring or discovering product candidates, research and development activities for an oral KIT inhibitor and other compounds, establishing arrangements with third parties for the manufacture of its product candidates and component materials, and providing general and administrative support for these operations. As a result, the Company has incurred significant operating losses and negative cash flows from operations since its inception and anticipates such losses and negative cash flows will continue for the foreseeable future.

Since its inception, the Company has funded its operations primarily with proceeds from sales of shares of its redeemable convertible preferred stock and most recently with proceeds from the IPO. The Company has incurred recurring losses since its inception, including net losses of $29.6 million and $35.2 million for the years ended December 31, 2021 and 2022, respectively. As of December 31, 2022, the Company had an accumulated deficit of $83.4 million. To date the Company has not generated any revenues and expects to continue to generate operating losses for the foreseeable future. As of the issuance date of these consolidated financial statements, the Company expects that its existing cash and cash equivalents of $288.9 million as of December 31, 2022, will be sufficient to fund its operating expenses and capital expenditure requirements for at least the next 12 months from the issuance date of these consolidated financial statements.

COVID-19 Pandemic

The global coronavirus disease 2019, or COVID-19, pandemic continues to evolve, and the Company will continue to monitor the ongoing COVID-19 pandemic. The extent of the impact of the ongoing COVID-19 pandemic on the Company's business, operations and development timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the outbreak and its impact on the Company's contract development and manufacturing organizations, or CDMOs, contract research organizations, or CROs, and other third parties with whom the Company does business, as well as its impact on regulatory authorities and key scientific and management personnel. The ultimate impact of the ongoing COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. The Company's financial results for the year ended December 31, 2021 and 2022, were not significantly impacted by the ongoing COVID-19 pandemic, however, the Company cannot at this time predict the specific extent, duration, or full impact that the ongoing COVID-19 pandemic will have on its financial condition, operations, and business plans for 2023, including the timing and enrollment of patients in its planned clinical trials and other expected milestones of its future product candidates.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America, or GAAP, and include the operations of Third Harmonic Bio, Inc. and its wholly-owned subsidiary. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the ASC and as amended by Accounting Standards Updates, or ASUs, of the Financial Accounting Standards Board, or FASB. All intercompany accounts, transactions, and balances have been eliminated in consolidation.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual of research and development expenses, and the valuations of common stock, preferred stock tranche liability, and anti-dilution right liability. The Company bases its estimates on historical experience when available, known trends and other market-specific data, or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates when there are changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

Segment Information

Operating segments are defined as components of an enterprise for which separate and discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company has one operating segment. The Company's focus is the research and development of the treatment of mast cell driven inflammatory diseases. The Company's chief operating decision maker, its chief executive officer, manages the Company's operations on a consolidated basis for the purpose of allocating resources.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include standard checking accounts and amounts held in money market funds. These accounts are guaranteed by the Federal Deposit Insurance Corporation, or FDIC, up to $250,000 per account per institution. At December 31, 2022, we held deposits in excess of FDIC insured limits.

Restricted Cash

As of December 31, 2022, the Company was required to maintain a separate cash balance of $0.3 million and $0.2 million in the form of a letter of credit, for the benefit of the landlord in connection with the Company's Prospect Street office space lease in Cambridge, Massachusetts, or the Prospect Street Lease, and the Company's Montgomery Street office space lease in San Francisco, California, or the Montgomery Street Lease, respectively, which are each classified as restricted cash (non-current) on the consolidated balance sheets (see Note 12).

	December 31, 2021	December 31, 2022
Cash and cash equivalents	$ 128,280	$ 288,877
Restricted cash	—	441
Cash, cash equivalents and restricted cash	$ 128,280	$ 289,318

Concentration of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash, cash equivalents and short term marketable securities. The Company regularly maintains deposits in accredited financial institutions in excess of federally insured limits. The Company invests its excess cash primarily in money market funds, U.S. treasury notes, and high quality, marketable debt instruments of corporations in accordance with the Company's investment policy. The Company's investment policy defines allowable investments and establishes guidelines relating to credit quality, diversification, and maturities of its investments to preserve principal and maintain liquidity. The Company has not experienced any losses related to its cash equivalents and marketable securities and management believes the Company is not exposed to significant risks of losses.

As of December 31, 2022, the Company held cash deposits at Silicon Valley Bank, or SVB, in excess of FDIC insured limits. On March 10, 2023, SVB was closed by the California Department of Financial Protection and Innovation, and the Federal Deposit Insurance Corporation, or FDIC, was appointed as receiver. No losses were incurred by the Company on deposits that were held at SVB. Management believes that the Company is not currently exposed to significant credit risk as the vast majority of the Company's deposits were either owned directly by the Company or held in custody at a third-party financial institution. As of March 27, 2023, the Company has approximately $3.4 million on deposit with SVB and is currently evaluating its banking relationships in light of recent events.

The Company is dependent on third-party CDMO's and CROs with whom it does business. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements of active pharmaceutical ingredients and formulated drugs in order to perform research and development activities in its programs. The Company also relies on a limited number of third-party CROs to perform research and development activities on its behalf. These programs could be adversely affected by significant interruption from these providers.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on 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—Quoted prices in active markets for identical assets or liabilities.

Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. The Company's preferred stock tranche liability and anti-dilution right liability were carried at fair value, determined according to Level 3 inputs in the fair value hierarchy described above.

An entity may choose to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings.

Research and Development Expenses

Research and development costs are charged to expense as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities, including personnel-related costs, stock-based compensation expense, clinical trial costs, contracted research services, research-related manufacturing, and other external costs.

The Company has entered into various research and development and other agreements with commercial firms, researchers, universities, and others for provisions of goods and services. These agreements are generally cancellable, and the related costs are recorded as research and development expenses as incurred. Research and development expenses include costs for salaries, employee benefits, subcontractors, facility-related expenses, depreciation and amortization, stock-based compensation, laboratory supplies, and external costs of outside vendors engaged to conduct discovery, nonclinical and clinical development activities, and clinical trials as well as to manufacture clinical trial materials, and other costs.

Nonrefundable advance payments for goods and services to be received in the future for use in research and development activities are recorded as prepaid expenses and expenses as the related goods are delivered or the services are performed.

Accrued Research and Development Expenses

The Company has entered into various research and development contracts. The payments under these contracts are generally cancellable and are recorded as research and development expenses as incurred. The Company records accrued liabilities for estimated ongoing research and development costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes the progress of the research and development activities, including the phase or completion of events, invoices received and contracted costs. Significant judgements and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications such as direct application fees, and legal and consulting expenses are expensed as incurred due to the uncertainty about the recovery of the expenditure. Patent-related costs are classified as general and administrative expenses within the Company's consolidated statements of operations.

Property, Plant and Equipment

Property and equipment are stated at cost, less accumulated depreciation and amortization, and comprise of furniture and equipment for use in the Company's office space, as well as leasehold improvements made by the Company to the leased office space. Depreciation is provided using the straight-line method over the estimated useful lives of the assets, which is generally five years for furniture and equipment and three years for computer equipment. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the improvements. Depreciation and amortization begin at the time the asset is placed in service.

Leases

The Company adopted FASB ASC 842 with an effective date of January 1, 2020, using the modified retrospective transition approach which uses the effective date as the date of initial application. In accordance with ASC 842, the Company determines whether an arrangement is or contains a lease at inception. A contract is or contains a lease if the contract conveys the right to control the use of an identified asset for a period of time in exchange for consideration. The Company classifies leases at the lease commencement date, when control of the underlying asset is transferred from the lessor to the lessee, as operating or finance leases and records a right-of-use, or ROU, asset and a lease liability on the consolidated balance sheet for all leases with an initial lease term of greater than 12 months. The Company has elected to not recognize leases with a lease term of 12 months or less on the balance sheet.

The Company enters into contracts that contain both lease and non-lease components. Non-lease components may include maintenance, utilities, and other operating costs. For leases of real estate, the Company combines the lease and associated non-lease components in its lease arrangements as a single lease component. Variable costs, such as utilities or maintenance costs, are not included in the measurement of right-of-use assets and lease liabilities, but rather are expensed when the event determining the amount of variable consideration to be paid occurs.

Lease assets and liabilities are recognized at the lease commencement date based on the present value of the lease payments over the lease term using the discount rate implicit in the lease if readily determinable. If the rate implicit is not readily determinable, the Company utilizes an estimate of its incremental borrowing rate based upon the available information at the lease commencement date. ROU assets are further adjusted for initial direct costs, prepaid rent, or incentives received. Operating lease payments are expensed using the straight-line method as an operating expense over the lease term. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option.

Redeemable Convertible Preferred Stock

The Company classified redeemable convertible preferred stock, or Preferred Stock, as temporary equity in the accompanying consolidated balance sheets due to terms that allowed for redemption of the shares upon certain events that are outside of the Company's control. Costs incurred in connection with the issuance of redeemable convertible preferred stock, as well as the recognition of the preferred stock tranche liability, were recorded as a reduction of gross proceeds from issuance. The Company did not accrete the carrying values of the preferred stock to the redemption values since the occurrence of these events were not considered probable as of December 31, 2021. Immediately prior to the closing of the initial public offering on September 19, 2022, all outstanding shares of our redeemable convertible preferred stock were converted into common stock (see Note 7).

Preferred Stock Tranche Liability

The Company classified the preferred stock tranche liability for the future purchase, and option to purchase, preferred stock as a liability on its balance sheets as the preferred stock tranche liability was a freestanding financial instrument that would have required the Company to transfer equity instruments upon subsequent closings of the preferred stock financings. The preferred stock tranche liability was initially recorded at fair value upon the date of issuance and was subsequently remeasured to fair value at each reporting date. Changes in the fair value of the preferred stock tranche liability were recognized as a component of other income and expense in the statements of operations. Changes in the fair value of the preferred stock tranche liability were recognized until the tranche liability was fulfilled or otherwise extinguished. As of December 31, 2021, the preferred stock tranche liability has been fulfilled or otherwise extinguished (see Note 7) in full.

Anti-Dilution Right Liability

The Company classified the anti-dilution right under its license agreement with Novartis International Pharmaceutical Ltd., or Novartis, as a derivative liability on its consolidated balance sheets as the anti-dilution right represented a freestanding financial instrument that may have required the Company to transfer equity instruments upon future equity closings. The anti-dilution right liability was initially recorded at fair value upon the date of issuance and was subsequently remeasured to fair value at each reporting date. The issuance date fair value of the anti-dilution right liability was recognized as a research and development expense upon entering into the agreement with Novartis. Changes in the fair value of the anti-dilution right liability were recognized as a component of other income and expense in the statements of operations. Changes in the fair value of the antidilution right liability were recognized until the anti-dilution right with Novartis was satisfied in the first quarter of 2021, in connection with the closing of the second tranche of the Series A-2 redeemable convertible preferred stock, or Series A-2 Preferred Stock, and the issuance and sale of the Series A-3 redeemable convertible preferred stock, or Series A-3 Preferred Stock. As of December 31, 2021, the anti-dilution liability was fulfilled (see Note 6).

Stock-Based Compensation

The Company accounts for all share-based payment awards granted to employees and non-employees as stock-based compensation expense at fair value, based on the date of the grant, and recognizes compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. The Company's share-based payments include stock options and grants of restricted stock awards. For stock-based awards with service-based vesting conditions, the Company recognizes compensation expense using the straight-line method. For awards with both performance and service-based vesting conditions, the Company records expense using an accelerated attribution method, once the performance conditions are considered probable of being achieved, using management's best estimates.

The fair value of each stock option is estimated on the grant date using the Black-Scholes option pricing model, which requires inputs based on certain subjective assumptions, including:

- *Fair Value of Common Stock*—Prior to the Company's IPO, the Company determined that based on the stage of development and other relevant factors, it was most appropriate to prepare the common stock valuations using the option-pricing method, or OPM, which used a market approach to estimate our enterprise value. After the completion of the Company's IPO, the Company will determine the fair value of the common stock based on the quoted market price of the common stock.
- *Expected Term*—The expected term represents the period that the stock-based awards are expected to be outstanding. We use the simplified method to determine the expected term, which is based on the average of the time-to-vesting and the contractual life of the options.
- *Expected Volatility*—Due to our limited operating history and lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the average volatility for comparable publicly traded biotechnology companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on the similar size, stage in life cycle or area of specialty. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.
- *Risk-Free Interest Rate*—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the awards.
- *Dividend Yield*—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

Significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date.

The Company adopted ASU No. 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting, or ASU No. 2018-07, at inception of the 2019 Stock Incentive Plan, prior to the issuance of any stock option grants. The measurement date for non-employee awards is the date of grant. Stock-based compensation costs for non-employees are recognized as expense over the vesting period on a straight-line basis.

Stock-based compensation expense is classified in the accompanying consolidated statement of operations in the same manner in which the award recipient's payroll costs are classified or in which the award recipients service payments are classified.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the financial statement and tax bases of assets and liabilities by using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

Deferred tax assets are recognized to the extent that the Company believes that these assets are more likely than not to be realized. In making such a determination, the Company considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If the Company determines that it would be able to realize deferred tax assets in the future in excess of their net recorded amount, the Company would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company records uncertain tax positions in accordance with ASC 740 on the basis of a two-step process in which (i) the Company determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (ii) for those tax positions that meet the more-likely-than-not recognition threshold, the Company recognizes the largest amount of tax benefit that is more than 50 percent likely to be realized upon ultimate settlement with the related tax authority.

Interest and penalties are recognized related to unrecognized tax benefits on the income tax expense line in the accompanying consolidated statement of operations. As of December 31, 2021 and 2022, no accrued interest or penalties are included on the related tax liability line in the consolidated balance sheet.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' deficit that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2021 and 2022, there was no difference between net loss and comprehensive loss and accordingly a statement of comprehensive loss is not presented.

Net Income (Loss) Per Share

The Company follows the two-class method when computing net income (loss) per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities, which included the Company's redeemable convertible preferred stock, 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.

The Company's redeemable convertible preferred stock contractually entitled the holders of such shares to participate in dividends but did not contractually require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss attributable to common stockholders, such losses are not allocated to such participating securities. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is antidilutive. The Company reported a net loss attributable to common stockholders for years ended December 31, 2021, and 2022.

Basic net income (loss) per share attributable to common stockholders is computed by dividing net income (loss) by the weighted-average number of common shares outstanding during the period. Diluted net income (loss) attributable to common stockholders is computed by adjusting net income (loss) attributable to common stockholders to reallocate undistributed earnings based on the potential impact of diluted securities. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the weighted-average number of common shares outstanding for the period, including potential dilutive common shares. For the purpose of this calculation, unvested restricted common stock, outstanding stock options, and redeemable convertible preferred stock are considered potential dilutive common shares.

Emerging Growth Company Status

The Company is an emerging growth company, as defined in the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an emerging growth company or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these consolidated financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

Recently Adopted 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 impact of recently issued standards that are not yet effective will not have a material impact on the Company's consolidated financial statements upon adoption. Under the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act, the Company meets the definition of an emerging growth company and has elected the extended transition period for complying with certain new or revised accounting standards pursuant to Section 107(b) of the JOBS Act.

In December 2019, the FASB issued ASU No. 2019-12, or ASU-2019-12, *Simplifying the Accounting for Income Tax*, which contains several provisions that reduce financial statement complexity including removing the exception to the incremental approach for intra-period tax expense allocation when a company has a loss from continuing operations and income from other items not included in continuing operations. The Company adopted this accounting standard as of January 1, 2022 with no material impact on its consolidated financial statements.

Recently Issued Accounting Pronouncements Not Yet Adopted

Management evaluated other recently issued accounting pronouncements and does not believe that any of these pronouncements will have a significant impact on the consolidated financial statements and related disclosures.

3. Fair Value Measurements

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

		December 31, 2021		
Description	**Total**	**Quoted Prices in Active Markets for Identical Assets (Level 1)**	**Significant Other Observable Inputs (Level 2)**	**Significant Other Observable Inputs (Level 3)**
Money market funds	$ 22,505	$ 22,505	$ —	$ —
Total financial assets	$ 22,505	$ 22,505	$ —	$ —

		December 31, 2022		
Description	**Total**	**Quoted Prices in Active Markets for Identical Assets (Level 1)**	**Significant Other Observable Inputs (Level 2)**	**Significant Other Observable Inputs (Level 3)**
Money market funds	$ 286,580	$ 286,580	$ —	$ —
Total financial assets	$ 286,580	$ 286,580	$ —	$ —

As of December 31, 2021 and December 31, 2022, the Company had no financial liabilities that required fair value measurement. As of December 31, 2021 and December 31, 2022, the Company's cash equivalents consisted of money market funds, classified as Level 1 financial assets, as these assets are valued using quoted market prices in active markets without any valuation adjustment.

During the year ended December 31, 2021 and year ended December 31, 2022 there were no transfers or reclassifications between fair value measurement levels of assets or liabilities. The carrying values of prepaid expenses and other current assets, accounts payable and accrued expenses and other current liabilities approximate their fair values due to the short-term nature of these assets and liabilities.

4. Property, Plant and Equipment

Property, plant and equipment consisted of the following (in thousands):

	December 31, 2021	December 31, 2022
Construction in progress	$ —	$ 16
Office furniture	—	—
Computer equipment	—	20
Lab equipment	—	—
Property, plant and equipment, gross	—	36
Less: Accumulated depreciation	—	(1)
Property, plant and equipment, net	$ —	$ 35

Depreciation expense was $1 for the year ended December 31, 2022, which has been recorded within general and administrative expenses.

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2021	December 31, 2022
Accrued research and development expenses	$ 2,685	$ 1,444
Professional fees	450	339
Employee compensation and related benefits	752	1,165
Other	2	233
Total accrued expenses and other current liabilities	$ 3,889	$ 3,181

6. Novartis License Agreement

On June 28, 2019, the Company entered into a License Agreement, or the Novartis License Agreement, with Novartis Pharma AG, formerly known as Novartis International Pharmaceutical Ltd, or Novartis. Pursuant to the Novartis License Agreement, the Company has been granted an exclusive, worldwide, royalty-bearing, sublicensable license under specified patent rights and know-how related to two licensed compounds, to develop, make, use and sell certain products incorporating or comprising a licensed compound, including THB001, to certain intellectual property rights owned or controlled by Novartis, or the Licensed IP, to research, develop, make, use, sell, and commercialize products containing the Licensed IP.

Under the Novartis License Agreement, the Company is solely responsible for all research, development, regulatory and commercialization activities related to the Licensed IP. The Company is required to use commercially reasonable efforts to develop and seek regulatory approval for, and commercialize, at least one licensed product in each of the United States, France, Germany, Italy, Spain, the United Kingdom, and Japan.

In exchange for these rights, the Company made an upfront cash payment of $0.4 million and issued 3,449,808 shares of Series A-1 Preferred Stock with a fair value of $3.0 million to Novartis. Upon entering into the Novartis License Agreement in 2019, the total initial consideration of $3.4 million transferred to Novartis was charged to expenses as research and development expense. The Company determined that the Novartis License Agreement represented an asset acquisition as it did not meet the definition of a business. The Company recorded the initial consideration transferred to Novartis as research and development expense in the statement of operations because the acquired Licensed IP represented in-process research and development with no alternative future use.

In addition, under the Novartis License Agreement, an anti-dilution right was issued to Novartis, in which Novartis is entitled to receive shares of Series A-1 Preferred Stock, guaranteeing them a 15% ownership interest of the fully diluted capitalization of the Company. The Company was obligated to issue additional shares of Series A-1 Preferred Stock until the Company had (1) raised aggregate cumulative proceeds of $30.0 million from sales of equity securities since its inception; or (2) issued and sold any securities that generate proceeds in excess of $30.0 million. Additionally, the Company was not obligated to issue more than 6,383,142 shares of the Series A-1 Preferred Stock to Novartis under the anti-dilution right. The Company assessed the Novartis anti-dilution right and determined that the right (i) meets the definition of a freestanding financial instrument that is not indexed to the Company's own stock and (ii) meets the definition of a derivative and does not qualify for equity classification. The initial fair value of the anti-dilution right liability of $1.0 million was recorded as research and development expense in July 2019, as part of the initial consideration in the license agreement. The Company remeasured the liability associated with the anti-dilution right at each reporting date and at each issuance of Series A-1 Preferred Stock under the anti-dilution right. Changes in the fair value were recorded as other income and expense in the statement of operations until the anti-dilution right was satisfied in February 2021 upon the Company raising aggregate cumulative proceeds of $30.0 million in sales of equity securities. As part of the anti-dilution right, the Company issued a total of 5,970,000 shares of Series A-1 Preferred Stock to Novartis. During the year ended December 31, 2021, the Company recorded an expense associated with changes in fair value of the anti-dilution right liability of $0.7 million. No expense was recognized during the year ended December 31, 2022 as the anti-dilution liability was satisfied in February 2021.

Under the Novartis License Agreement, the Company is obligated to make aggregate milestone payments of up to $231.7 million related to the achievement of specified development, commercialization, and sales milestones. The Company records the milestone payments as research and development expenses when the milestones occur and consideration is paid or becomes payable. As of December 31, 2022, the Company has made two development milestone payments under the Novartis Agreement totaling $1.0 million, of which $0.4 million was achieved and paid in 2019, and $0.6 million was achieved and paid in 2020, which have been recorded as research and development expense. No other milestones have occurred or have been paid under the Novartis License Agreement.

As part of the Novartis License Agreement, the Company also agreed to pay tiered royalties based on future net sales of all products licensed under the agreement, of which the royalty percentage ranged within the single digits.

7. Redeemable Convertible Preferred Stock

As of December 31, 2021, the redeemable convertible preferred stock consisted of the following (in thousands, except share amounts):

	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Value	Common Stock Issuable Upon Conversion
Series A-1 Preferred Stock	13,970,000	13,970,000	$ 12,574	$ 13,970	6,184,150
Series A-2 Preferred Stock	13,750,000	13,750,000	19,476	22,000	6,086,762
Series A-3 Preferred Stock	7,812,501	7,812,501	33,288	20,000	3,458,386
Series B Preferred Stock	14,091,689	14,091,686	104,846	105,000	6,238,018
Total	49,624,190	49,624,187	$ 170,184	$ 160,970	21,967,316

Immediately prior to the closing of the initial public offering on September 19, 2022, all outstanding shares of our redeemable convertible preferred stock were converted into 21,967,316 shares of common stock and the related carrying value was reclassified to common stock and additional paid-in capital. Accordingly, there were no shares of redeemable convertible preferred stock outstanding as of December 31, 2022.

8. Stockholder's Equity (Deficit)

Common stock

As of December 31, 2021 and December 31, 2022, the Company's Amended and Restated Certificate of Incorporation authorized the Company to issue 72,731,000 and 500,000,000 shares of common stock, with a par value of $0.0001, respectively. The voting, dividend and liquidation rights of the holders of the Company's common stock were subject to and qualified by the rights, preferences and privileges of the holders of the redeemable convertible preferred stock.

The holders of the common stock are entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders. There are not cumulative voting rights for the election of directors in the restated certificate of incorporation, which means that holders of a majority of the shares of the common stock will be able to elect all of the directors. Common stockholders are entitled to receive dividends, as may be declared by the board of directors, or the Board, if any, subject to the preferential dividend rights of redeemable convertible preferred stock. Through December 31, 2022, no cash dividends had been declared or paid.

On September 19, 2022, the Company completed its IPO, at which time the Company issued 12,535,000 shares of common stock, including the exercise in full by the underwriters of their option to purchase up to 1,635,000 additional shares of common stock, at a public offering price of $17.00 per share. The Company received $198.2 million, net of underwriting discounts and commissions, but before deducting offering costs payable by the Company, which were $2.3 million. Upon the closing of the IPO, all outstanding shares of redeemable convertible preferred stock converted into 21,967,316 shares of common stock (see Note 6). As of December 31, 2021 and December 31, 2022, there were 4,237,290 and 39,377,222 shares of common stock issued and outstanding, respectively.

The following shares of common stock were reserved for issuance as follows:

	December 31, 2021	December 31, 2022
Conversion of outstanding shares of preferred stock	21,967,316	—
Options to purchase common stock	394,254	3,644,500
Unvested restricted common stock	1,907,102	964,992
Remaining shares reserved for future issuance	2,065,764	3,801,282
Total	26,334,436	8,410,774

Undesignated preferred stock

As of December 31, 2022, the Company’s Amended and Restated Certificate of Incorporation authorized the Company to issue up to 10,000,000 shares of undesignated preferred stock, par value $0.0001 per share. There were no undesignated preferred shares issued or outstanding as of December 31, 2022.

9. Stock-Based Compensation

2019 Stock Incentive Plan

The Company's 2019 Stock Incentive Plan, or the 2019 Plan, provided for the Company to grant incentive stock options, stock appreciation rights, restricted stock, restricted stock units, and other stock-based awards. The 2019 Plan was administered by the Board or, at the discretion of the Board, by a committee delegated by Board. The exercise prices, vesting and other restrictions were determined at the discretion of the Board, or its committee if so delegated. The Company’s Board valued the Company’s common stock, taking into consideration its most recently available valuation of common stock performed by third party valuation specialists as well as additional factors which may have changed since the date of the most recent contemporaneous valuation through the date of grant.

The total number of shares of common stock that could have been issued under the 2019 Plan was 5,317,559 shares, of which 283,808 shares remained available for grant on September 19, 2022, the date that the Company's 2022 Equity Incentive Plan, or the 2022 Plan, became effective. Upon the effectiveness of the 2022 Plan, the 283,808 remaining shares available under the 2019 Plan were transferred and became available for issuance under the 2022 Plan. Shares of common stock underlying outstanding awards under the 2019 Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of stock, expire or are otherwise terminated (other than by exercise) will be added to the shares of common stock available for issuance under the 2022 Plan.

2022 Plan

The 2022 Plan was approved by the Board and stockholders in August 2022. The 2022 Plan became effective on September 14, 2022 and replaced the Company's 2019 Plan on that date. The 2022 Plan authorizes the award of incentive stock options, or ISOs, non-qualified stock options, or NQSOs, Restricted Stock Awards, or RSAs, Stock Appreciation Rights, or SARs, Restricted Stock Units, or RSUs, performance awards and stock bonus awards. Pursuant to the 2022 Plan, ISOs may be granted only to employees.

The number of shares initially reserved for issuance under the 2022 Plan is 4,710,545 shares of common stock, which includes the 283,808 shares transferred from the 2019 Plan, and shall automatically increase on January 1 of each of 2023 through 2032 by the number of shares equal of the lesser of 5% of the aggregate number of shares of all classes of the common stock, plus the total number of shares of common stock issuable upon conversion of any preferred stock (if any) or exercise of any pre-funded warrants, as issued and outstanding as of the immediately preceding December 31, or a number as may be determined by the Board.

The 2022 Plan is administered by the Board or, at the discretion of the Board, by a committee of the Board. The exercise prices, vesting and other restrictions are determined at the discretion of the Board, or its committee if so delegated, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the share of common stock on the date of grant and the term of stock option may not be greater than ten years.

Shares that are expired terminated, surrendered or cancelled under the 2022 Plan without having been fully exercised will be available for future awards.

Stock Options

The assumptions that the Company used to determine the grant-date fair value of stock options awarded to employees, were as follows for the year ended December 31, 2021 and 2022:

	Year Ended December 31,	
	2021	2022
Expected term (in years)	6.06-6.53	5.19-6.53
Expected volatility	82.4 - 84.2%	72.8-83.5%
Risk-free interest rate	0.87-1.20%	1.70-4.21%
Expected dividend yield	—	—
Fair value of common stock	$ 1.90	$4.30-18.40

The following table summarizes the Company's stock option activity since December 31, 2021:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2021	394,254	$ 0.85	9.08	$ 3,294
Granted	3,448,476	11.41		
Exercised	(13,283)	7.92		
Forfeited or cancelled	(184,947)	8.19		
Outstanding as of December 31, 2022	3,644,500	10.45	9.51	1,283
Options vested and exercisable as of December 31, 2022	173,529	6.82	8.93	581
Options unvested as of December 31, 2022	3,470,971	10.70	9.57	769

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock.

The weighted-average grant-date fair value per share of stock options granted during the year ended December 31, 2022 was $8.27. As of December 31, 2022, there was $25.3 million of unrecognized stock-based compensation expense related to unvested stock options, to be recognized over a weighted-average period of 3.70 years.

The total fair value of options vested during the year ended December 31, 2022 was $1.9 million.

Included within the total stock options outstanding are 115,580 stock options to purchase common stock which have performance-based vesting criteria and were granted to certain employees, officers and consultants of the Company on various dates during the years ended December 31, 2020 and 2021, collectively, the Performance Stock Options. Vesting of 37,133 of the Performance Stock Options was contingent on the closing of the Series A-2 Second Tranche, which occurred on February 24, 2021, and vesting of the remaining 97,938 Performance Stock Options was contingent on the closing of the Series A-3 Second Tranche, which occurred on November 15, 2021. The vesting commencement date of the Performance Stock Options was the date in which the performance condition is met, and vesting occurs based on the accelerated attribution method over four years from the vesting commencement date. The Company began to recognize expense associated with the Performance Stock Options on the date in which each respective performance criteria was met and recognized total stock-based compensation expense associated with the Performance Stock Options of less than $0.1 million for the year ended December 31, 2021 and $0.1 million for the year ended December 31, 2022. No expense associated with the Performance Stock Options was recognized prior to the year ended December 31, 2021.

Restricted Common Stock Awards

The Company has granted restricted common stock awards with service and performance and service based vesting conditions to employees of the Company. Unvested shares of restricted common stock may not be sold or transferred by the holder, except for transfers for estate planning purposes in which the transferee agrees to remain bound by all restrictions set forth in the original common stock purchase agreement. These restrictions lapse over the vesting term of each award, which is typically four years. The purchase price of each share of restricted common stock was $0.0001 per share.

On August 9, 2021, the Company's chief executive office, or CEO, purchased 1,218,836 shares of common stock at a purchase price of $1.44 per share, under the terms of a restricted common stock award granted under the 2019 Plan. These shares were purchased in exchange for a promissory note, or the Promissory Note, of $1.8 million. The shares granted include both service and performance-based vesting criteria and accrued at an interest rate of 0.76% per annum, compounded annually and were accounted for as restricted stock.

On August 22, 2022, the Company forgave the entire promissory note, including principal and accrued and unpaid interest. As a result this is considered a modification to the original awards, and the Company recognized the grant date fair value plus any incremental fair value due to the modification. The incremental cost was measured as the difference between the fair value of the award at modification date and the fair value of the original award immediately prior to modification. As a result of accounting for the modification, the Company recorded an incremental stock based compensation charge of $1.0 million, which will be recognized over the remaining requisite service period of the award from the date of the modification.

The CEO was paid a one-time special bonus of $1.9 million to offset the CEO's tax liability as a result of the forgiveness of the promissory note, or the Tax Payment, which is subject to a three-year vesting schedule with six-month cliffs. The Company is allowed to claw-back the unvested portion of the Tax Payment in the event that the CEO's employment is terminated before the end of the three-year vesting period, provided that the CEO's employment is terminated by the Company other than for cause, or if the CEO resigns for a good reason (a) within 12 months following a change of control, or (b) within 3 months preceding a change in control but as to only if the separation occurs after a potential change in control. In the event the CEO's employment is terminated, the unvested portion of the Tax Payment will accelerate and will not be subject to the claw back provision. The clawback provision will be accounted for if and when the CEO leaves under the relevant circumstances and the payment amount will be capitalized and recognized over the related service period as G&A employee salary expense.

A summary of the activity of the restricted common stock since December 31, 2021:

	Number of Shares	Weighted-Average Grant Date Fair Value Per Share
Unvested at December 31, 2021	1,907,102	$ 1.17
Granted	—	—
Vested	(624,334)	1.33
Cancelled or forfeited	(317,776)	0.71
Unvested at December 31, 2022	964,992	$ 0.59

The weighted-average grant-date fair value per share of restricted common stock awards granted during the year ended December 31, 2022 was zero as no shares were granted in the period. The aggregate fair value of restricted stock awards that vested during the year ended December 31, 2022 was $0.7 million. Stock-based compensation expense recognized for the restricted stock granted was $1.1 million for the year ended December 31, 2022. As of December 31, 2022, there was unrecognized expense of $1.2 million related to the restricted stock, which is expected to be recognized over a weighted-average period of 2.29 years.

Stock-Based Compensation Expense

Stock-based compensation expense included in the Company's consolidated statements of operations was as follows (in thousands):

	Year Ended December 31,	
	2021	2022
Research and development	224	1,650
General and administrative	286	3,101
Total stock-based compensation expense	510	4,751

10. Income Taxes

Income (loss) before provision for income taxes consisted of the following (in thousands):

	Year ended December 31,	
	2021	2022
Domestic	$ (29,609)	$ (35,155)
Foreign	—	—
Loss before provision for income taxes	$ (29,609)	$ (35,155)

A reconciliation of the Company's statutory income tax rate to the Company's effective income tax rate is as follows:

	Year ended December 31,	
	2021	2022
Income at US statutory rate	21.00%	21.00%
State taxes, net of federal benefit	3.43%	3.60%
Change in tranche liability	-7.04%	0.00%
Non-deductible Compensation	-0.21%	-3.31%
Tax credits	1.03%	0.50%
Valuation allowance	-18.21%	-21.78%
Other	0.00%	-0.01%
	0.00%	0.00%

The net deferred income tax asset balance related to the following (in thousands):

	Year ended December 31,	
	2021	2022
Net operating loss carryforwards	$ 7,935	$ 10,336
Research and development credits	774	1,006
Intangibles	1,613	1,422
Capitalized research and development	—	5,433
Right of use liabilities	—	1,087
Stock-based compensation	—	211
Accrued expenses & other	252	274
Total deferred tax assets	10,574	19,769
Right of use assets	—	(1,084)
Deferred compensation	—	(445)
Other	—	—
Total deferred tax liabilities	—	(1,529)
Net Deferred Tax assets	10,574	18,240
Valuation allowance	(10,574)	(18,240)
Deferred Tax Assets, Net of Valuation Allowance	$ —	$ —

As of December 31, 2021 and 2022, the Company had a federal net operating loss carryforward of $29.8 million and $38.9 million, respectively, which can be carried forward indefinitely. As of December 31, 2021 and 2022, the Company has state NOL carryforwards of $26.7 million and $34.1 million, respectively. The state net operating loss carryforwards begin to expire in 2039.

As of December 31, 2022, the Company also has federal and state tax credits of $0.8 million and $0.2 million, which begin to expire in 2039 and 2039, respectively.

The Tax Cuts and Jobs Act contained a provision which requires the capitalization of Section 174 costs incurred in years beginning on or after January 1, 2022. Section 174 costs are expenditures which represent research and development costs that are incident to the development or improvement of a product, process, formula, invention, computer software, or technique. This provision changes the treatment of Section 174 costs such that the expenditures are no longer allowed as an immediate deduction but rather must be capitalized and amortized. The Company has included the impact of this provision, which results in a deferred tax asset of approximately $5.4 million as of December 31, 2022.

Future realization of the tax benefits of existing temporary differences and net operating loss carryforwards ultimately depends on the existence of sufficient taxable income within the carryforward period. As of December 31, 2021 and 2022, the Company performed an evaluation to determine whether a valuation allowance was needed. The Company considered all available evidence, both positive and negative, which included the results of operations for the current and preceding years. The Company determined that it was not possible to reasonably quantify future taxable income and determined that it is more likely than not that all of the deferred tax assets will not be realized. Accordingly, the Company maintained a full valuation allowance as of December 31, 2021 and 2022.

Under Internal Revenue Code Section 382, if a corporation undergoes an “ownership change,” the corporation’s ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income may be limited. The Company has not completed a study to assess whether an “ownership change” has occurred or whether there have been multiple ownership changes since we became a “loss corporation” as defined in Section 382. Future changes in the Company's stock ownership, which may be outside of the Company's control, may trigger an “ownership change.” In addition, future equity offerings or acquisitions that have equity as a component of the purchase price could result in an “ownership change.” If an “ownership change” has occurred or does occur in the future, utilization of the NOL carryforwards or other tax attributes may be limited, which could potentially result in increased future tax liability to the Company.

The calculation of our tax liabilities involves dealing with uncertainties in the application of complex tax laws and regulations for both federal taxes and the many states in which we operate or do business in. ASC 740 states that a tax benefit from an uncertain tax position may be recognized when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, on the basis of the technical merits.

The Company records uncertain tax positions as liabilities in accordance with ASC 740 and adjust these liabilities when our judgment changes as a result of the evaluation of new information not previously available. Because of the complexity of some of these uncertainties, the ultimate resolution may result in a payment that is materially different from the Company's current estimate of the unrecognized tax benefit liabilities. These differences will be reflected as increases or decreases to income tax expense in the period in which new information is available. As of December 31, 2021 and 2022, the Company has not recorded any uncertain tax positions in our financial statements.

The Company recognizes interest and penalties related to unrecognized tax benefits on the income tax expense line in the accompanying consolidated statement of operations. As of December 31, 2021 and 2022, no accrued interest or penalties are included on the related tax liability line in the consolidated balance sheet.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. The Company’s tax years are still open under statute from December 31, 2019, to the present. The resolution of tax matters is not expected to have a material effect on the Company’s consolidated financial statements.

11. Net Loss Per Share

The following table sets forth the computation of the Company's basic and diluted net loss per share for the periods presented (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2021	2022
Numerator:		
Net loss	$ 29,609	$ 35,155
Net loss attributable to common stockholders, basic and diluted	$ 29,609	$ 35,155
Denominator:		
Weighted-average number of common shares used in net loss per share, basic and diluted	4,043,416	13,426,066
Net loss per share of common stock, basic and diluted	$ 7.32	$ 2.62

The Company excluded the following shares from the computation of diluted net loss per share attributable to common stockholders during the year ended December 31, 2021 and 2022 because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2021	2022
Redeemable convertible preferred stock	21,967,316	—
Options to purchase common stock	394,254	3,644,500
Unvested restricted stock	1,907,102	964,992
Total	24,268,672	4,609,492

12. Leases

Operating Leases for Office Space

In October 2022, the Company entered into an office space lease approximating 10,356 of rentable square feet, located at 130 Prospect Street in Cambridge, Massachusetts. The lease commenced on December 1, 2022 when the Company took occupancy of the space, and has an initial lease term of 63 months, expiring on February 29, 2028 with no renewal options.

Also in October 2022, the Company entered into an office space lease approximating 4,703 of rentable square feet located at 1700 Montgomery Street in San Francisco, California. The lease commenced on December 20, 2022 when the Company took occupancy of the space, and has an initial lease term of 63 months, expiring on February 20, 2028 with no renewal options.

The Company also leased various office suites on a month-to month basis from Atlas Venture Life Science Advisors, or Atlas, and other third parties during the years ended December 31, 2021 and 2022. As the Company elected to not recognize leases with a lease term of 12 months or less on the balance sheet, no operating lease right of use assets and liabilities were recognized.

During the year ended December 31, 2021 and 2022, the components of operating lease cost were as follows, and are reflected in general and administrative expenses and research and development expenses, as determined by the underlying activities:

	December 31, 2021	December 31, 2022
Lease Cost:	$ —	$ —
Operating lease cost	—	75
Variable operating lease cost	—	—
Short-term operating lease cost	97	195
Total operating lease cost	$ 97	$ 270

The following table summarizes information related to the measurement of the Company's operating leases for the years ended December 31, 2021 and 2022:

	December 31, 2021	December 31, 2022
Weighted-average remaining lease term	—	5.20
Weighted-average discount rate	—	10.5%
Cash paid for amounts included in the measurement of operating lease liabilities	$ —	$ —

Maturities of operating lease liabilities at December 31, 2022 are as follows (in thousands):

2023	$ 826
2024	1,116
2025	1,145
2026	1,176
Thereafter	1,445
Total lease payments	5,708
Less: interest	(1,369)
Total lease liability	$ 4,339

13. Commitments and Contingencies

Legal Proceedings

From time to time, in the ordinary course of business, the Company is subject to litigation and regulatory examinations as well as information gathering requests, inquiries and investigations. As of December 31, 2021 and 2022, there were no litigation matters which would have a material impact on the Company’s financial results.

14. Related Party Transactions

Entities Affiliated with Atlas Venture Fund XI, L.P.

Entities affiliated with Atlas Venture Fund XI, L.P. are a significant beneficial owner of the Company, holding more than 5% of the total outstanding stock of the Company, as of December 31, 2021 and 2022. The Company leased various office space from Atlas for use in its daily operations through September 2022.

During the year ended December 31, 2021 and 2022, the Company made payments of $0.2 million and $0.1 million, respectively associated with the lease agreements with Atlas, which was recorded within the general and administrative expense.

Novartis

Novartis is a significant beneficial owner of the Company, holding more than 5% of the total outstanding stock of the Company, as of December 31, 2021 and December 31, 2022. The Company has an in-license agreement with Novartis, which required the Company to make an upfront payment and issue shares of Series A-1 Preferred Stock to Novartis, and further includes future milestone payments upon the occurrence of certain events and royalty payments upon future sales. Refer to Note 6.

CEO Promissory Note

On August 9, 2021, the Company entered into the Promissory Note with the CEO for an amount of $1.8 million, which was used to allow the CEO to purchase 1,218,836 shares of common stock granted in the form of a restricted stock award under the 2019 Plan. The Promissory Note had a stated interest rate of 0.76%, which was compounded annually. The entire Promissory Note, including principal and accrued and unpaid interest, was forgiven on August 22, 2022. The Company has paid the CEO a one-time special bonus of $1.9 million, which was paid to offset the CEO's tax liability as a result of the forgiveness of the Promissory Note. This is subject to a three-year vesting schedule with six-month cliffs, as well as continued employment with the company on the relevant vesting dates. Refer to Note 15 Employee Benefit Plans.

15. Employee Benefit Plans

Effective January 1, 2019, the Company adopted a 401(k) Plan for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the 401(k) Plan within statutory and 401(k) Plan limits. Since inception of the plan and through the year ended December 31, 2022 the Company has not made any contributions to the 401(k) Plan.

16. Subsequent Events

On March 6, 2023, the Board of Directors of the Company approved the reduction in exercise price of certain options that had been granted under the 2019 Plan and the 2022 Plan, that have an exercise price greater than or equal to $8.61 per share, which were each repriced at an exercise price of $4.20. There were no changes in the vesting schedule or maturity term of the options. The Company expects to record the impact of the option repricing in the quarter ending March 31, 2023.

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

As of December 31, 2022, management, with the participation of our Principal Executive Officer and Principal Financial and Accounting Officer, performed an evaluation of the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including the Principal Executive Officer and the Principal Financial and Accounting Officer, to allow timely decisions regarding required disclosures. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Principal Executive Officer and Principal Financial and Accounting Officer concluded that, as of December 31, 2022, our disclosure controls and procedures were effective at a reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

This Annual Report does not include a report of management's assessment regarding our internal control over financial reporting or an attestation report of our independent registered accounting firm due to a transition period established by rules of the SEC for newly public companies. Additionally, our independent registered accounting firm will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an "emerging growth company" as defined in the JOBS Act.

Changes in Internal Control over Financial Reporting

Management determined that, as of December 31, 2022, there were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter then ended that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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.

The information required by this item will be included in our Proxy Statement for the 2023 Annual Meeting of Stockholders, to be filed with the SEC within 120 days of the fiscal year ended December 31, 2022, and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this item will be included in our Proxy Statement for the 2023 Annual Meeting of Stockholders, to be filed with the SEC within 120 days of the fiscal year ended December 31, 2022, 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 will be included in our Proxy Statement for the 2023 Annual Meeting of Stockholders, to be filed with the SEC within 120 days of the fiscal year ended December 31, 2022, and is incorporated herein by reference.

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

The information required by this item will be included in our Proxy Statement for the 2023 Annual Meeting of Stockholders, to be filed with the SEC within 120 days of the fiscal year ended December 31, 2022, and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be included in our Proxy Statement for the 2023 Annual Meeting of Stockholders, to be filed with the SEC within 120 days of the fiscal year ended December 31, 2022, and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

The following documents are filed as part of this Annual Report:

1. Financial Statements

See Index to Financial Statements under Part II, Item 8 of this Annual Report.

2. Financial Statement Schedules

Schedules not listed above have been omitted because they are not required, not applicable, or the required information is otherwise included.

3. Exhibits

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed herewith
3.1	Restated Certificate of Incorporation.	10-Q	001-41498	3.1	11/9/2022	
3.2	Amended and Restated Bylaws.	8-K	001-41498	3.1	12/21/2022	
4.1	Form of Common Stock Certificate.	S-1/A	333-267022	4.1	09/08/2022	
4.2	Description of Registrant's Securities.					X
4.3	Amended and Restated Investors' Rights Agreement, dated December 17, 2021 by and among the Registrant and certain of its stockholders.	S-1	333-267022	4.2	8/23/2022	
10.1+	Form of Indemnity Agreement.	S-1/A	333-267022	10.1	09/08/2022	
10.2+	2019 Stock Incentive Plan, as amended, and forms of award agreements.	S-1	333-267022	10.2	08/23/2022	
10.3+	2022 Equity Incentive Plan and forms of award agreements.	S-1/A	333-267022	10.3	09/08/2022	
10.4+	2022 Employee Stock Purchase Plan and forms of award agreements.	S-1/A	333-267022	10.4	09/08/2022	
10.5^	Use and Occupancy Agreement, dated February 1, 2021, by and among and Registrant and Atlas Venture Life Science Advisors, LLC.	S-1	333-267022	10.5	08/23/2022	
10.6^	Use and Occupancy Agreement, dated July 1, 2021, by and between the Registrant and Atlas Venture Life Science Advisors, LLC.	S-1	333-267022	10.6	08/23/2022	
10.7†^	License Agreement, dated June 28, 2019, by and between the Registrant and Novartis International Pharmaceutical Ltd.	S-1	333-267022	10.7	08/23/2022	
10.8+	Offer Letter, dated July 2, 2021, by and between the Registrant and Natalie Holles.	S-1	333-267022	10.8	08/23/2022	
10.9+	Amended and Restated Employment Agreement, dated August 22, 2022, between the Registrant and Natalie Holles.	S-1/A	333-267022	10.9	09/08/2022	
10.10+	Offer Letter, dated February 14, 2022, by and between the Registrant and Robert Ho.					X
10.11+	Offer Letter, dated May 12, 2022, by and between the Registrant and Edward Conner.					X
10.12+	Form of Change in Control and Severance Agreement.	S-1/A	333-267022	10.10	09/08/2022	
10.13+	Consulting Agreement, dated June 14, 2019, by and between the Registrant and Mark Iwicki.	S-1	333-267022	10.11	08/23/2022	

10.14+	Consulting and Scientific Advisory Board Agreement, dated July 25, 2019, by and between the Registrant and H. Martin Seidel.	S-1	333-267022	10.10	08/23/2022	
10.15†^	Lease Agreement, dated October 21, 2022, between 130 Prospect Limited Partnership and the Registrant.					X
10.16†^	Office Lease Agreement, dated October 21, 2022, between JPPF Waterfront Plaza, L.P. and the Registrant.					X
21.1	Subsidiaries of the Registrant.					X
23.1	Consent of Deloitte & Touche LLP.					X
24.1	Power of Attorney (reference is made to the signature page hereto).					X
31.1	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.					X
31.2	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.					X
32.1*	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.					X
32.2*	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.					X
101.INS	Inline XBRL Instance Document.					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Cover Page Interactive Data File (formatted in iXBRL and contained in Exhibit 101).					X

† The Registrant has omitted portions of the exhibit as permitted under Item 601(b)(10) of Regulation S-K.

^ The Registrant has omitted schedules and exhibits pursuant to Item 601(b)(2) of Regulation S-K. The Registrant agrees to furnish supplementally a copy of the omitted schedules and exhibits to the SEC upon request.

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

* This certification is deemed not filed for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Annual Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Third Harmonic Bio, Inc.

Date: March 29, 2023

By: /s/ Natalie Holles
Natalie Holles
Chief Executive Officer and Director *(Principal Executive Officer)*

Date: March 29, 2023

By: /s/ Robert Ho
Robert Ho
Chief Financial Officer *(Principal Financial and Accounting Officer)*

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Natalie Holles and Robert Ho, and each of them, as her or his true and lawful attorneys-in-fact, proxies and agents, each with full power of substitution and resubstitution, for her or him and in her or his name, place and stead, in any and all capacities, to sign any and all amendments to this report and to file the same, with any exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto such attorneys-in-fact, proxies and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact, proxies and agents, or their or his or her substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Natalie Holles Natalie Holles	Chief Executive Officer and Director (*Principal Executive Officer*)	March 29, 2023
/s/ Robert Ho Robert Ho	Chief Financial Officer and Treasurer (*Principal Financial and Accounting Officer*)	March 29, 2023
/s/ Mark Iwicki Mark Iwicki	Director	March 29, 2023
/s/ David P. Bonita David P. Bonita	Director	March 29, 2023
/s/ Michael Gladstone Michael Gladstone	Director	March 29, 2023
/s/ Rob Perez Rob Perez	Director	March 29, 2023
/s/ H. Martin Seidel H. Martin Seidel	Director	March 29, 2023
/s/ Thomas M. Soloway Thomas M. Soloway	Director	March 29, 2023

Third Harmonic
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