
# 2022 Annual Report

# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**Washington, DC 20549**

# FORM 10-K

**(Mark One)**

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

**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: 001-40869**

# Theseus Pharmaceuticals, Inc.

**(Exact Name of Registrant as Specified in Its Charter)**

| **Delaware** | **83-0712806** |
|---|---|
| **(State or Other Jurisdiction of Incorporation or Organization)** | **(IRS Employer Identification No.)** |
| **314 Main Street Cambridge, Massachusetts** | **02142** |
| **(Address of Principal Executive Offices)** | **(Zip Code)** |

**(857) 400-9491**

**(Registrant's Telephone Number, Including Area Code)**

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 | THRX | The Nasdaq Global Select Market |

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. **Yes** ☐ **No** ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 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, a smaller reporting company, or an emerging growth company. See the definitions of the "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 the 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 Act). **Yes** ☐ **No** ☒

The aggregate market value of the voting and non-voting common stock held by non-affiliates of the registrant based on the closing price of the registrant's common stock as reported on the Nasdaq Global Select Market on June 30, 2022, was $85.6 million. For purposes of this disclosure, shares of common stock held by each executive officer, director and stockholder known by the registrant to be affiliated with such individuals based on public filings and other information known to the registrant have been excluded since such persons may be deemed affiliates. This determination of executive officer or affiliate status is not necessarily a conclusive determination for other purposes.

As of March 1, 2023, there were 43,561,124 shares of the registrant's common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive Proxy Statement relating to its 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2022 are incorporated herein by reference in Part III of this Annual Report on Form 10-K.

**Theseus Pharmaceuticals, Inc.**
**FORM 10-K**
**INDEX**

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, including the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," as well as information included in oral statements or other written statements made or to be made by us, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. All statements contained in this Annual Report other than statements of historical fact, including statements regarding our future operating results and financial position, our business strategy and plans, market growth, and our objectives for future operations, are forward-looking statements. The words "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "target," "plan," "expect," and similar expressions are intended to identify forward-looking statements.

Forward-looking statements contained in this Annual Report include, but are not limited to, statements about:

- the ability of our preclinical studies and clinical trials to demonstrate safety and efficacy of product candidates and other positive results;
- the initiation, timing, progress, results and cost of our research and development programs and our current and future preclinical studies and clinical trials for current product candidates and other product candidates we may develop, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the studies or trials will become available, and our research and development programs;
- the timing, scope and likelihood of regulatory filings and approvals, including timing of investigational new drug applications, or INDs, and final approval by the US Food and Drug Administration, or the FDA, of our current product candidates and any future product candidates we may develop;
- our ability to develop and advance our current product candidates and development programs into, and successfully complete, clinical trials;
- our manufacturing, commercialization, and marketing capabilities and strategy;
- our plans relating to commercializing product candidates, if approved, including the geographic areas of focus and sales strategy;
- the need to hire additional personnel and our ability to attract and retain such personnel;
- the size of the market opportunity for our product candidates and development programs, including our estimates of the number of patients who suffer from the diseases we are targeting;
- our competitive position and the success of competing therapies that are or may become available;
- the beneficial characteristics, and the potential safety, efficacy and therapeutic effects of product candidates;
- the potential advantages of our integrated research and development approach;
- our ability to obtain and maintain regulatory approval of product candidates;
- our plans relating to the further development of product candidates, including additional indications we may pursue;

- existing regulations and law and regulatory developments in the United States, or US, Europe and other jurisdictions;

- our expectations regarding the impact of the COVID-19 pandemic on our business and the timing and enrollment of our clinical trials;

- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering our current product candidates and other product candidates we may develop, including the extensions of existing patent terms where available, the validity of intellectual property rights held by third parties, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;

- our continued reliance on third parties to conduct additional preclinical studies and clinical trials of product candidates;

- our ability to contract with third-party suppliers and manufacturers for the manufacture of product candidates for preclinical studies and clinical trials and their ability to perform timely and adequately as a result of supply chain constraints or otherwise;

- our ability to obtain, and negotiate favorable terms of, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize product candidates;

- the pricing and reimbursement of current product candidates and other product candidates we may develop, if approved;

- the rate and degree of market acceptance and clinical utility of current product candidates and other product candidates we may develop;

- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;

- our expected use of proceeds from sales of our common stock in “at-the-market” offerings and the period over which such proceeds, together with existing cash, will be sufficient to meet our operating needs;

- our financial performance;

- the period over which we estimate our existing cash, cash equivalents, and marketable securities will be sufficient to fund our future operating expenses and capital expenditure requirements;

- our expectations regarding the period during which we will remain an emerging growth company under the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act;

- our anticipated use of our existing cash resources;

- developments relating to our competitors, our industry or the economy; and

- other risks and uncertainties, including those listed in the section titled “Risk Factors” in Part I, Item 1A of this Annual Report.

We caution you that the foregoing list may not contain all of the forward-looking statements made in this Annual Report.

These forward-looking statements are subject to a number of risks, uncertainties, and assumptions, including those described in the section titled “Risk Factors” in Part I, Item 1A 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 future events and trends 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. The events and circumstances reflected in the forward-looking statements may not be achieved or occur. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, performance or achievements. We undertake no obligation to update any of these forward-looking statements for any reason after the date of this Annual Report or to conform these statements to actual results or to changes in our expectations, except as required by law.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

You should read this Annual Report and the documents that we reference in this Annual Report and have filed with the Securities and Exchange Commission with the understanding that our actual future results, performance and events and circumstances may be materially different from what we expect.

## RISK FACTOR SUMMARY

Our business and our ability to execute our business strategy are subject to numerous risks. These risks include, among others:

- We are very early in our development efforts, have a limited operating history, have not completed any clinical trials, have no products approved for commercial sale and have not generated any revenue, which may make it difficult for investors to evaluate our current business and likelihood of success and viability.

- We have incurred significant net losses in each period since our inception, and we expect to continue to incur significant net losses for the foreseeable future.

- Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve in a timely manner our objectives relating to the discovery, development and commercialization of our product candidates and development programs.

- We will need to obtain substantial additional funding to complete the development and, if approved, any commercialization of our product candidates. If we are unable to raise this capital when needed, we may be forced to delay, reduce or eliminate our product development programs or other operations.

- We are very early in our development efforts and are substantially dependent on THE-630, our pan-variant KIT product candidate for gastro-intestinal stromal tumors, or GIST, and THE-349, our fourth-generation epidermal growth factor receptor, or EGFR, product candidate, for non-

small cell lung cancer, or NSCLC. If we are unable to advance any product candidates through preclinical and clinical development, obtain regulatory approval and ultimately commercialize such product candidates, or experience significant delays in doing so, our business will be materially harmed.

- We may not be able to submit INDs for our EGFR inhibitor product candidate, THE-349, or for our BCR-ABL or other discovery programs, to commence clinical trials on the timelines we expect, and even if we are able to submit an IND, the FDA may not permit us to initiate clinical trials.

- Our ongoing and anticipated preclinical studies and clinical trials may fail at any time, and because our most advanced product candidates THE-630 and THE-349 are in a very early stage of development, there is a high risk of failure, and we may never succeed in developing marketable products.

- We have limited experience as a company in conducting clinical trials.

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

- We have never commercialized a product candidate as a company before and currently lack the necessary expertise, personnel and resources to successfully commercialize any products on our own or together with suitable collaborators.

- We may be unable to obtain US or foreign regulatory approval and, as a result, may be unable to commercialize product candidates.

- We depend on intellectual property licensed from ARIAD Pharmaceuticals, Inc., or ARIAD, the termination of which could result in the loss of significant rights, which would harm our business.

- If we and our licensors and collaborators, if any, are unable to obtain and maintain sufficient patent and other intellectual property protection for product candidates and technology, our competitors could develop and commercialize products and technology similar or identical to ours, and we may not be able to compete effectively in our market or successfully commercialize any product candidates we may develop.

## PART I

### ITEM 1. Business

#### Overview

We are a clinical-stage biopharmaceutical company focused on improving the lives of cancer patients through the discovery, development, and commercialization of transformative targeted therapies. Our development programs are designed to address drug resistance mutations in key driver oncogenes, which are mutated genes that cause cancer. Resistance mutations limit the efficacy of existing targeted therapies by rendering tumor cells unresponsive to drugs, and therefore present a critical challenge in cancer treatment today. Our initial focus is on developing the next generation of tyrosine kinase inhibitors, or TKIs, and is rooted in the critical role that tyrosine kinases play in the development of cancer. Despite the commercial success of approved TKIs, the development of drug resistance is a persistent limitation, narrowing the number of effective treatment options available to patients as they progress through subsequent lines of therapy.

Our goal is to develop “pan-variant” kinase inhibitors-inhibitors that target all major cancer causing and drug resistance mutations in clinically significant protein kinases. We believe that truly pan-variant inhibitors are required to effectively inhibit the heterogeneous mix of resistance mutations found in patients, and may also suppress the emergence of new mutations when used in earlier lines of therapy. To develop such inhibitors, we deploy our novel Predictive Resistance Assay™, or PRA, a highly differentiated cell-based method for testing TKIs that we believe is predictive for “pan-ness”. We also employ structure-guided drug design, and, coupled with our PRA, we believe our approach has the potential to optimize molecules for pan-variant activity while maintaining selectivity and tolerability.

Our most advanced product candidate, THE-630, is a pan-variant inhibitor of all major classes of activating and resistance mutations of the KIT kinase for the treatment of GIST, a type of cancer most often characterized by oncogenic activation of KIT. GIST is the most common sarcoma of the gastrointestinal tract and often initiates in the stomach or small intestines. We are currently enrolling patients in a Phase 1/2 dose escalation and dose expansion clinical trial for the evaluation of THE-630 in patients with advanced GIST whose disease has developed resistance to prior KIT-targeting therapies. As of December 31, 2022, we were treating patients in cohort 5 of dose escalation, with all seven planned Phase 1 sites in the US open and enrolling patients. We expect to present initial data from the Phase 1 dose escalation portion of the clinical trial at an academic meeting in the second quarter of 2023, and to report additional data from the dose escalation study at an academic meeting in the fourth quarter of 2023. The primary objective of the Phase 1 dose escalation portion of the study are to evaluate the safety profile of THE-630, including the determination of a recommended Phase 2 dose, or RP2D, in GIST patients who have received imatinib and at least one other TKI. Secondary objectives include determining the pharmacokinetic, or PK, profile of THE-630, and to characterize preliminary evidence of antitumor activity of THE-630. Once an RP2D is determined, the study will transition into the Phase 2 portion consisting of three expansion cohorts in patients with second-line GIST, third or fourth-line GIST, and fifth (or greater) line GIST. The Phase 2 dose expansion portion is expected to include sites in the US and Europe. The FDA has granted orphan drug designation to THE-630 for the treatment of GIST.

Our second product candidate is THE-349, a fourth-generation EGFR inhibitor for the treatment of NSCLC. THE-349 is designed to address on-target treatment resistance to existing EGFR inhibitors by targeting the common activating mutations in exons 19 and 21 alone or in combination with the most frequently observed resistance mutations, T790M and C797X. Preclinical characterization of THE-349 as central nervous system, or CNS active, and mutant-selective inhibitor with potent activity against single-, double-, and triple-mutant EGFR variants, including T790M and C797X, was shared in a poster presentation at the 34th EORTC-NCI-AACR, or ENA, Symposium in Barcelona on October 26-28, 2022. We have initiated IND-enabling studies, and expect to file an IND application for this product candidate with the FDA in the fourth quarter of 2023. We plan to pursue initial clinical development as monotherapy in patients with C797X-mediated resistance after treatment with osimertinib, or another third-generation inhibitor, and then, assuming positive clinical data and subject to discussions with the FDA, expand into evaluation of combination treatment with other relevant

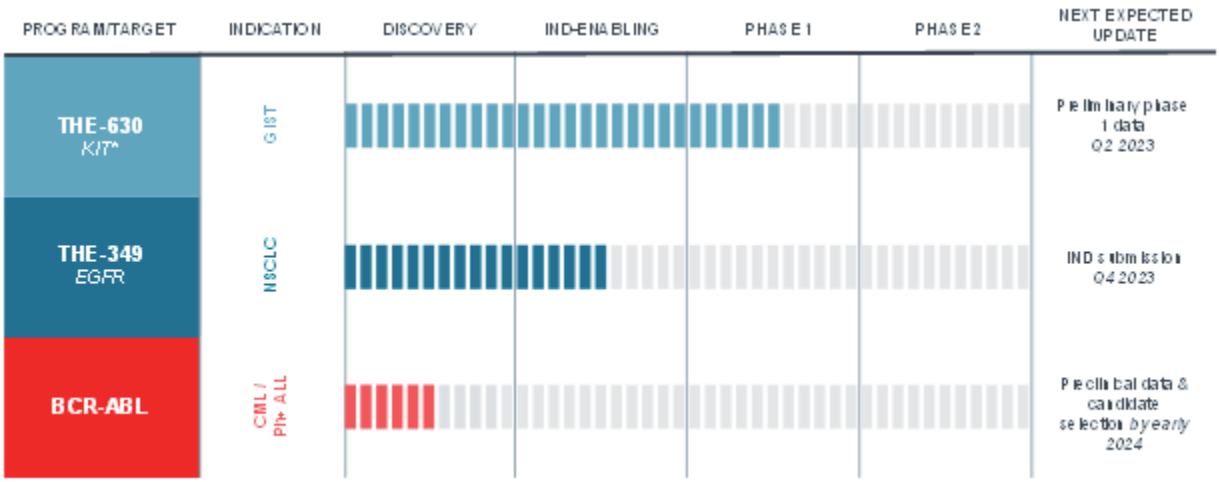
modalities and, if clinical data support, target a broader second-line patient population to address the unmet need of patients who have been previously treated with osimertinib, but progress with either on-target or off-target resistance.

Our third program is a next-generation BCR-ABL TKI that we are designing to be potent, selective, and pan-variant—features that we believe would balance safety and efficacy—for patients with relapsed/refractory chronic myeloid leukemia, or CML, and Philadelphia chromosome-positive, or Ph+, acute lymphoblastic leukemia, or ALL. We expect to nominate a development candidate for this program by early 2024, with the goal of pursuing clinical development in patients with CML who have been previously treated with a second-generation TKI or have the T315I mutation, and in combination therapy for newly diagnosed patients with Ph+ ALL.

Our differentiated approach to addressing drug resistance is built on three strategic pillars: (1) targeting clinically-validated oncogenic drivers that have a clear unmet need; (2) integrating structure-guided drug design with our predictive screening methodologies, including our PRA; and (3) pursuing translationally-driven, biomarker-guided clinical development strategies. We believe our research and development approach, honed over years of our management team's experience in developing approved therapeutics at ARIAD, positions us well to develop a pipeline of drugs to address the challenges posed by resistance mutations.

**Our Pipeline**

Our current product candidates, targeting KIT (THE-630) and EGFR (THE-349), and our BCR-ABL program, are next-generation TKIs that aim to address the key limitation of drug resistance, and are summarized below:




* We hold exclusive rights to all our programs. For THE-630, we hold a worldwide exclusive license in our therapeutic area of focus through the ARIAD License Agreement, as defined and described in the section titled "Business—ARIAD License Agreement."

***THE-630: Pan-Variant KIT Inhibitor***

Our most advanced product candidate, THE-630, is a pan-variant KIT inhibitor for the treatment of patients with advanced GIST. GIST is the most common sarcoma of the gastrointestinal tract and is often initiates in the stomach or small intestines. Current estimates for the total number of GIST cases diagnosed each year in the US range from approximately 4,000 to 6,000. Prevalence is estimated to be 13.5 to 15.5 cases per 100,000 people, and therefore approximately 48,000 patients are estimated to be living with GIST in the US each year. Front-line intervention is surgical removal of cancerous tissue when possible. In cases where the

tumor has spread and/or surgery cannot be performed, the TKI imatinib is often used as first-line therapy. However, most patients receiving imatinib relapse and subsequent lines of therapy are less effective.

THE-630 is a novel small molecule TKI that has been designed to block activity of all major classes of activating and resistance mutations of KIT that drive GIST. Existing TKIs for GIST are limited by the emergence of resistance mutations, as clinical data have demonstrated their inability to inhibit disease progression as these mutations arise in tumor cell populations. THE-630 is a pan-variant KIT inhibitor for GIST, with potent activity demonstrated in cellular assays and strong anti-tumor activity demonstrated in animal models against both activating and resistance mutations. We believe THE-630, if approved, has the potential to overcome limitations of existing TKIs based on its promising inhibitory profile and favorable drug-like properties, as well as its potential to achieve predicted pan-variant KIT inhibitory blood concentrations at tolerable doses in preclinical safety studies.

We are currently enrolling patients in a Phase 1/2 dose escalation and dose expansion clinical trial for the evaluation of THE-630 in patients with advanced GIST whose disease has developed resistance to prior KIT-targeting therapies. We expect to present initial data from the Phase 1 portion of the clinical trial at an academic meeting in the second quarter of 2023, and to report additional data from the dose escalation study at an academic meeting in the fourth quarter of 2023. As of December 31, 2022, we were treating patients in cohort 5 of dose escalation, with all seven planned Phase 1 sites in the US open and enrolling patients. The primary objective of the Phase 1 dose escalation portion of the study is to evaluate the safety profile of THE-630, including determination of an RP2D, in GIST patients who have received imatinib and at least one other TKI. Secondary objectives include determining the PK profile of THE-630, and to characterize preliminary evidence of antitumor activity of THE-630. Once an RP2D is determined, the study will transition into the Phase 2 portion consisting of three expansion cohorts in patients with second-line GIST, third or four-line GIST and fifth (or greater) line GIST. The Phase 2 dose expansion portion is expected to include sites in the US and Europe.

Assuming positive clinical data and subject to discussions with the FDA, our registration strategy will evaluate THE-630 in two different GIST populations. One population will be GIST patients who have already received four prior lines of therapy, or fifth-line GIST, where there is currently no available therapy and therefore a significant unmet medical need. Given its broad mutational coverage as a pan-variant KIT inhibitor, we also plan to evaluate THE-630 in GIST patients who only received prior imatinib, or in second-line GIST. Our goal is to pursue our registrational trials in fifth-line and second-line GIST in parallel. Based on the preclinical profile and known clinical limitations of marketed therapies for GIST, we believe THE-630 has the potential to deliver meaningful clinical benefit over the currently available standards of care.

The FDA has granted orphan drug designation to THE-630 for the treatment of GIST.

***THE-349: Fourth-Generation EGFR Inhibitor***

Our second product candidate is THE-349, which is a fourth-generation inhibitor of EGFR that is active against 1) C797X, the most common EGFR mutation that causes resistance to osimertinib in patients with NSCLC, 2) the most common activating mutations in EGFR, and 3) T790M, the most common mutation that confers resistance to first- and second-generation EGFR inhibitors. In addition, preclinical data have demonstrated that THE-349 has a high degree of kinome and wild-type EGFR selectivity, and exhibits substantial CNS activity.

NSCLC is the most common form of lung cancer with approximately 10% to 50% of NSCLC tumors driven by activating mutations in EGFR, depending on geographic region. Treatment of EGFR-mutant metastatic NSCLC patients with first- and second-generation EGFR TKIs, such as erlotinib, gefitinib, afatinib and dacomitinib, substantively improved outcomes for patients compared to chemotherapy. However, resistance eventually develops in most patients, leading to disease progression, with about half of patients' tumors developing the T790M EGFR mutation. Osimertinib, a third-generation TKI, was initially developed to treat T790M-positive disease in patients progressing on a first- or second-generation TKI. Subsequently, it was

approved in the first-line setting in the US where it improved progression-free and overall survival compared to earlier-generation inhibitors. However, most patients receiving treatment eventually progress. A subset of patients on osimertinib, either in first- or later-line therapy, will still progress due to further EGFR resistance mutations, with C797X being the most common of such mutations. A significant unmet medical need remains for patients with this subset of EGFR-mutant NSCLC.

To address this problem of on-target resistance, we have developed THE-349, a TKI designed to inhibit the full range of single-, double- and triple-mutant variants found in the tumors of patients with EGFR-mutant NSCLC that have developed resistance to osimertinib in first- or later-line therapy, including the C797X and T790M mutations. Preclinical data demonstrate THE-349 can potently inhibit these major classes of EGFR activating and resistance mutations, possesses kinome and wild-type EGFR selectivity, and has CNS activity. We expect to file an IND for this product candidate with the FDA in the fourth quarter of 2023, and to initiate the Phase 1/2 trial as soon as possible thereafter, subject to clearance of the IND by the FDA. We plan to pursue an initial clinical development as monotherapy in patients with C797X-mediated resistance, and then, assuming positive clinical data and subject to discussions with the FDA, expand into evaluation of combination treatment with other relevant modalities and, if clinical data support, target a broader second-line patient population to address the unmet need of patients who have been previously treated with osimertinib, but progress with either on-target or off-target resistance. We believe that continued EGFR inhibition, in combination with other relevant effective modalities, will be necessary to optimally treat patients who develop off-target resistance to osimertinib, given the clonal heterogeneity of the disease.

**Our Strategy**

We are a biopharmaceutical company focused on improving the lives of cancer patients through the discovery, development, and commercialization of transformative targeted therapies. Our development programs are designed to address drug resistance mutations in key driver oncogenes, which are mutated genes that cause cancer. The key elements of our strategy to achieve our mission are:

- ***Advance the development of our most advanced product candidate, THE-630, for GIST patients.*** We designed THE-630 as a differentiated TKI for the treatment of patients with previously-treated GIST. We believe that the broad inhibitory profile of THE-630 against all major classes of activating and resistance mutations in KIT has the potential to generate robust and durable responses for advanced GIST patients across the spectrum of previously-treated patient populations. Our registration strategy is expected to be focused on fifth-line and second-line GIST. There is currently no available therapy and therefore a significant unmet medical need in the fifth-line GIST setting. Given its broad mutational coverage as a pan-variant KIT inhibitor, we also plan to evaluate THE-630 in second-line GIST. We plan to pursue our fifth-line and second-line registrational trials in parallel.

- ***Advance THE-349, our fourth-generation EGFR inhibitor product candidate for NSCLC patients.*** We have developed THE-349, a TKI designed to inhibit the full range of single-, double- and triple-mutant variants found in the tumors of patients with EGFR-mutant NSCLC that have developed resistance to osimertinib in first- or later-line therapy, including the C797X and T790M mutations. We believe that THE-349 has the potential to meaningfully improve patient outcomes in EGFR-mutant NSCLC patients who have progressed on osimertinib given its broad and potent EGFR mutation coverage, its selectivity, and CNS activity. We expect to file an IND for this product candidate with the FDA in the fourth quarter of 2023.

- ***Leverage our differentiated research and discovery approach to advance our BCR-ABL program and expand our pipeline.*** Mutational resistance has the potential to affect the therapeutic utility of a broad range of existing oncology therapies. Our structure-guided drug design approach, integrated with our PRA, allows us to efficiently design and validate novel inhibitors against known targets that target all major activating and resistance mutations. In January 2023, we announced that our next program will be a TKI to inhibit BCR-ABL fusions, which are implicated in two diseases, CML

and Ph+ ALL, for which there are significant unmet needs for therapies that optimally balance safety and efficacy. Beyond BCR-ABL, we expect to initially focus on discovering additional kinase inhibitors, and we may also explore other oncogenic driver targets. In addition to our in-house research, we may evaluate in-licensing opportunities that could be synergistic with our pipeline.

- ***Build a leading, fully integrated precision oncology company to maximize the clinical impact and value of our pipeline.*** We believe the targeted nature of our research and discovery approach allows for efficient and focused clinical development. By developing drugs for known targets where TKI activity has previously been established, we believe we can minimize biology risk in our product development lifespan. We continue to build a lean, experienced team to rapidly advance product candidates in a capital-efficient manner. We currently intend to retain the commercialization rights to our product candidates in the US; however, we may opportunistically enter into strategic collaborations in certain geographic or clinical settings to maximize the value of our pipeline.

**Our Research and Discovery Approach**

Our approach to drug discovery is characterized by the identification of therapeutic solutions responsive to resistance mutations in certain cancers with clear unmet need. Our drug discovery approach is built on three pillars:

- ***Clinically validated targets with clear unmet need.*** We are focused exclusively on well-validated targets that are directly linked to the proliferation and survival of a tumor, known as driver oncogenes, for which the clinical activity of TKI therapies has already been established, and where there is a clear unmet need. We believe this approach can allow us to identify targets more reliably for our programs since data in patients have shown that successful inhibition of these targets will typically have the intended biological effect. We further focus on targets where there is documented observation of resistance mutations, no pan-variant TKI available to patients and lack of further treatment options for patients that have been failed by existing standards of care. These settings have a clear unmet need with a strong rationale for the development of a pan-variant inhibitor.

- ***Structure-guided drug design integrated with predictive screening methodologies.*** We design small molecule inhibitors based on deep structural knowledge of our targets and candidate molecules at the molecular level. We acquire high-resolution, atom-level structural maps of activated and mutated target proteins using techniques such as X-ray crystallography, and we supplement these with computational modeling to understand the precise changes induced by mutations. We use these approaches to guide iterative rounds of synthesis and testing of molecules. This allows us to design novel small molecule inhibitors that target all major activating and resistance mutations. To test these molecules, we deploy our PRA, a novel screening and characterization approach that incorporates two critical human serum proteins that can affect drug activity. We believe our PRA is a highly differentiated cell-based method for testing small molecule TKIs under conditions that mimic the physiological setting and that it is predictive for “pan-ness”, the ability to inhibit all major classes of activating and resistance mutations in a given target. By comparing TKI inhibitory values in this assay to achievable human blood levels of TKIs, our approach allows us to select TKIs for clinical testing that we believe have the potential to perform best in cancer patients, irrespective of mutational status. As such, although to date our PRA has not been clinically validated, we believe it allows us to apply our drug discovery expertise in selecting small molecule inhibitors that have the optimal properties for further development and testing.

- ***Translationally-driven, biomarker-guided clinical development.*** We design clinical development programs that are intended to supply rich biomarker datasets to provide us with an early assessment of activity against individual mutant variants. By monitoring mutational status of patients before and during treatment, we aim to validate the inhibition of individual mutant forms of the target protein, then correlate this with overall clinical response. We believe this will provide us with insights of potential

clinical pan-inhibitory activity and inform our investment decisions given that the process of clinical development is inherently uncertain.

**THE-630: Our Pan-Variant KIT Inhibitor**

***Summary Overview***

Our most advanced product candidate, THE-630, is a next-generation KIT inhibitor for the treatment of patients with advanced GIST. GIST is the most common sarcoma of the gastrointestinal tract and often initiates in the stomach or small intestines. The worldwide annual incidence of GIST is estimated to be between 11 and 19.6 cases per million people. Current estimates for the total number of GIST cases diagnosed each year in the US range from approximately 4,000 to 6,000. Prevalence is estimated to be 13.5 to 15.5 cases per 100,000 people, and therefore approximately 48,000 patients are estimated to be living with GIST in the US each year. We estimate that the annual addressable population for first- and second-line unresectable or metastatic GIST in the US is approximately 3,200 and 2,200 patients, respectively. Approximately 80% are driven by activating mutations in the KIT kinase. Front line intervention is surgical removal of cancerous tissue when possible. In cases where the tumor has spread and/or surgery cannot be performed, the TKI imatinib is often used as first-line therapy. Most patients receiving imatinib relapse, often with multiple KIT kinase resistance mutations, and subsequent lines of therapy are typically less effective due to a lack of coverage over all major resistance mutations in KIT, meaning that all patients who relapse are expected to ultimately succumb to their cancer. Therefore, a significant unmet need exists for GIST patients.

THE-630 is a novel small molecule TKI that blocks activity of all major classes of KIT activating and resistance mutations that drive GIST. Existing TKIs are limited by the emergence of resistance mutations, as clinical data have demonstrated their inability to inhibit disease progression as these mutations arise in tumor cell populations. THE-630 is a pan-variant KIT inhibitor for GIST, with potent activity demonstrated in cellular assays and strong anti-tumor activity in animal models against both activating and resistance mutations. We believe THE-630, if approved, has the potential to be a best-in-class KIT inhibitor for GIST patients based on its promising inhibitory profile and favorable drug-like properties, as well as its ability to achieve predicted pan-variant KIT inhibitory blood concentrations at tolerable doses in preclinical safety studies.

We are currently enrolling patients in the Phase 1 portion of a Phase 1/2 dose escalation and dose expansion clinical trial in patients with previously-treated GIST. The Phase 1 portion is enrolling patients with prior treatment with imatinib and at least one of the following: sunitinib, regorafenib, ripretinib, or avapritinib. We expect to present initial data from the Phase 1 dose escalation portion of the clinical trial in an academic meeting in the second quarter of 2023 and to report additional data from the dose escalation study at an academic meeting in the fourth quarter of 2023. As of December 31, 2022, we were treating patients in cohort 5 of dose escalation, with all seven planned Phase 1 sites in the US open and enrolling patients. The primary objective of the Phase 1 dose escalation portion of the study is to evaluate the safety profile of THE-630, including determination of an RP2D. Secondary objectives include determining the PK profile of THE-630, and to characterize preliminary evidence of antitumor activity of THE-630. Once an RP2D is determined, the study will transition into the Phase 2 portion consisting of three expansion cohorts in patients with second-line GIST, third- or four-line GIST, and fifth- (or greater) line GIST. The Phase 2 dose expansion portion is expected to include sites in the US and Europe.

Assuming positive clinical data and subject to discussions with the FDA, our registration strategy will evaluate THE-630 in two different GIST populations. One population will be GIST patients who have already received four prior lines of therapy, or fifth-line GIST, where there is currently no available therapy and therefore a significant unmet medical need. Given its broad mutational coverage as a pan-variant KIT inhibitor, we also plan to evaluate THE-630 in GIST patients who have only received prior imatinib, or second-line GIST. We plan to pursue our registrational trials in fifth-line and second-line GIST in parallel. Based on the preclinical profile and known limitations to marketed therapies for GIST, we believe THE-630 has the potential to deliver meaningful clinical benefit over the currently available standards of care.

***Overview of GIST and KIT Mutations***

GIST is the most common tumor of the gastrointestinal tract and presents most often in the stomach or small intestine. In adult GIST patients, approximately 95% of tumors overexpress the tyrosine kinase receptor KIT, while approximately 80% have KIT gene mutations that activate the KIT receptor. In normal cells, KIT receptor tyrosine kinase, or RTK, activity is regulated by binding of the endogenous ligand for the receptor. Activation of the KIT kinase caused by mutations leads to uncontrolled cancer cell growth, leading to tumor formation. As shown in Figure 1 below, there are two major classes of activating mutations in KIT that occur in different exons of the gene:

- **KIT exon 11 activating mutations** occur in approximately 70% of newly diagnosed GIST patients. These mutations are located in an intracellular domain of the receptor that usually has an inhibitory effect on kinase activation, thereby interfering with this normal inhibitory function.

- **KIT exon 9 activating mutations** occur in approximately 10% of newly diagnosed GIST patients. These mutations affect an extracellular domain, which results in ligand-independent KIT activation.

Successful targeting of KIT activating mutations by existing KIT inhibitors almost always leads to the emergence of one or more additional mutations, at separate sites in the protein, that make the tumor resistant to the inhibitor. As shown in Figure 1 below, there are also two major classes of resistance mutations that occur in different exons of the gene:

- **KIT exon 13 and exon 14 resistance mutations** are seen in up to approximately 45% of GIST patients who develop resistance to imatinib. These mutations occur in a region of the protein known as the ATP-binding pocket and block, or reduce, the ability of inhibitors to bind and impede kinase activity.

- **KIT exon 17 and exon 18 resistance mutations** are also seen in up to approximately 45% of GIST patients who develop resistance to imatinib. These mutations occur in a region of the protein known as the activation loop and block, or reduce, the ability of inhibitors to bind and impede kinase activity.

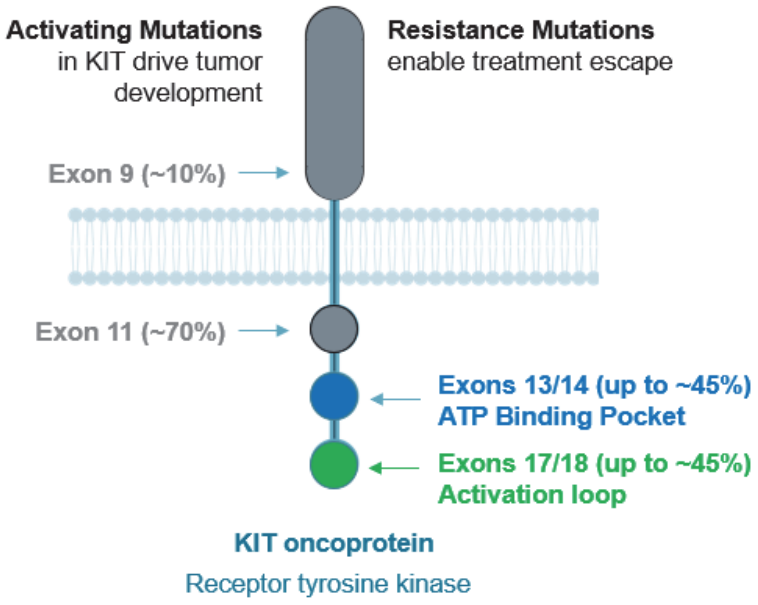



**Figure 1. The major classes of activating mutations in the KIT gene in GIST patients are found in exons 9 and 11 and the major classes of resistance mutations in the KIT gene in GIST patients are found in exons 13/14 and 17/18.**

### *Current Treatment Paradigm in GIST*

Patients diagnosed with localized GIST will typically undergo surgery to remove their tumor lesions, and those at high risk of recurrence may then receive post-operative imatinib as adjuvant therapy. Patients who present with metastatic disease at diagnosis or those who are not eligible to undergo surgical resection have several systemic treatment options at different lines of therapy. As summarized in Figure 2 below, the majority of patients receiving imatinib therapy will experience tumor progression and then progress relatively rapidly on second-, third-, and fourth-line treatments, successively. Patient outcomes are substantially worse following imatinib failure, with response rates of less than 10% for each successive line of therapy.

| LINE | THERAPY | ORR | MEDIAN PFS |
|---|---|---|---|
| First-line | Imatinib | 51.4% | 18.9 months |
| Second-line | Sunitinib | 6.8% | 5.5 months |
| Third-line | Regorafenib | 4.5% | 4.8 months |
| Fourth-line | Ripretinib | 9.4% | 6.3 months |

**Figure 2. Response rate and progression-free survival, or PFS, in successive lines of KIT-targeting therapies. Overall response rate, or ORR, includes all patients who had a 30% or greater reduction in tumor size. PFS is the length of time after initiation of treatment that a patient lives with the cancer but it does not get worse.**

### *Limitations of Current Treatment Options and Unmet Medical Need in GIST*

Despite the availability of multiple TKIs as treatment options across various lines of disease, the five-year overall survival rate of patients with unresectable or metastatic GIST is less than 60%.

Disease progression is most often driven by mutations in KIT that create resistance to the currently approved KIT targeting therapies. Such resistance mutations are found in up to 90% of tumors after imatinib failure. The resistance mutations are mainly found in two regions of the kinase domain: the ATP-binding pocket encoded within exons 13 and 14 and the activation loop encoded within exons 17 and 18.

In addition, the heterogeneity of tumor cell populations complicates the treatment of resistant GIST. Patients frequently have multiple subclones of their cancer, each with a different resistance mutation in KIT. As a result, the treatment with a TKI that only inhibits some of the resistance mutations, and therefore growth of only some of the tumor cells, will likely result in rapid outgrowth of unaffected subclones and overall disease progression.

Imatinib and sunitinib have activity against the activating mutations in exons 9 and 11, although potency against exon 9 mutations is reported to be lower for imatinib. Imatinib has relatively weak activity against resistance mutations in both the ATP-binding pocket and the activation loop, located in exons 13, 14, 17 and 18. Sunitinib is active against imatinib-resistant GIST subclones with resistance mutations in exons 13 and 14 that encode the ATP-binding pocket, including the common V654A mutation. However, it has poor activity against subclones with KIT activation loop mutations encoded by exons 17 and 18. Compared to sunitinib, regorafenib has somewhat more potent activity against activation loop mutations, but is less potent against ATP-binding pocket mutations. In the fourth-line setting, ripretinib yielded a 9.4% response rate and clinical benefit was relatively limited, with half of ripretinib-treated patients in a Phase 3 clinical trial experiencing progression within the first six months of treatment. Furthermore, in preclinical studies, ripretinib reportedly showed relatively low potency against ATP-binding-pocket mutations in exons 13 and 14.

The toxicity profile of some of these therapies also significantly limits their utility in treating patients with advanced GIST. In particular, sunitinib and regorafenib are multi-kinase inhibitors that are associated with more toxicity than imatinib, with side effects including severe hand-foot syndrome, thrombocytopenia, thyroid dysfunction and liver enzyme elevation.

The clinical benefits of second-line sunitinib and third-line regorafenib are limited: reported median PFS is six months or less in each case, and dose reductions and dose interruptions due to toxicity are commonly reported. Ripretinib has a similar median PFS of approximately six months in patients who have relapsed following treatment with imatinib, sunitinib and regorafenib. In a retrospective subgroup analysis from a recent clinical trial in second-line GIST, ripretinib was shown to provide meaningful clinical benefit over sunitinib in the subset of patients with an activating exon 11 mutation and resistance mutations in exons 17/18 only, which would be predicted by our PRA. Median PFS was shown to be 14.2 months and the ORR was 44% for ripretinib. We believe that a pan-variant KIT inhibitor such as THE-630 has the potential to show strong efficacy more broadly in second-line GIST patients, irrespective of the KIT activating and resistance mutations present.

***Our Solution: THE-630, a Pan-Variant KIT Inhibitor***

THE-630 is a pan-variant KIT inhibitor designed to address the limitations of previous generations of TKIs for patients with GIST. We designed THE-630 to have potent activity against both major classes of activating KIT mutations (exons 9 and 11), and both major classes of KIT resistance mutations that arise in: (1) the ATP-binding pocket (exons 13 and 14) and (2) the activation loop (exons 17 and 18). In preclinical studies, THE-630 achieved the predicted pan-variant KIT inhibitory blood concentrations at tolerable doses and induced significant anti-tumor activity. Given the heterogeneity of the tumor cell populations in GIST patients whose tumors progress on imatinib, and the incomplete KIT mutational coverage provided by later lines of therapy, we believe developing a next-generation KIT compound that effectively inhibits all major classes of KIT activating and resistance mutations should improve response rates and increase PFS in GIST patients in both later and earlier lines of therapy.

***Broad KIT Mutation Coverage Supported by In Vitro Data***

To accurately measure the activity of product candidates, we developed the PRA, a novel screening and characterization approach that incorporates two critical human serum proteins that can affect drug activity. Using this approach, we believe we can accurately predict the clinical activity of current TKI therapies, including imatinib, sunitinib, regorafenib and ripretinib. In so doing, we believe that we can better understand the therapeutic strengths and weaknesses of each compound, thereby allowing us to design THE-630 with an improved product profile.

To evaluate specific TKI activity, we engineered a panel of cell lines, derived from the commonly used murine Ba/F3 cell line, each of which is dependent on the activity of a different KIT variant for survival. These variants include combinations of different activating mutations and ten different resistance mutations known to arise after first and later lines of current TKI therapies in patients with GIST, as shown in Figure 3 below.

| KIT MUTANT ABBREVIATION | ACTIVATING MUTATION | | RESISTANCE MUTATION | |
|---|---|---|---|---|
| | LOCATION | GENOTYPE | LOCATION | GENOTYPE |
| **Ex11Del** | Exon 11 (JM) | Del 557_558 | — | — |
| **Ex11Del + V654A** | | | Exon 13 (ATP pocket) | V654A |
| **Ex11Del + T670I** | | | Exon 14 (ATP pocket) | T670I |
| **Ex11Del + D816G** | | | Exon 17 (A-loop) | D816G |
| **Ex11Del + D816H** | | | | D816H |
| **Ex11Del + D816Y** | | | | D816Y |
| **Ex11Del + D820A** | | | | D820A |
| **Ex11Del + D820G** | | | | D820G |
| **Ex11Del + N822K** | | | | N822K |
| **Ex11Del + Y823D** | | | | Y823D |
| **Ex11Del + A829P** | | | Exon 18 (A-loop) | A829P |
| **V560D** | | V560D | — | — |
| **V560D + V654A** | | | Exon 13 (ATP pocket) | V654A |
| **V560D + D816H** | | | Exon 17 (A-loop) | D816H |
| **Ex9Ins** | Exon 9 (ECD) | Ins 502AY | — | — |
| **Ex9Ins + V654A** | | | Exon 13 (ATP pocket) | V654A |
| **Ex9Ins + D816H** | | | Exon 17 (A-loop) | D816H |

Del (deletion); Ins (insertion); JM (juxtamembrane domain); ECD (extracellular domain); ATP pocket (ATP binding pocket); A-loop (activation loop)

**Figure 3. List of clinically relevant activating and resistant KIT mutations in GIST incorporated into our engineered Ba/F3 cell lines.**

To assess the cellular potency of TKIs against each KIT variant, we measure IC50 values, which is the TKI concentration that inhibits cell survival by 50%. To better mimic the functional effects of protein binding on drug activity in humans, we performed the cell survival assays in cell culture medium supplemented with physiologic concentrations of two critical human serum proteins. We then compared these IC50 values to TKI concentrations achieved in patients treated at the clinically utilized dose. TKI concentrations in patients are represented by the average concentration, or Cav, which is calculated as the Area Under the Curve, or AUC, over a 24-hour period and divided by 24. In the context of our PRA, we believe Cav to be a more reliable clinical predictor of therapeutic benefit than the maximum or minimum concentrations observed in patients. Using this measure, we calculated the Cav for imatinib, sunitinib, regorafenib and ripretinib in patients at the approved clinical doses as set forth in Figure 4 below.

| BENCHMARK TKIS | Cav IN PATIENTS |
|---|---|
| Imatinib | 3,385 nM |
| Sunitinib | 136 nM |
| Regorafenib | 5,027 nM |
| Ripretinib | 2,126 nM |

nM (nanomolar)

**Figure 4. The table shows Cav values for approved TKI therapies for GIST, or benchmark TKIs, as calculated from the clinical literature. Ripretinib is known to have an active metabolite, and this was included in the analysis.**

We used our PRA to predict the clinical activity of individual approved TKI therapies for GIST against specific KIT variants by comparing TKI potency, as assessed in Ba/F3 cells, to the Cav values in patients. We predicted that KIT variants inhibited by a TKI at a concentration substantially below the patient Cav would be highly sensitive to that TKI but that KIT variants inhibited at a concentration substantially above the Cav would be highly resistant. We further predicted that KIT variants inhibited with a TKI IC50 at a concentration that is

within approximately two-fold of the Cav would initially be associated with a stable disease outcome but ultimately would confer tumor resistance and progression.

To illustrate how we use this methodology, we compared Cav levels of sunitinib in GIST patients, and sunitinib potency against several KIT resistance mutations as determined in our cellular assay. As shown in Figure 5 below, our *in vitro* PRA predicted that sunitinib would have strong activity against ATP-binding pocket mutations but weak activity against activation loop mutations, consistent with the reported clinical data.

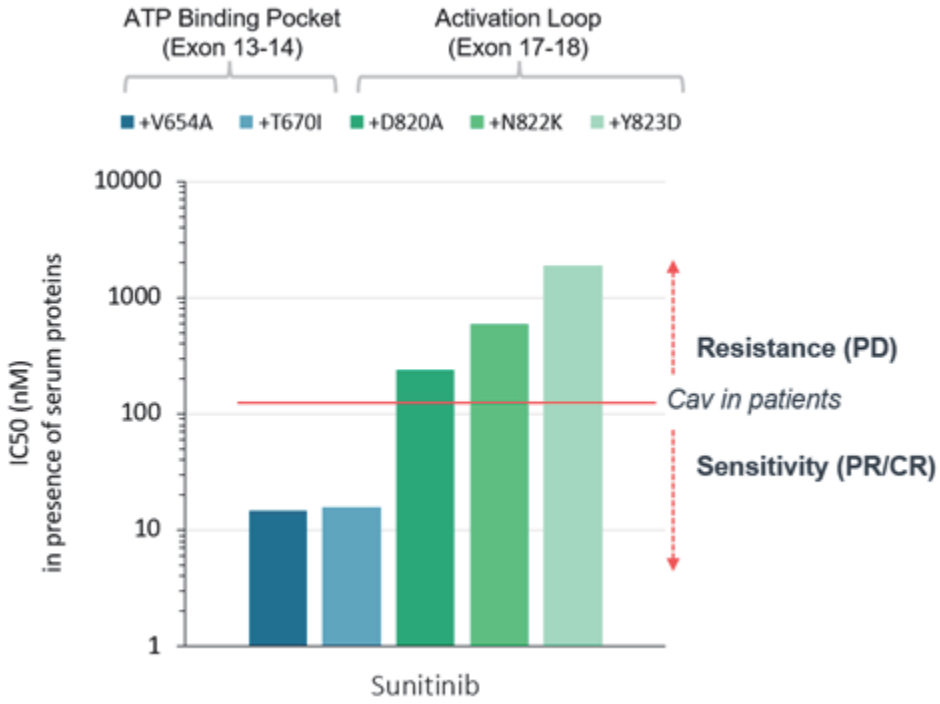



**Figure 5. Our *in vitro* PRA correctly recapitulated the clinical patterns of resistance of sunitinib. The prediction of resistance or sensitivity to sunitinib is shown relative to the Cav. The y-axis shows the IC50 values range using a log10 scale. PR/CR means partial/complete response; PD means progressive disease.**

Next, we expanded our analysis to include all four approved KIT TKIs against a broad panel of KIT variants. Figure 6 below shows the IC50 values for imatinib, sunitinib, regorafenib and ripretinib against all 17 KIT variants, as well as the Cav values for these TKIs in patients. The resulting predictions of TKI activity against each class of activating and resistance mutations, using the approach described above, are shown in Figure 7 below.

As was the case for sunitinib, the results of our PRA accurately recapitulated the known clinical patterns of resistance of imatinib and regorafenib, including overall insensitivity against ATP-binding pocket mutations and activation loop mutations. For ripretinib, our PRA predicts only modest clinical activity against activating mutations in exon 9 and against resistance mutations in the ATP-binding pocket, which is consistent with the results seen in the INTRIGUE study evaluating ripretinib versus sunitinib in the second-line GIST setting.

We then evaluated the same panel of KIT mutations in our PRA against our lead TKI product candidate, THE-630, which demonstrated activity against all major classes of activating and resistance mutations at a target Cav of 100 nM.

THE-630 showed a wide breadth of inhibitory activities, demonstrating potent activity against the most common activating mutation of exon 11 deletions as well as ten different known resistance mutations. THE-

630 also demonstrated potent activity against an alternate exon 11 activating mutation at V560D plus two known resistance mutations. THE-630 also showed potent activity against an exon 9 activating mutation plus two resistance mutations.

Based on the activity profile, we believe that if a Cav of 100 nM is achieved in patients, THE-630 will be able to potently inhibit all major classes of activating and resistance mutations. While two mutational combinations of exon 11 deletion plus the exon 17 D816Y mutation, and of exon 9 insertion plus the exon 17 D816H mutation, were not as potently inhibited by THE-630, we note that these variants are very rarely seen in GIST patients, despite being inhibited even less potently by imatinib, sunitinib, and regorafenib.

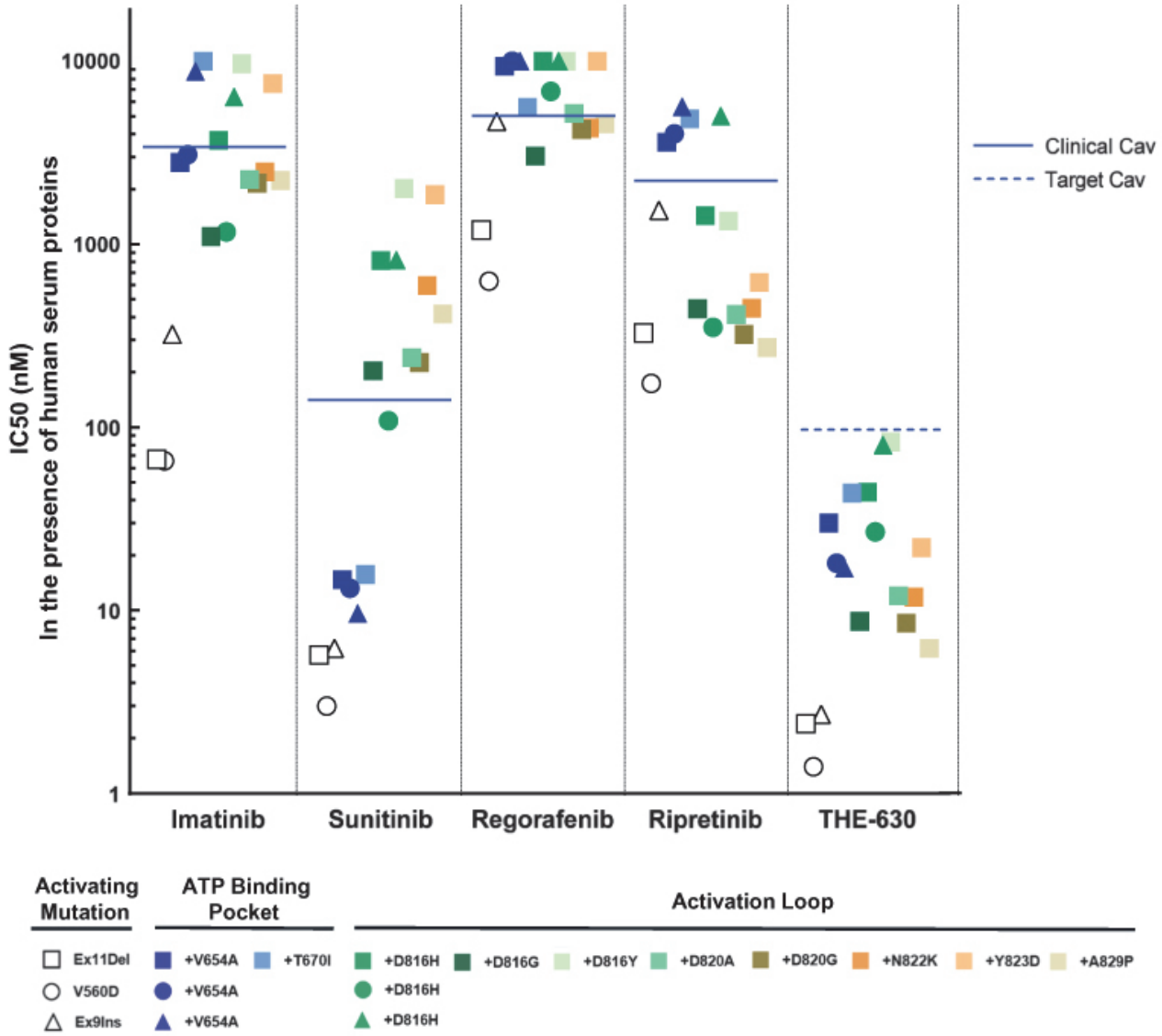
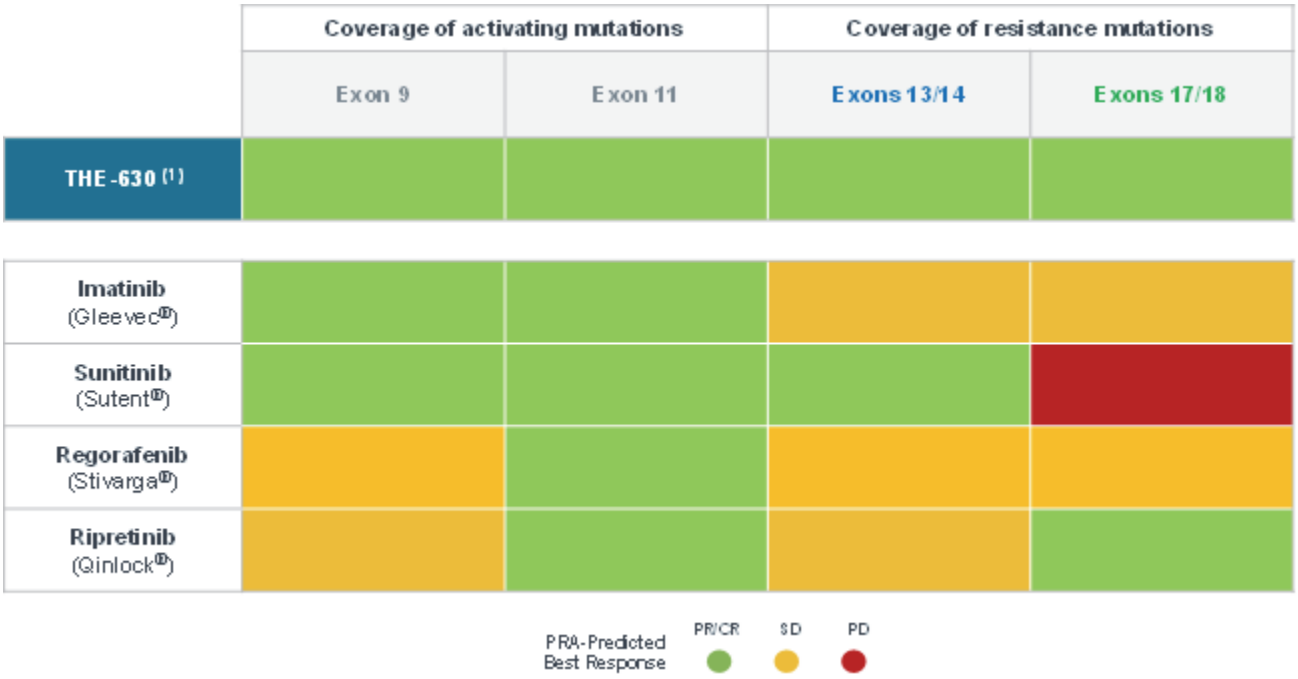



**Figure 6. Activity of THE-630 and benchmark TKIs in the PRA of cytotoxicity against KIT activation and resistance mutations showing a broad activity profile. The y-axis shows the IC50 value range using a $\log_{10}$ scale.**




(1) Assumes target Cav of 100 nM

**Figure 7. Clinical activity profile predicted by our PRA for benchmark TKIs and THE-630 against all major classes of KIT activating and resistance mutations. PR/CR means partial/complete response; SD means stable disease; PD means progressive disease.**

### *Tumor Regression in In Vivo Mouse Models Harboring KIT Activating and Resistance Mutations*

We expanded upon the results generated using our PRA by examining the *in vivo* activity of THE-630 in seven tumor models expressing KIT variants containing both major classes of activating mutations and both major classes of resistance mutations. To do this, we implanted GIST-T1 cells, which express KIT with an activating mutation in exon 11, or Ba/F3 cells engineered with six different KIT variants, subcutaneously into the right flank of female immunocompromised mice, and orally administered THE-630 and other TKIs to groups of mice. Based on a pilot study in mice, which showed that once daily dosing, or QD, of THE-630 at 30 mg/kg exceeded the maximum tolerated dose, all subsequent preclinical efficacy studies used a top dose of either 20 mg/kg or 25 mg/kg of THE-630 QD. At these dose levels, there were no signs of overt toxicity associated with THE-630 treatment in the mice.

When sunitinib or ripretinib were included as comparators, mice were dosed orally using standard regimens reported in the literature. For sunitinib, this was 20 mg/kg QD and for ripretinib it was 50 mg/kg twice a day, or BID. Our pharmacokinetic analysis on the treated mice showed the drug exposure levels exceeded that achieved in patients by three-fold for sunitinib and two-fold for ripretinib.

Data from all seven models are shown in Figures 8, 9 and 10 below. Also shown is the degree of anti-tumor activity for each TKI, which was calculated as the percent tumor growth inhibition, or TGI, relative to tumors in control mice, unless tumors regressed relative to the first day of treatment, in which case the percent tumor regression, or TR, was calculated. In each study, the control group of mice was dosed orally with the vehicle that each TKI was dissolved in, and on the same schedule.

THE-630 demonstrated anti-tumor activity in all seven models. As shown in Figure 8 below, THE-630 had strong anti-tumor activity in models containing an exon 11 activating mutation (85% TR) or an exon 9 activating mutation (58% TR). In contrast, ripretinib demonstrated weak anti-tumor activity in the exon 9

model (17% TGI). As shown in Figure 9 below, THE-630 had strong activity in a model containing a KIT exon 11 activating mutation plus the most common resistance mutation observed in the ATP-binding pocket, V654A (86% TGI), and moderate activity in a model containing the T670I mutant (39% TGI). In contrast, ripretinib had modest or weak activity in both models (26% TGI and 8% TGI). Finally, as shown in Figure 10 below, THE-630 had strong activity in three models containing a KIT exon 11 activating mutation and a resistance mutation in the activation loop, with 83% TR, 59% TR, and 90% TGI seen in models containing N822K, D820A, and A829P, respectively. In contrast, sunitinib had weak or no activity against N822K (25% TGI) and A829P (0% TGI).

Therefore, consistent with the results of our *in vitro* PRA, sunitinib and ripretinib showed *in vivo* activity only against a subset of activating and resistance mutations. In contrast, THE-630 demonstrated *in vivo* activity against all major classes of activating and resistance mutations observed in KIT-mutant GIST, consistent with the profile of a pan-variant inhibitor.

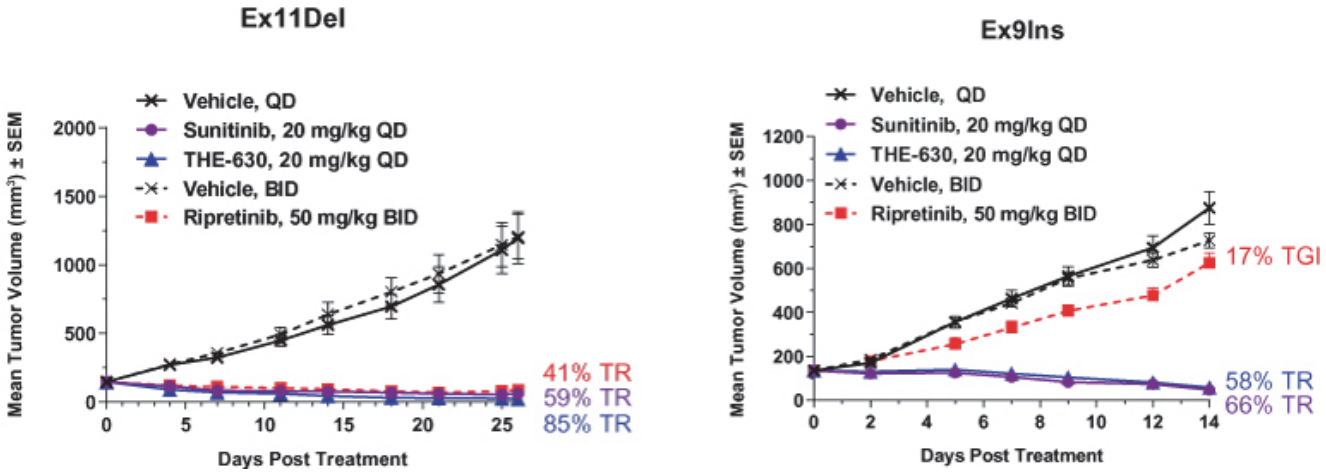



**Figure 8.** ***In vivo*** **activity of THE-630 and benchmark TKIs in tumor models with both classes of KIT activating mutations.**

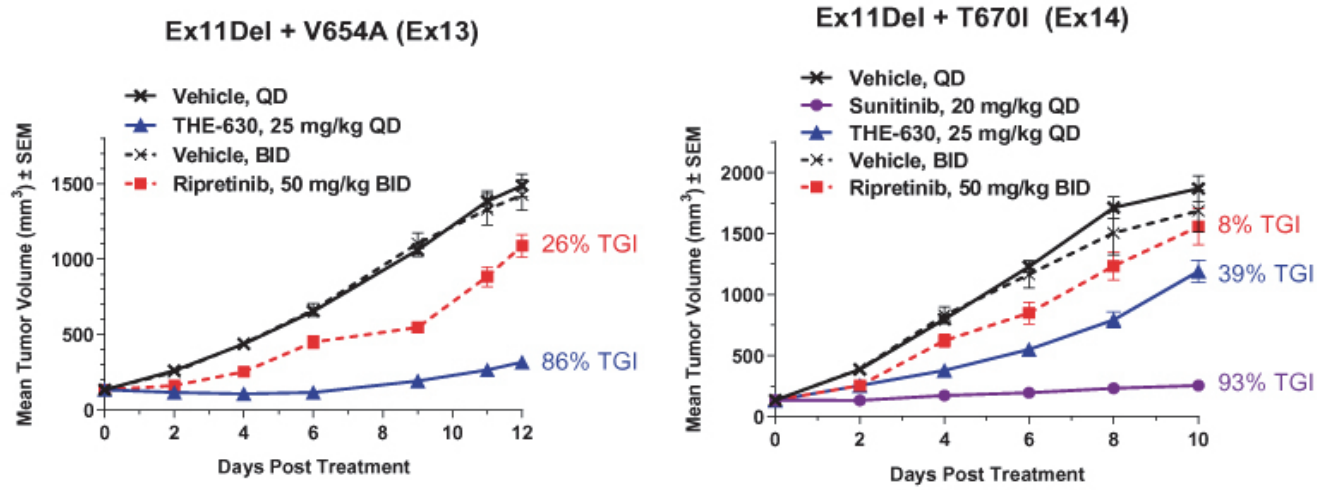



**Figure 9.** ***In vivo*** **activity of THE-630 and benchmark TKIs in tumor models containing resistance mutations in the KIT ATP-binding pocket.**

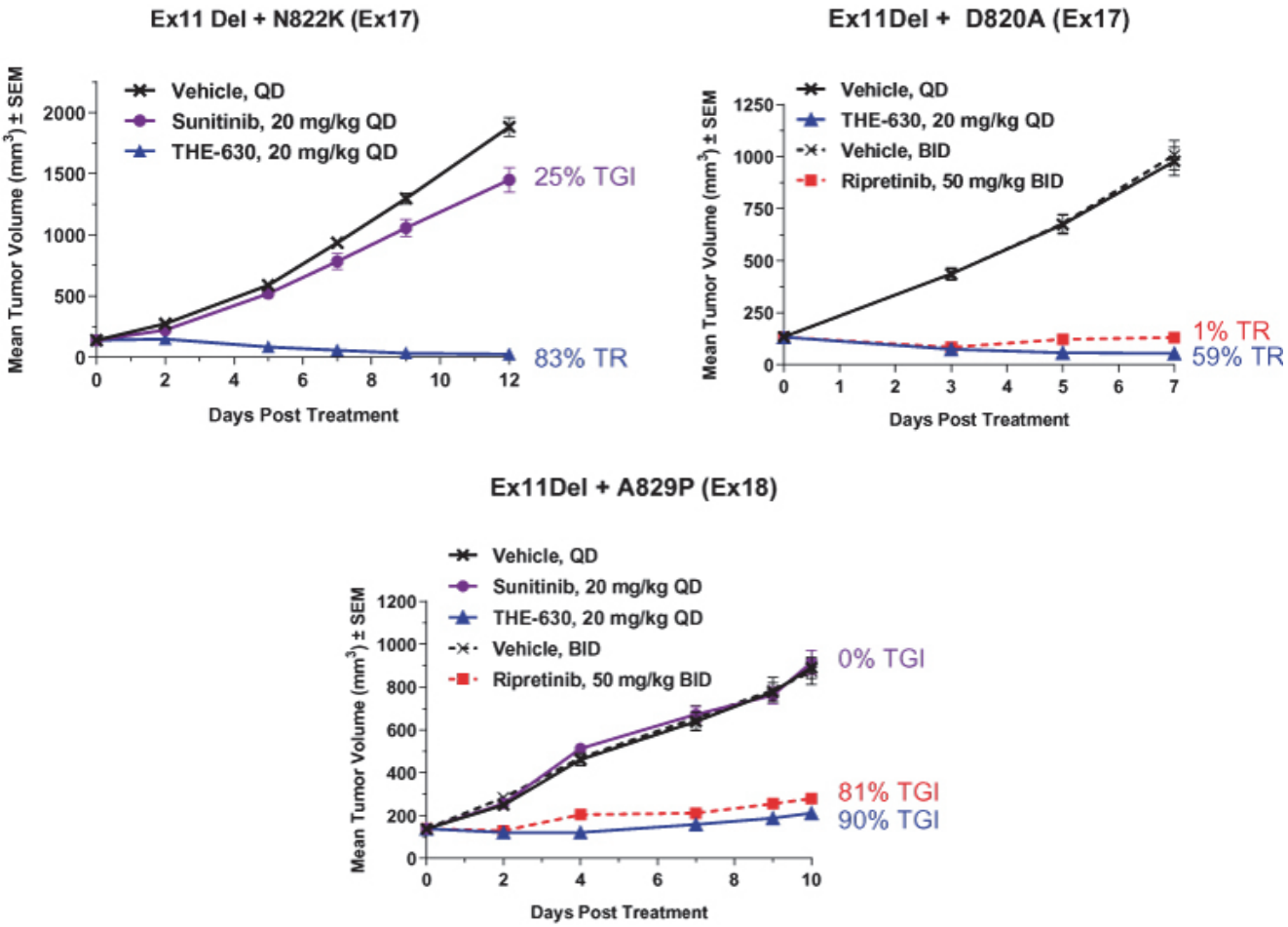



**Figure 10.** ***In vivo*** **activity of THE-630 and benchmark TKIs in tumor models containing resistance mutations in the KIT activation loop.**

To evaluate the kinase selectivity of THE-630, we conducted a single point screen against 330 kinases at 100 nM, using a commercially available screening panel. For comparison, we included ripretinib. Against this panel, THE-630 inhibited the activity of 50 out of 330 kinases by more than 50%. Similarly, ripretinib inhibited the activity of 43 out of 330 kinases by more than 50%.

Next, we tested THE-630 in a series of standard *in vitro* pharmacology screens with targets including receptors, transporters and enzymes, with no liabilities identified. In addition, THE-630 was screened for potential drug-drug interactions and cardiac toxicity with standard *in vitro* safety pharmacology assays and no liabilities were identified.

***Preclinical Pharmacokinetic and Tolerability Profile of THE-630***

Pharmacokinetic, or PK, studies of THE-630 were performed in rats and non-human primates, or NHPs, to evaluate bioavailability and compound half-life *in vivo*. Single doses were given at 3 mg/kg intravenously and 8 to 10 mg/kg orally. THE-630 demonstrated favorable oral PK in both species, with NHPs showing higher bioavailability (approximately 60%, compared to approximately 36% in rats) and longer half-life ($t_{1/2}$) (13.1 hours, compared to 5.8 hours in rats), as shown in Figure 11 below.

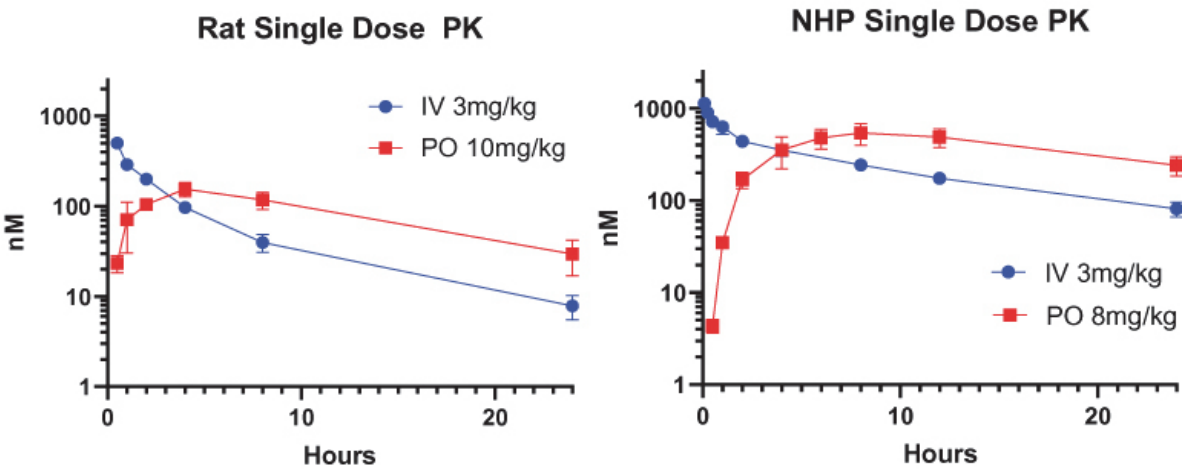



**Figure 11. Rats or NHPs were dosed intravenously, or IV, and orally, or PO, with THE-630 in order to evaluate bioavailability and half-life. The concentration of THE-630 in plasma was measured and plotted against time elapsed after administration of THE-630.**

We have also completed a 28-day good laboratory practice, or GLP, toxicology study of THE-630 in rats and a 28-day GLP toxicology study of THE-630 in NHPs. The no observed adverse effect level, or NOAEL, in our NHP toxicology study was used to derive our proposed first-in-human dose. The NOAEL in the NHP toxicology study was observed at dose level which provided a Cav of approximately 75 nM, indicating a favorable therapeutic index of at least 0.75 when compared to our target exposure level in humans (Cav) of 100 nM. 100 nM Cav is the exposure we expect to demonstrate pan-variant KIT activity and meaningfully improve patient outcomes. The exposure levels achieved in NHPs at the NOAEL met or exceeded the *in vitro* IC50 values, measured in the presence of human serum proteins, for all KIT mutants evaluated. No adverse effects were seen in standard GLP safety *in vivo* pharmacology studies.

***Clinical Development Plan for THE-630 in GIST***

We designed our initial first-in-human Phase 1/2 clinical trial with the goal of evaluating monotherapy THE-630 in patients with advanced GIST across the spectrum of previously-treated populations. The clinical trial commenced with the dosing of the first patient in the Phase 1 portion in January 2022, and will consist of two phases:

- Phase 1—Dose Escalation: patients with previously-treated, unresectable or metastatic GIST will be enrolled in the Phase 1 portion of the trial. Patients must have disease progression on or be intolerant to imatinib therapy and have also received at least 1 of the following: sunitinib, regorafenib, ripretinib, or avapritinib. The primary objective of the dose escalation phase is to determine the safety profile of oral THE-630, including the dose limiting toxicities, or DLTs, maximum tolerated dose, or MTD, the RP2D, as well as PK and preliminary anti-tumor activity. We expect to report initial data from the Phase 1 portion of the trial at an academic meeting in the second quarter of 2023, and expect to report additional data through cohort 8 at an academic meeting in the fourth quarter of 2023. We believe that an important early pharmacodynamic indicator to provide proof of mechanism will be circulating tumor DNA, or ctDNA, analyses. We are currently and will continue to be collecting ctDNA samples before, during, and after treatment to be analyzed by next-generation sequencing, or NGS, to characterize the KIT variants that are present and the effects of THE-630 on variant allele fraction over time. Given the heterogeneity of GIST, we believe that ctDNA analyses can help support our preclinical hypothesis that THE-630 has pan-variant KIT inhibition, as it will allow us to examine its effects on the spectrum of individual KIT variants seen in GIST patients. As of December 31, 2022, we were dosing patients in cohort 5 of the Phase 1 dose escalation portion of the Phase 1/2 clinical trial, and we believe, based on data collected to date, that we will require 7 or 8 cohorts to reach the

target Cav of 100 nM, which is predicted to yield pan-variant KIT activity based on preclinical modeling in our PRA.

- Phase 2—Dose Expansion: patients with unresectable or metastatic GIST will be enrolled at the RP2D into cohorts defined by prior therapy, including: (1) patients with second-line GIST who have had only prior imatinib therapy; (2) patients with fifth- or later-line GIST; and (3) patients with third- or fourth-line GIST. The Phase 2 portion of the clinical trial will further characterize the anti-tumor activity, PK and safety profile of THE-630 in these defined populations.

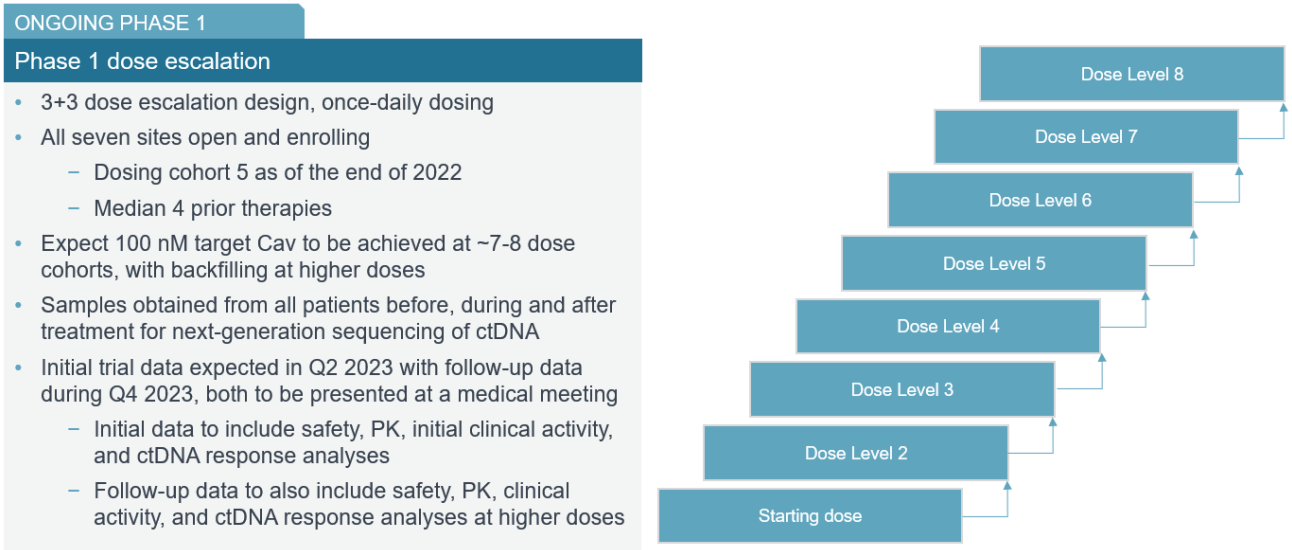
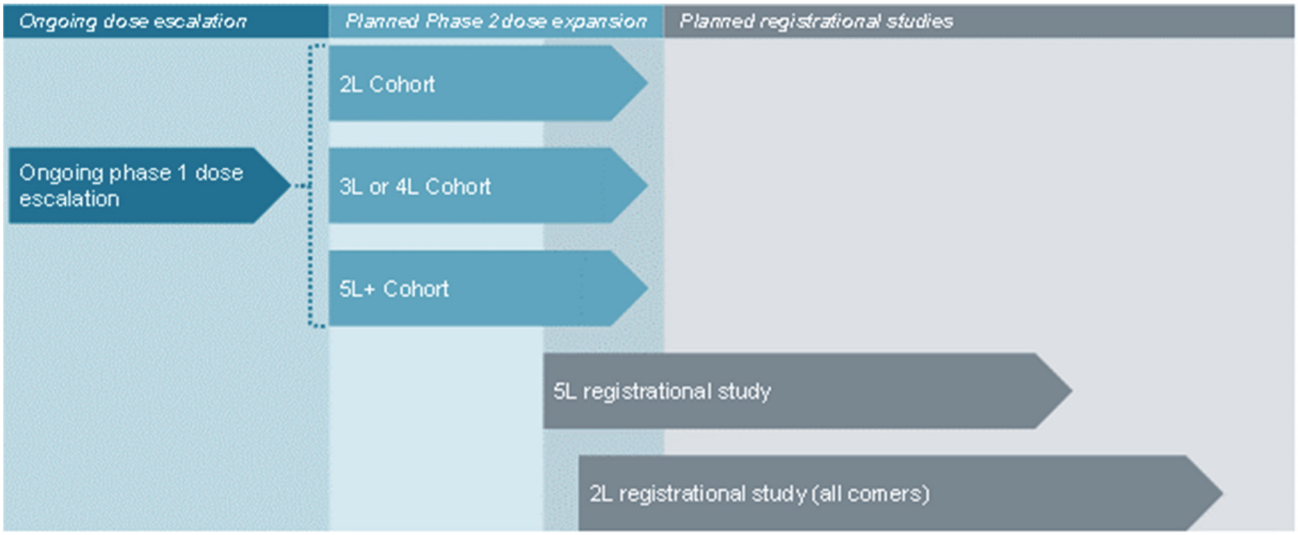



**Figure 12. Outline of the design of our ongoing first-in-human clinical trial of THE-630. Our dose escalation and expansion cohorts are designed to evaluate the safety and efficacy of THE-630 in advanced GIST patients in second- through fifth- or later-lines of therapy.**

Assuming positive clinical data and subject to discussions with the FDA, our registration strategy will evaluate THE-630 in two different GIST populations, fifth-line and second-line. There is currently no available therapy and therefore a significant unmet medical need in the fifth-line GIST setting. The data from the proposed Phase 1/2 clinical trial and feedback from regulatory authorities will inform the design of a potential registration trial in fifth-line GIST. We also plan to prioritize the evaluation of THE-630 in second-line GIST, where we believe our pan-variant KIT inhibitor, with activity against all major classes of activating and resistance mutations, has the potential to deliver meaningful clinical benefit over the current standard of care. We expect to run registrational studies in fifth-line and second-line GIST in parallel.




2L (second-line); 3L (third-line); 4L (fourth-line); 5L (fifth-line)

**Figure 13. Overview of the registration strategy for THE-630. Based on data from the ongoing Phase 1/2 trial in patients with advanced GIST and regulatory feedback we intend to commence a registration trials in fifth-line GIST and in second-line GIST.**

## THE-349: Our Fourth-Generation EGFR Inhibitor

### *Summary Overview*

Our second product candidate is THE-349, which is a fourth-generation inhibitor of EGFR that is active against C797X, the most common EGFR mutation that causes resistance to first- or later-line osimertinib treatment in patients with NSCLC, as well as the most common activating and resistance mutations seen in patients prior to treatment with osimertinib. Additionally, preclinical data has demonstrated that THE-349 has a high degree of kinome and wild-type EGFR selectivity, and exhibits substantial CNS activity.

NSCLC is the most common form of lung cancer with up to 50% of NSCLC tumors driven by activating mutations in EGFR, depending on geographic region. Treatment of EGFR-mutant metastatic NSCLC patients with first- and second-generation EGFR TKIs, such as erlotinib, gefitinib, afatinib and dacomitinib, substantively improved outcomes for patients compared to chemotherapy. However, resistance eventually develops in most patients, leading to disease progression, with about half of patients' tumors developing the T790M EGFR mutation. Osimertinib, a third-generation TKI, was initially developed to treat T790M positive disease in patients progressing on a first- or second-generation TKI. Subsequently, it was approved in the first-line setting where it improved PFS and overall survival compared to earlier-generation inhibitors. However, most patients receiving treatment eventually progress. A subset of patients on osimertinib, either in first- or later-line therapy, will progress with EGFR-mediated resistance, primarily with the C797X mutation. A significant unmet medical need remains for patients with this subset of EGFR-mutant NSCLC.

Our target product profile for THE-349 is below:

- potent activity against all major classes of mutated EGFR that could contribute to disease progression in osimertinib-resistant patients:
    - the common activating mutations (deletions in exon 19 or the L858R substitution in exon 21);
    - double mutations (activating mutation with either T790M or C797X); and

- triple mutations (activating mutation with T790M and C797X);

- kinome and wild-type EGFR selectivity; and

- ability to penetrate the blood-brain barrier, or BBB, with activity against CNS metastases.

We intend to file an IND with the FDA for THE-349 in the fourth quarter of 2023.

***The Market Opportunity in NSCLC for EGFR Inhibitors***

Lung cancer is the second most commonly diagnosed cancer worldwide and its incidence continues to grow. In 2020, an estimated 2.2 million new cases of lung cancer were diagnosed globally, accounting for approximately 11.4% of the global cancer burden. An estimated 1.8 million lung cancer deaths occurred in 2020. Among all cancers, lung cancer is currently the most common cause of cancer deaths in most countries, with North America and Europe having the highest rates. NSCLC is the most common form of lung cancer, accounting for approximately 85% of all lung cancers. Up to 50% of NSCLC tumors are driven by activating mutations in EGFR, depending on geographic region. Approximately 90% of these mutations are in exon 19 (exon 19 deletions) or exon 21 (L858R) of the gene that encodes EGFR. In patients whose tumors progress on osimertinib, C797X and other resistance mutations in EGFR have been observed at a frequency of up to approximately 12% after first-line osimertinib and 20% after second-line osimertinib.

***Current Treatment Paradigm in EGFR-mutant NSCLC and Limitations***

*EGFR biology and means of inhibiting EGFR.* EGFR, a member of the RTK family, plays a critical role in maintaining normal cell physiology in many organs and tissues. Since EGFR signaling is implicated in the genesis and progression of many cancers, it has led to the development of several classes of EGFR inhibitors. For example, the discovery of ligand-independent EGFR signaling in cancers led to the development and clinical characterization of EGFR TKIs, particularly in NSCLC. In particular, activating mutations within the EGFR kinase domain were found in approximately 10% to 15% of caucasian NSCLC patients and up to 50% of East-Asian NSCLC patients, and it was in these patients where strong response to first-generation EGFR TKIs, such as gefitinib and erlotinib, was observed.

*The mutations targeted by marketed EGFR inhibitors and the resulting levels of efficacy.* The major EGFR genetic alterations observed in NSCLC, the exon 19 deletions and the exon 21 L858R substitution, are mutations that cause ligand-independent activation of EGFR. The activation causes downstream signaling that promotes cancer cell survival and proliferation. First- and second-generation EGFR TKIs bind to the EGFR kinase domain's ATP-binding pocket to inhibit activity and signal transduction. These first- and second-generation TKIs, which include gefitinib, erlotinib, afatinib and dacomitinib, induce a high response rate of approximately 70% to 75% and provide a median PFS of approximately 10 months to 14 months. These clinical results are superior to the previous standard of care front-line treatment with platinum-based chemotherapy in EGFR-mutant metastatic NSCLC.

*Resistance and unmet need in EGFR-driven lung cancer.* Despite these advances, resistance to first- and second-generation EGFR TKIs has been observed, resulting in patient relapse, disease progression and death. The most common resistance mutation that arises in response to first- and second-generation EGFR TKIs is the T790M mutation, a gatekeeper mutation in exon 20 that blocks TKI access to the ATP-binding pocket. Osimertinib was developed initially to counter this resistance mutation. Osimertinib was first approved in the US and globally for the treatment of patients with metastatic EGFR T790M mutation-positive NSCLC whose disease has progressed on or after EGFR TKI therapy. In this setting, osimertinib yielded a high response rate (approximately 65%) and improved PFS compared to chemotherapy. Subsequently, osimertinib was approved in the first-line metastatic setting for EGFR exon 19 deletion or exon 21 L858R substitution NSCLC after showing improved efficacy compared to earlier-generation TKIs, with a median PFS of 19 months and median overall survival, or OS, of over three years. More recently, osimertinib was approved as an adjuvant treatment after tumor resection for patients with EGFR exon 19 deletion or exon 21 L858R substitution NSCLC. Lazertinib and almonertinib are two additional third-generation TKIs approved for

EGFR-mutant NSCLC, both with similar mechanisms of action to osimertinib. Lazertinib monotherapy is approved in South Korea for patients with EGFR T790M mutation positive disease who have previously been treated with an EGFR TKI, and the drug is also being evaluated in combination with a MET/EGFR bispecific antibody, amivantamab, in EGFR-mutant NSCLC. Almonertinib is approved in China for patients with EGFR T790M mutation positive disease who have previously been treated with an EGFR TKI.

Resistance to osimertinib and other third-generation TKIs is an emerging limitation to the success of current EGFR TKI therapy, as shown in Figure 13 below. Several of the resistance mechanisms that have been seen to arise in response to osimertinib are EGFR-independent, involving amplification or oncogenic changes in other signaling pathways, such as the MET gene. However, in both treatment-naïve patients and patients with EGFR T790M-positive disease who progress on osimertinib, EGFR resistance mutations have also been observed. The C797X mutation results in the conversion of the targeted cysteine, or C, at position 797 of EGFR, into another amino acid, or X, with conversion to serine, or S, being observed in the vast majority of cases. In addition, several other EGFR mutations are found in osimertinib-resistant patients. C797X and other resistance mutations in EGFR have been observed at a frequency of up to approximately 12% after first-line osimertinib and approximately 20% after second-line osimertinib. Therefore, we believe that there is a critical need for a fourth-generation EGFR TKI that can block the array of resistance mutations in EGFR that arise across the first- through third-generation EGFR TKI therapeutic landscape. A summary of the major classes of activating and resistance mutations that must be inhibited by a fourth-generation EGFR TKI is shown in Figure 14 below.

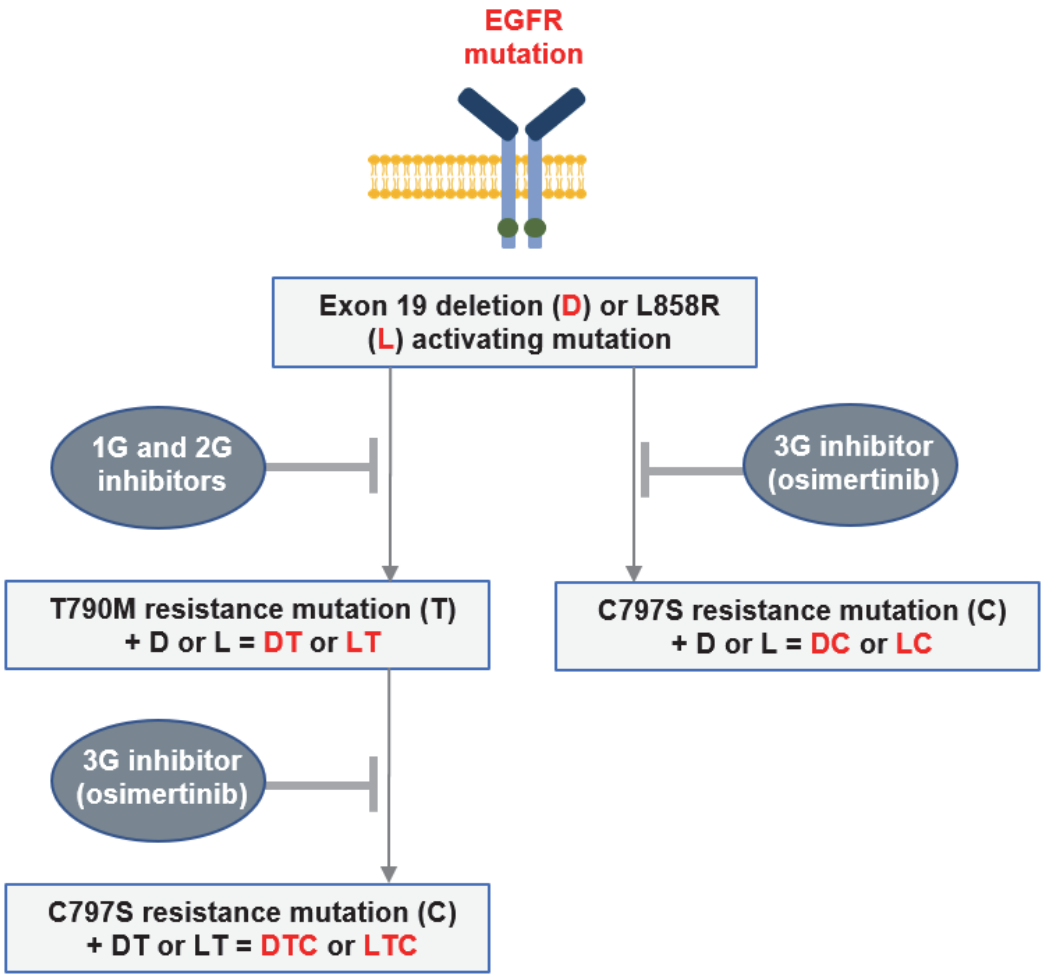



**Figure 14. Schematic of activating EGFR mutations and resistance mutations that arise following treatment with first-, second- and third-generation EGFR inhibitors. Activating deletions in exon 19 are referred to as Del19 mutations.**

| CLASS | SPECIFIC MUTATION(S) | ABBREVIATION | DESCRIPTION |
|---|---|---|---|
| Single mutant | L858R | L | Activating mutation only |
| | Del19 | D | |
| Double mutant | L858R + T790M | LT | Activating mutation plus T790M or C797S |
| | Del19 + T790M | DT | |
| | L858R + C797S | LC | |
| | Del19 + C797S | DC | |
| Triple mutant | L858R + T790M + C797S | LTC | Activating mutation plus T790M and C797S |
| | Del19 + T790M + C797S | DTC | |

**Figure 15. Nomenclature used to describe the major classes of EGFR activating and resistance mutations.**

An important element in the development of EGFR inhibitors is ensuring selectivity for mutant EGFR compared to the wild-type, or non-mutated, EGFR that is normally expressed in human tissues. Inhibition of wild-type EGFR leads to gastrointestinal and skin toxicities that can be serious and dose-limiting. First- and second-generation EGFR inhibitors are limited by this toxicity, although third-generation EGFR inhibitors, such as osimertinib, have improved selectivity for mutant, activated EGFR and therefore improved tolerability.

***Our Solution: THE-349, a Fourth-Generation EGFR Inhibitor with broad mutational coverage, wild-type selectivity, and CNS activity***

Using our structure-guided approach, we have developed intricate computer models of the EGFR binding site that have provided a map of potential residues to target for increased molecular interaction. We have leveraged these detailed maps in the design of THE-349, which inhibits activating forms of EGFR and mutant forms with C797X and T790M resistance mutations, with wild-type EGFR selectivity. Using the triple-mutant Del19/T790M/C797X, or DTC mutant, as an *in vivo* screen, we have shown that THE-349 is orally bioavailable and shows strong tumor growth inhibition *in vivo*. For example, THE-349 was profiled against a series of mutant EGFR variants *in vivo*, including the single-mutant variant L858R, or L mutant, the double-mutant variant L858R/T790M, or LT mutant, and the triple-mutant variant L858R/T790M/C797X, or LTC mutant, and was shown to have strong anti-tumor activity against all three. THE-349 demonstrated significant anti-tumor activity in two intracranial models in mice, with increased survival highlighting CNS activity/penetration.

***Broad EGFR Mutation Coverage and Wild-type Selectivity Supported by In Vitro Data***

To determine the ability of THE-349 to broadly inhibit single-, double- and triple-mutant EGFR variants, we first evaluated its activity in a kinase inhibition assay using EGFR kinases containing various combinations of activating mutations (L858R or L; Del19, or D) alone, or in combination with a T790M, or T, resistance mutation and/or a C797X resistance mutation. In addition to testing C797S, or C, the most common C797X resistance mutation, we also tested variants with a C797G or a C797A resistance mutation. Activity in these assays is reported as IC50 values, which is the TKI concentration that inhibits kinase activity by 50%. Erlotinib and osimertinib, two approved EGFR inhibitors, were included as controls. As shown in Figure 16 below, erlotinib and osimertinib did not potently inhibit mutants with a T790M or a C797X mutation, respectively. In contrast, THE-349 demonstrated low nanomolar IC50 values against all single-, double- and triple-mutant EGFR variants tested.

| EGFR variant | Biochemical $IC_{50}$ (nM) | | |
|---|---|---|---|
| | Erlotinib | Osimertinib | THE-349 |
| L | 0.2 | 0.6 | 0.7 |
| LT | 207 | 0.2 | 0.1 |
| LC | 0.3 | 746 | 0.6 |
| L-C797G | 0.5 | 824 | 0.8 |
| LTC | 345 | 360 | 0.4 |
| D | 0.3 | 0.6 | 0.6 |
| DC | 0.6 | 418 | 0.9 |
| D-C797A | 2.8 | 1258 | 3.2 |

Purple indicates IC50 >100 nM

**Figure 16. Summary of biochemical IC50 values of THE-349 and controls (erlotinib and osimertinib) against a panel of mutant EGFR variants**

To determine the ability of THE-349 to broadly inhibit single-, double- and triple-mutant EGFR variants in a cellular context, we engineered a panel of Ba/F3 cell lines so their survival is dependent on different mutant EGFR variants. We then used these cell lines to assess cellular potency as represented by the IC50 value. We also measured the potency of each TKI against wild-type EGFR, also represented by the IC50 value, by determining the concentration required to inhibit phosphorylation of wild-type EGFR by 50% in A431 cells. We had previously observed that clinical efficacy of first-, second-, and third-generation TKIs against specific mutant EGFR variants is associated with a substantially lower IC50 value against the mutant variant than against wild-type EGFR as measured using these assays.

Figure 16 below shows the potency of erlotinib and osimertinib against wild-type EGFR, as well as against eight EGFR variants representing all major classes of activating and resistance mutations. These include: (1) a Del19 activating mutation alone, or D mutant, L858R activating mutation alone, or L mutant; (2) four double-mutant variants, Del19/T790M, or DT mutant, and Del19/C797S, or DC mutant, L858R/C797S, or LC mutant, L858R/T790M, or LT mutant; and (3) two triple-mutant variants, Del19/T790M/C797S, or DTC mutant, and the LTC mutant. As expected, based on its clinical profile, erlotinib had potent activity against the D, L, LC and DC mutant variants, but not against any of the three variants that contain a T790M mutation. In contrast, osimertinib had potent activity against D, L, LT and DT mutant variants, but not against any of the three variants that contained a C797S mutation.

In contrast to erlotinib and osimertinib, as shown in Figure 16 below, THE-349 demonstrated potent activity against all eight mutant variants. That is, THE-349 potently inhibited EGFR with a common activating mutation and maintain potency in the presence of a T790M mutation, or a C797S mutation, or both T790M and C797S mutations in the same protein. In addition, in all cases, all five mutant EGFR variants are inhibited with potency at least ten-fold greater than that against wild-type EGFR, suggesting the potential for on target EGFR-driven efficacy without the toxicities associated with wild-type inhibition.

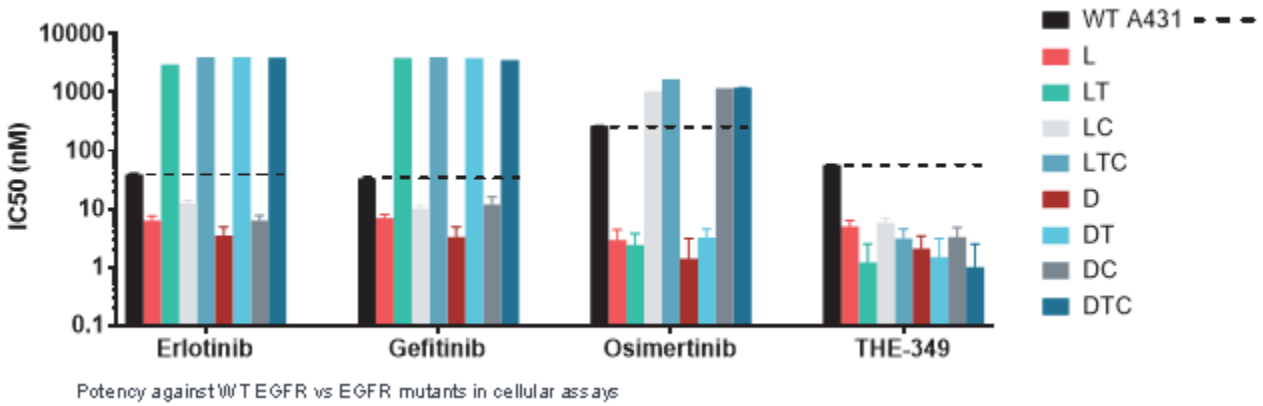



**Figure 17. Summary of cellular IC50 values including control (erlotinib and osimertinib) and THE-349 against wild-type (WT) EGFR and a panel of single- (D, L), double- (DT, DC, LT, LC) and triple- (DTC, LTC) mutant EGFR variants.**

### *Tumor Regression in In Vivo Mouse Models Harboring EGFR Activating and Resistance Mutations*

We evaluated the activity of THE-349 in mouse tumor models to determine whether it has the necessary pharmacologic activity *in vivo*. To do this, we subcutaneously implanted Ba/F3 cells engineered with EGFR-mutant variants into immunocompromised mice, then administered compounds orally to groups of mice. When osimertinib was included as a comparator, mice were dosed orally using a standard regimen reported in the literature, 25 mg/kg QD. The degree of anti-tumor activity for each TKI was calculated as the percent tumor growth inhibition, or TGI, relative to tumors in control mice, unless tumors regressed relative to the first day of treatment, in which case the percent tumor regression, or TR, was calculated. We did not observe any signs of overt toxicity associated with these treatments.

We next evaluated THE-349 in five *in vivo* models. As shown in Figure 18 below, THE-349 had strong anti-tumor activity in all five models. For example, in a triple-mutant model expressing an EGFR triple-mutant LTC variant, THE-349 induced 88% TR, while osimertinib had only modest anti-tumor activity. In models expressing an EGFR single-mutant L variant or an EGFR double-mutant LT variant, both THE-349 and osimertinib demonstrated strong anti-tumor activity.

THE-349, in agreement with our panel of *in vitro* data, suggests that it is possible to design compounds that are orally bioavailable, wild-type EGFR selectivity, and which have activity against single-, double- and triple-mutant EGFR variants.

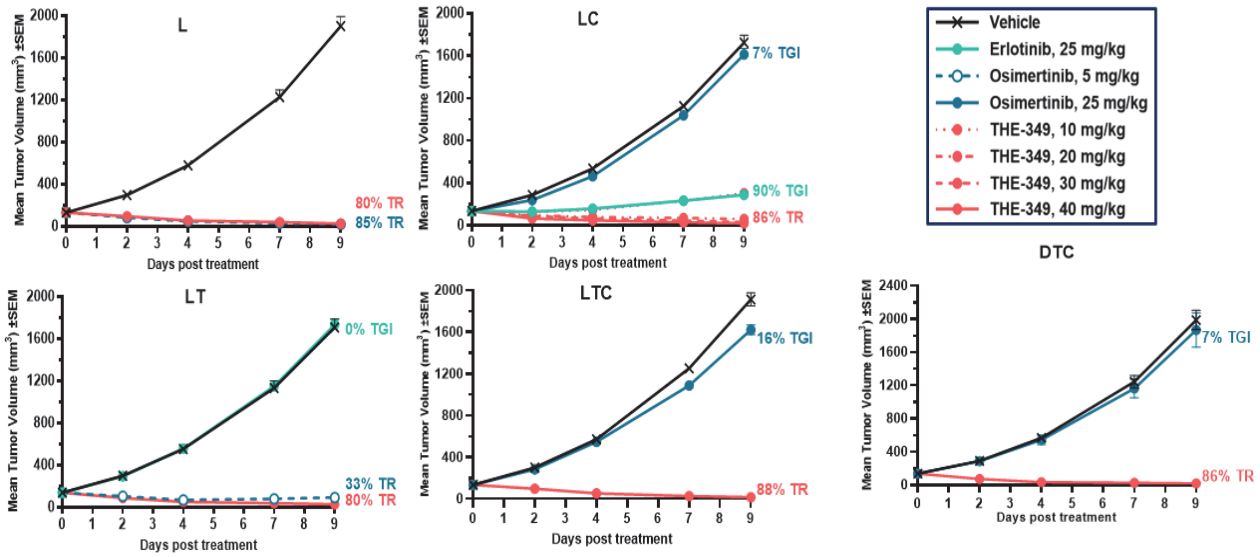



**Figure 18.** ***In vivo*** **activity, including osimertinib as a control, of THE-349 against single- (L), double- (LT) and triple- (LTC) mutant EGFR variants.**

### *Evaluation of CNS Activity*

EGFR-mutant NSCLC commonly metastasizes to the CNS, and the frequency increases with lines of therapy. Thus, CNS activity is an important attribute for drugs intended to treat this disease. To assess the potential of THE-349 to exhibit meaningful CNS activity, we measured its anti-tumor properties in two intracranial mouse models and measured drug concentrations in the brain and plasma compartments. THE-349 demonstrated significant anti-tumor activity in H1975 LTC and PC9 (D) intracranial models in mice, with increased survival highlighting CNS activity. CNS activity reflects the balance of strong potency and ~9% brain:plasma ratio (Kp) in mice, which was observed to be similar in rats.

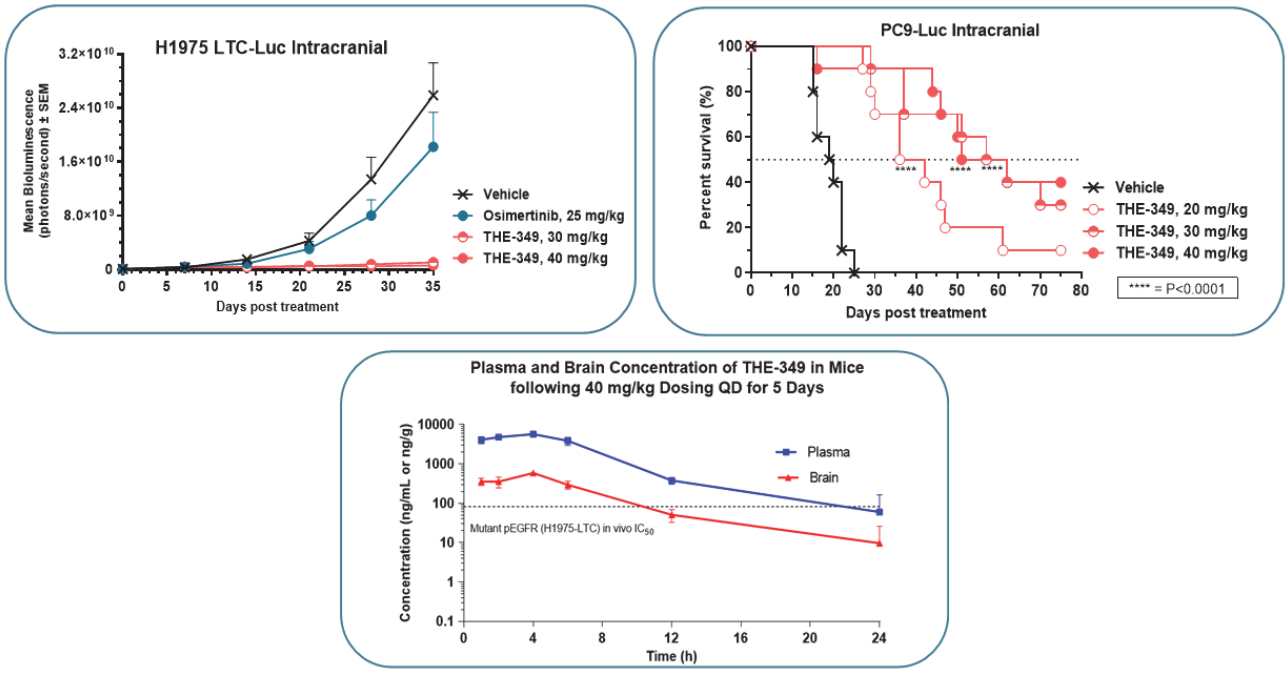



**Figure 19.** ***In vivo*** **activity of THE-349 in H1975 LTC-Luc intracranial model, PC9-Luc (D) intracranial model, and plasma and brain concentration of THE-349 in mice following 40mg/kg dosing QD for 5 days.**

***Clinical Development Plan***

We expect to submit an IND application for THE-349 to the FDA in the fourth quarter of 2023 and to initiate the Phase 1/2 trial as soon as possible thereafter. We plan to pursue initial clinical development as monotherapy in patients with on-target resistance, as well as rapidly expand into evaluation of combination treatment with other relevant modalities and, if clinical data support, target a broader second line patient population. Monotherapy dose escalation will enroll patients with EGFR-mutant NSCLC and prior Osimertinib/third-generation TKI, enriched for patients with the C797X with or without T790M mutations. Monotherapy dose expansion will enroll patients into cohorts defined by on-target resistance mutations (C797X and T790M), presence of active brain metastases, to characterize CNS activity, as well as a treatment naïve population. We plan to explore combination of THE-349 and other relevant modalities that are active in EGFR-mutant NSCLC in Phase 1b dose escalation and then expansion, in patients previously treated with osimertinib both with and without on-target resistance mechanisms. Our expected clinical development plan for THE-349 is summarized in Figure 20 below.

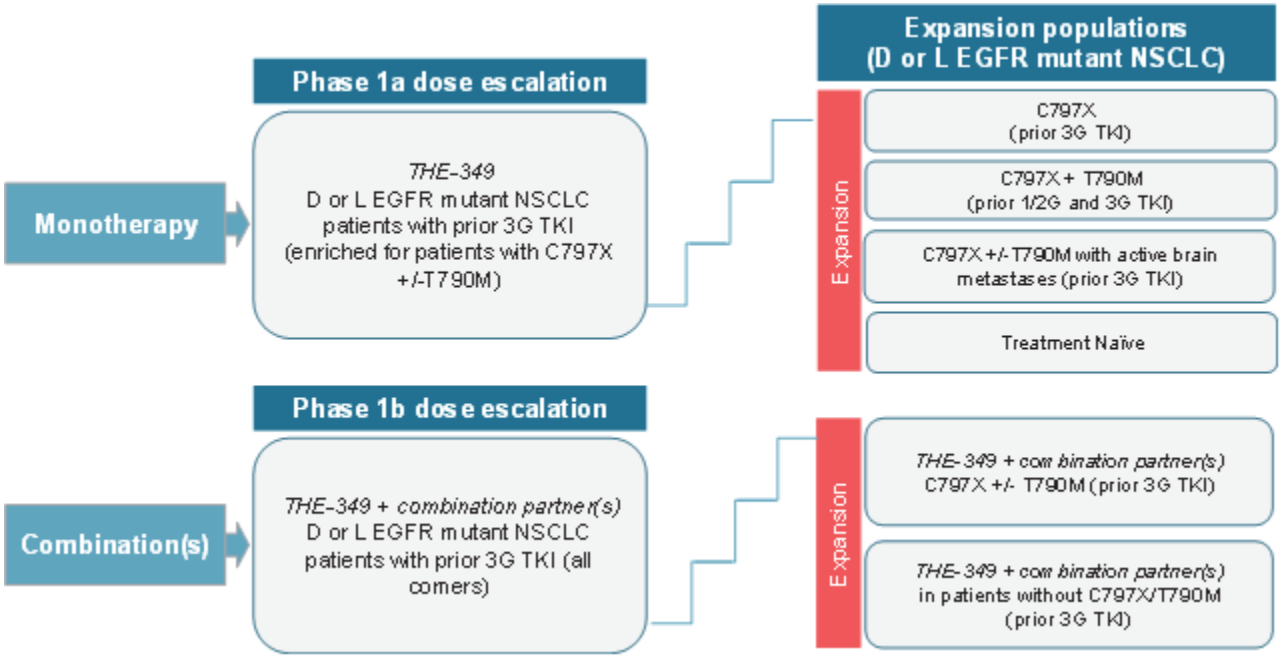



**Figure 20. Clinical development plan for THE-349.**

**Our Pan-variant BCR-ABL Program for Refractory CML and Ph+ ALL**

***Summary Overview***

Our third program is a pan-variant TKI for the treatment of refractory CML and Ph+ ALL. Both diseases are driven by the BCR-ABL fusion gene product. Our goal is to develop a next-generation pan-variant TKI for patients with relapsed/refractory CML and newly diagnosed Ph+ ALL.

CML is a disease which remains BCR-ABL driven through multiple lines of therapy, and patients commonly will relapse with a BCR-ABL resistance mutation. Multiple therapies for CML have been approved; however, approximately 30-40% of patients started on any TKI will switch to an alternative TKI due to side effects or inadequate response. For patients refractory to first-generation, or 1G, and second-generation, or 2G, TKIs, the treatment options include ponatinib or asciminib, but neither has an optimal balance of safety and efficacy.

Newly diagnosed Ph+ ALL adults have historically received chemotherapy followed by allogenic hematopoietic stem-cell transplant, or HSCT, and more recently the addition of BCR-ABL TKIs have improved outcomes in 1L treatment, despite their lack of FDA approval for this use, though five are National Comprehensive Cancer Network, or NCCN, recommended. However, in newly diagnosed patients treated in combination therapy with 1G or 2G TKIs, relapse is associated with BCR-ABL resistance mutations in up to 75% of patients, with the T315I mutation observed most frequently. Ponatinib, a pan-variant inhibitor, has been shown to improve clinical outcomes compared to 1G and 2G TKIs; however, toxicity limits optimal dosing.

Preclinically, our lead molecules have shown a high degree of potency against BCR-ABL and clinically relevant resistance mutations, and significant kinome selectivity, including against key off-target kinases. We expect to nominate a development candidate for this program by early 2024, with the goal of pursuing clinical development in patients with CML who have been previously treated with a 2G TKI or have the T315I mutation, and in combination therapy treatment for newly diagnosed patients with Ph+ ALL.

Our target product profile for BCR-ABL is below:

- Potent and pan-variant inhibition of BCR-ABL, including the T315I gatekeeper mutation;
- Tolerability profile compatible with long duration of treatment;
- For CML patients: Highly effective and well-tolerated option post-2G TKI; and
- For Ph+ ALL patients: A TKI that can provide durable, relapse-free, outcomes and reduce the need for HSCT.

A selective, well-tolerated, pan-variant BCR-ABL inhibitor could substantially improve clinical outcomes in refractory CML, and could reduce the need for HSCT in patients with Ph+ ALL when administered as a front-line therapy.

***The Market Opportunity and Treatment Paradigm in CML and Ph+ ALL***

CML is a disease which remains BCR-ABL driven through multiple lines of therapy, and patients commonly will relapse with a BCR-ABL resistance mutation. In the last decade, the annual incidence of CML has remained steady at approximately two cases per 100,000 adults and was estimated to be 9,000 people in the US in 2020. Multiple therapies have been approved and it is considered one of the great success stories in targeted oncology due to the prolonged life expectancy since imatinib's approval in 2001; however, approximately 30% to 40% of patients started on any TKI will switch to an alternative TKI because of side effects or inadequate response. For patients refractory to first- and second-generation TKIs, the treatment options include ponatinib or asciminib, but neither has an optimal balance of safety and efficacy. Asciminib is not pan-variant but is better tolerated. Ponatinib is a potent pan-variant BCR-ABL inhibitor but has a black box warning for vascular occlusion, heart failure, and hepatotoxicity. Despite the limitations of the currently approved BCR-ABL inhibitors for CML, the market opportunity is estimated to be greater than $5 billion based on global sales of the five approved TKIs for the treatment of CML in 2021.

Newly diagnosed Ph+ ALL adults have historically received chemotherapy followed by allogenic hematopoietic stem-cell transplant (HSCT), and more recently the addition of BCR-ABL TKIs have improved outcomes in 1L treatment, despite their lack of FDA approval for this use (five are NCCN recommended). However, in newly diagnosed patients treated in combination therapy with 1G or 2G TKIs, relapse is associated with BCR-ABL resistance mutations in up to 75% of patients, with the T315I mutation observed most frequently. Ponatinib, a pan-variant inhibitor, has been shown to improve clinical outcomes compared to 1G and 2G TKIs; however, toxicity limits optimal dosing. We believe that for newly diagnosed patients with Ph+ ALL, a pan-variant BCR-ABL TKI with a more favorable safety profile has the potential to provide durable, relapse-free, outcomes and potentially reduce the need for HSCT.

***In vitro characterization demonstrated pan-BCR-ABL activity with increased selectivity versus ponatinib***

To assess the on- and off-target potency of compounds, we engineered a panel of Ba/F3 cell lines so their survival is dependent on wild type or key mutant variants of BCR-ABL, or on activated variants of other "off-target" kinases that are also potently inhibited by ponatinib, the only approved pan-variant BCR-ABL TKI. We also assessed the degree of toxicity of compounds towards endothelial cells, using human umbilical vein endothelial cells (HUVEC), and assessed the degree of kinome selectivity in vitro using a panel of 330 kinases.

As shown in Figure 21, the on-target BCR-ABL potency of Compound 1 was similar to ponatinib as measured by IC50s, while the off-target potency of Compound 1, one compound in a series of molecules we are evaluating in lead optimization studied, was similar to that of ponatinib, while the off-target potency of Compound 1 was shown to be substantially lower than ponatinib in all of the off-target assays tested.

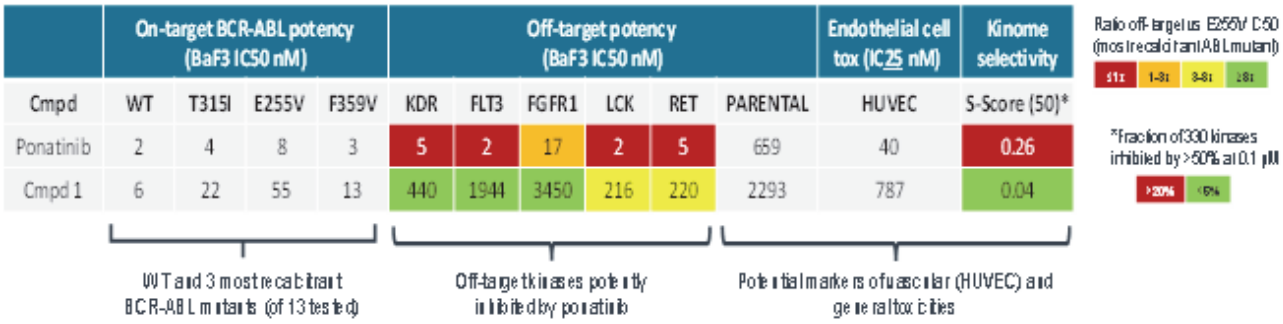



**Figure 21. In vitro characterization of Compound 1 versus ponatinib in Ba/F3 cell line.**

***In vivo model of Compound 1 showed similar tumor regression activity and superior tolerability to ponatinib***

To evaluate the in vivo activity of Compound 1 in mice, we subcutaneously implanted Ba/F3 cells engineered with a BCR-ABL E255V mutant, the mutant that Compound 1 had the lowest potency against, and then administered compounds orally to groups of mice. As shown in Figure 22, Compound 1 induced strong tumor regressions, comparable to those induced by ponatinib. Furthermore, Compound 1 demonstrated improved tolerability compared to ponatinib, with keratinized skin observed in 8 out of 10 mice dosed with 25 mg/kg of ponatinib, but in 0 out of 10 mice dosed with 120 mg/kg of Compound 1.

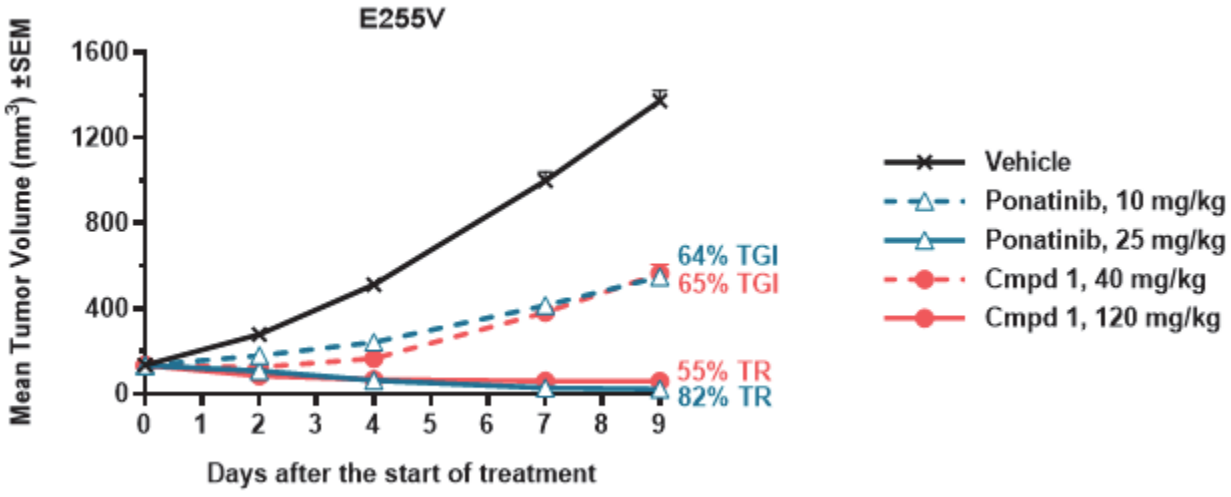



**Figure 22. *In vivo* mouse model of ponatinib and Compound 1 in mice with the E255V BCR-ABL variant.**

**Our Predictive Resistance Assay™ is Driving Development of Additional Novel Therapeutics**

Based on the use of our PRA for multiple TKI families, including our current programs, we believe the novel PRA approach we used to evaluate KIT, EGFR and BCR-ABL TKI therapies is suitable for the prosecution of diverse kinase targets, as well as targets from other oncogenic protein families. As we apply our PRA more widely, we are guided by the clear principles of our research and discovery approach. We will focus on clinically validated targets with clearly defined patient populations and significant unmet medical needs. We will leverage our core competencies in structure-guided design for novel small molecule development and use our PRA to identify candidates that demonstrate on-target pan-mutant activity against known activation and resistance mutations. We believe our insights into small molecule drug design allow us to design and develop small molecule inhibitors that address on-target mechanisms of resistance to prior generation inhibitors while maintaining selectivity and offering the potential for superior tolerability.

**Competition**

The pharmaceutical and biotechnology industries, particularly the field of oncology, are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. We believe that our pipeline, knowledge, experience and scientific resources provide us with differentiated competitive advantages. However, we have competitors both in the US and internationally, which include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, emerging and start-up companies, universities and other research institutions.

The key competitive factors that will affect the success of product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors. We also compete with these organizations to recruit and retain qualified scientific and management personnel. We will also face competition in establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our competitors have developed, are developing, or may develop products, product candidates and processes competitive with ours. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Many of our competitors, either alone or with their collaborators, have significantly greater financial resources, established presences in markets, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals, gaining reimbursement and marketing approved products than we do. Our competitors may succeed in obtaining approval from the FDA or other comparable foreign regulatory authorities or in discovering, developing and commercializing product candidates in our field before we do.

There are several approved therapies for the treatment of conditions for which we are attempting or may attempt to develop product candidates. In addition, we believe that a significant number of product candidates are currently under development, and may become commercially available in the future.

- With respect to our most advanced product candidate, THE-630, there are several large pharmaceutical companies and biotechnology companies marketing drugs for the treatment of GIST, including Blueprint Medicines, Inc., or Blueprint, Cogent Biosciences, Inc., or Cogent, Novartis AG, Pfizer, Inc., Deciphera Pharmaceuticals, Inc., or Deciphera, and Bayer AG. We are also aware of pharmaceutical and biotechnology companies developing drugs for the treatment of GIST, including AB Sciences S.A., Arog Pharmaceuticals, Inc., CTTP, Exelixis, Inc., IDRX, Inc., Immunicum AB, Jiangsu HengRui, Inc., Ningbo Tai Kang Medical Technology Co. Ltd., Taiho Pharmaceutical Co. Ltd, Xencor, Inc. and Merck KGaA. In particular, Cogent has disclosed its registrational trial evaluating bezuclastinib in combination with sunitinib, which is being conducted in patients with second-line GIST, and Deciphera has disclosed its plans to evaluate ripretinib in a subset of patients with second-

line GIST. If successful, these products may compete with THE-630 to the extent we are able to advance it into earlier lines of treatment for patients with GIST.

- With respect to THE-349, we are aware of other pharmaceutical companies with approved drugs for treatment-resistant EGFR-mutant NSCLC, including AstraZeneca plc's osimertinib, lazertinib, which is marketed by Yuhan Corp. in South Korea, and almonertinib, which is under collaboration between Jiangsu Hansoh Pharmaceutical Group Co., Ltd. and EQRx, Inc., which is approved in China. In addition, THE-349 may face competition from drug candidates in development for EGFR-mutated NSCLC, including those being developed by Alpha Biopharma Inc., Astellas Pharma Inc., Black Diamond Therapeutics, Inc., Blueprint, Boehringer Ingelheim RCV GmbH & Co KG, Bridge Biotherapeutics, Inc., C4 Therapeutics, Inc., CTTP, Genosco Inc., Genprex, Inc. and Janssen Pharmaceuticals, Inc.

- With respect to our BCR-ABL program, there are currently six BCR-ABL TKIs approved for use in CML: Novartis AG's Gleevec (imatinib), Tasigna (nilotinib), and Scemblix (asciminib), Bristol Myers Squibb's Sprycel (dasatinib), Pfizer's Bosulif (bosutinib), and Takeda's Iclusig (ponatinib). Iclusig (ponatinib) is indicated for patients with CML who have resistance or intolerance to at least two prior TKIs. It is also approved for patients with the T315I mutation. Scemblix (asciminib), is a fourth-generation TKI marketed by Novartis AG which was recently approved by the FDA. Other BCR-ABL TKIs under investigation include Enliven Therapeutics' ELVN-001 program, which is in Phase 1 studies, Sun Pharma Advanced Research Company's vodobatinib, Ascentage Pharma's olverembatinib, Terns Pharmaceuticals' TERN-701, and others at various stages of development. While there are no approved TKIs for Ph+ ALL, imatinib, dasatinib, nilotinib, bosutinib, and ponatinib are recommended by the National Comprehensive Cancer Network, and Takeda recently announced positive results in a registrational trial evaluating ponatinib versus imatinib that demonstrated ponatinib statistically superior efficacy to imatinib in newly diagnosed patients with Ph+ ALL.

We also face competition broadly across the oncology market for cost-effective and reimbursable cancer treatments. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While product candidates, if any are approved, may compete with these existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, product candidates may not be competitive with them. Additionally, product candidates may need to compete with drugs that physicians use off-label to treat the indications for which we seek approval. Moreover, many companies are developing new oncology therapeutics, and we cannot predict what the standard of care will be as product candidates progress through clinical development.

**ARIAD License Agreement**

In June 2018, we entered into a license agreement, or the ARIAD License Agreement, with ARIAD, a wholly-owned subsidiary of Takeda, for an exclusive, transferable (subject to certain restrictions), sublicensable (subject to certain conditions), worldwide license, under certain of ARIAD's patent rights, know-how and compounds and a certain ARIAD chemical library, to develop, use, manufacture, market and commercialize certain compounds, and products that contain such compounds, that are therapeutically useful for the treatment of diseases and disorders in humans, including with respect to KIT (referred to as C-KIT, CD117, and stem cell factor receptor in the ARIAD License Agreement). THE-630 is derived from intellectual property licensed to us under the ARIAD License Agreement and is therefore subject to the ARIAD License Agreement.

Pursuant to the terms of the ARIAD License Agreement and related stock purchase agreements, we issued an aggregate of 1,615,427 shares of our Series A Preferred Stock to ARIAD (which converted to shares of our common stock in connection with our initial public offering in October 2021). We are obligated to make tiered royalty payments to ARIAD that are low- to mid-single digits of our future net sales and those of our sublicensees of each product comprising a licensed ARIAD compound in each country, beginning on the first commercial sale of such product in such country and ending on the later of (1) ten years following such first

commercial sale and (2) the expiry of all patents that cover the product in such country, or the royalty term. Our royalty payment obligations are subject to reductions in certain circumstances.

During the term of the ARIAD License Agreement, we agreed not to use any intellectual property licensed to us, or any biological materials provided to us, thereunder to develop, use, manufacture, market or commercialize the same with respect to EGFR or any compounds or products that are potentially therapeutically useful for the treatment of diseases and disorders in humans with respect to EGFR (also known as ErbB1, ErbB and HER1). We did not use any intellectual property licensed to us, or any biological materials provided to us, under the ARIAD License Agreement to develop any of our other programs.

ARIAD may terminate the ARIAD License Agreement (1) for our uncured material breach of such agreement, (2) if we, or any of our affiliates or sublicensees, commence, and do not stop after receiving notice from ARIAD, any interference or opposition proceeding in relation to, challenges to the validity or enforceability of, or opposition to any extension of or the grant of a supplementary protection certificate with respect to, any ARIAD patent or patent application licensed under the ARIAD License Agreement, or (3) in the event of our bankruptcy.

We have the first right to control the prosecution of, and to bring enforcement actions for infringement by third parties with respect to, the patents licensed to us under the ARIAD License Agreement, with input from ARIAD. If we determine not to prosecute or enforce an ARIAD-licensed patent then ARIAD has the right to do so under certain conditions.

The ARIAD License Agreement terminates, on a product-by-product and country-by-country basis, on expiration of the royalty term for such product for the applicable country. Thereafter, the licenses from ARIAD to us with respect to such product for such country will convert to a fully paid, royalty-free, irrevocable, and perpetual license.

**Intellectual Property**

We seek to protect the intellectual property and proprietary technology that we consider important to our business, including by pursuing patent applications that cover THE-630, THE-349 and any additional product candidates we may develop, and methods of using the same, as well as any other relevant inventions and improvements that we believe to be commercially important to the development of our business. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications in the US and in jurisdictions outside of the US directed to our proprietary technology, inventions, improvements, and product candidates (including compositions, methods of use, dosing and formulations) that are important to the development and implementation of our business. We may also pursue patent protection with respect to manufacturing and drug development processes and technologies. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. We also plan to rely on data exclusivity, market exclusivity and patent term extensions when available. Our commercial success depends, in part, on our ability to obtain, maintain, enforce and protect our intellectual property and other proprietary rights for the technology, inventions and improvements we consider important to our business, and to defend any patents we may own or in-license in the future, prevent others from infringing any patents we may own or in-license in the future, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and proprietary rights of third parties.

As of December 31, 2022, our worldwide patent portfolio consisted of seventeen issued patents and 54 pending patent applications that we own or license related to our KIT and EGFR inhibitor product candidates. Specifically, as of that date, we owned or licensed two issued US patents, three pending US non-provisional patent applications, one pending US provisional patent application, three pending PCT patent applications, fifteen issued foreign patents, and 47 pending foreign patent applications.

More specifically, with respect to our KIT inhibitor product candidate, we own one pending PCT patent application and two foreign patent applications in Argentina and Taiwan and we license two issued US patents, two pending US non-provisional patent applications, fifteen foreign patents and 38 pending foreign patent applications, including Australia, Brazil, Canada, China, Eurasia, Europe, Israel, India, Japan, Mexico, New Zealand, Singapore, South Africa, and South Korea. Any patents that may issue from our pending patent applications are expected to have nominal expiration dates ranging from 2037 to 2042, absent any patent term adjustments or patent term extensions for regulatory delay. The KIT portfolio includes filings covering compositions of matter and methods of using our most advanced product candidate, THE-630, including one licensed patent with issued claims directed to composition of matter that encompass THE-630.

With respect to our EGFR inhibitor product candidate, we own one pending US provisional patent application, one pending US non-provisional patent application, and two pending PCT patent applications, and 7 pending foreign patent applications, including China, Europe, Israel, India, Japan, South Korea, and Mexico. Any patents that may issue from our pending patent applications are expected to have nominal expiration dates ranging from 2041 to 2043, absent any patent term adjustments or patent term extensions for regulatory delay.

Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In the US, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest US non-provisional filing date. In addition, in certain instances, the term of an issued US patent that covers or claims an FDA approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called patent term extension. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The term of patents outside of the US varies in accordance with the laws of the foreign jurisdiction, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications and those of our licensors and collaborators may not result in patents being issued which protect product candidates or which effectively prevent others from commercializing competitive product candidates. Moreover, obtaining and enforcing patents in the pharmaceutical and biotechnology industries is inherently uncertain, due in part to ongoing changes in the patent laws. Changes in either the patent laws or in the interpretations of patent laws in the US and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities.

**Commercial Strategy**

We intend to retain significant development and commercial rights to product candidates and, if marketing approval is obtained, to commercialize product candidates on our own, or potentially with a partner, in the US and other regions. We currently have no sales, marketing, or commercial product distribution capabilities. However, we intend to build a focused sales and marketing organization and the necessary infrastructure and capabilities over time in the US, and potentially other regions, following further advancement of product candidates. We believe that such an organization will be able to address the community of oncologists who are the key specialists in treating the patient populations for which product candidates and programs are

being developed. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with researchers and practitioners in relevant fields of medicine. Clinical data, the size of the addressable patient population, the size of the commercial infrastructure and manufacturing needs may all influence or alter our commercialization plans.

**Manufacturing**

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of THE-630, THE-349, as well as any other product candidates we may develop through our programs, for preclinical and clinical testing. We also expect to rely on third parties for the manufacture of our product candidates and any other product candidates we may develop through our programs for commercial supply, if any product candidates obtain marketing approval. We also rely, and expect to continue to rely, on third parties to package, label, store and distribute our product candidates and any other product candidates we may develop through our programs and, if marketing approval is obtained, our commercial products.

However, as we progress towards commercialization of product candidates, we anticipate expanding the supply chain to include multiple contract manufacturing organizations, or CMOs. We believe this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities and equipment, while also enabling us to focus our expertise and resources on the development of product candidates.

Manufacturing is subject to extensive regulations that impose procedural and documentation requirements. These regulations govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance. Our CMOs are required to comply with these regulations and are assessed through regular monitoring and formal audits. Our third-party manufacturers are required to manufacture any product candidates we develop under current Good Manufacturing Practice, or cGMP, requirements and other applicable laws and regulations.

We generally expect to rely on third parties for the manufacture of companion diagnostics, which are assays or tests that identify an appropriate patient population, if needed for any product candidates that receive marketing approval.

**Government Regulation**

The FDA, and other regulatory authorities in and outside the US, extensively regulate, among other things, the research, development, manufacture, import, export, labeling, packaging, storage, distribution, advertising, and promotion of drugs and biologics. We, along with third parties we work with, will be required to navigate the various preclinical, clinical, manufacturing, and commercial approval requirements of the governing regulatory agencies of the jurisdictions in which we wish to conduct studies or seek marketing approval of drug product candidates. The process of obtaining regulatory approvals of drugs and biologics and ensuring subsequent compliance with applicable legal requirements presents a variety of risks and requires the expenditure of substantial time and financial resources.

In the US, where we are initially focusing our drug development and commercialization, we believe our product candidates, as small molecule drugs, would be regulated as new drugs rather than biologics. If we fail to comply with applicable FDA or other requirements at any time with respect to product development, clinical testing, approval or any other regulatory requirements relating to product manufacture, handling, safety, advertising, promotion, packaging, labeling, export, import, distribution, or sale, we may become subject to administrative or judicial sanctions or other legal consequences. These sanctions or consequences could include, among other things, the FDA's refusal to approve pending applications, issuance of clinical holds for proposed or ongoing studies, suspension or revocation of approvals, warning or untitled letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties, or criminal prosecution.

***Preclinical Studies and Clinical Trials for Drugs***

Before testing any drug in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of product chemistry, formulation and stability, as well as in vitro and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulation and requirements, including good laboratory practice, or GLP, requirements under 21 C.F.R. Part 58 and animal testing requirements under the Animal Welfare Act Amendments of 1976 (7 U.S.C. 2131 et seq.). The results of the preclinical studies, together with manufacturing information and analytical data, must be submitted to the FDA as part of an IND.

An IND is a submission to the FDA under which a sponsor proposes to administer an investigational product to humans. An IND must become effective before the proposed clinical trials may begin. The IND becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns about the conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks, and imposes a full or partial clinical hold. The FDA must notify the sponsor of the grounds for the hold, and any identified deficiencies must be resolved before the clinical trial can begin. Submission of an IND may result in the FDA not allowing clinical trials to commence or not allowing clinical trials to commence on the terms originally specified in the IND. After the 30-day time period, the FDA can still raise concerns about the conduct of a proposed or ongoing trial and impose a full or partial clinical hold.

The clinical stage of development involves the administration of the product candidate to study subjects under the supervision of qualified investigators, who generally are physicians not employed by or under the trial sponsor's control, in accordance with good clinical practice, or GCP, requirements, which include the requirements that all research subjects provide their informed consent for their participation in a clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND.

Furthermore, each clinical trial must be reviewed and approved by an institutional review board, or IRB, or independent ethics committee, or IEC, for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable compared to the anticipated benefits. The IRB or IEC also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. The FDA, the IRB or IEC, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. There also are requirements governing the reporting of ongoing clinical trials, including the reporting of certain types of adverse events to the FDA, as well as reporting completed clinical trials to public registries such as www.ClinicalTrials.gov, a clinical trials database maintained by the National Institutes of Health.

A sponsor who wishes to conduct a clinical trial outside of the US is subject to the requirements of the applicable jurisdiction and may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the FDA may nevertheless accept the results of the study in support of an NDA if the FDA determines that the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if one is deemed necessary.

Clinical trials to evaluate therapeutic indications to support NDAs for marketing approval are typically conducted in three sequential phases, which may overlap.

- Phase 1—Phase 1 clinical trials involve initial introduction of the investigational product in a limited population of healthy human volunteers or patients with the target disease or condition. These studies are typically designed to test the safety, dosage tolerance, absorption,

metabolism, and distribution of the investigational product in humans, evaluate the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.

- Phase 2—Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the drug's potential efficacy, to determine the optimal dosages and dosing schedule, and to identify possible adverse side effects and safety risks.

- Phase 3—Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy, and to further test for safety, generally at multiple geographically dispersed clinical trial sites. Phase 3 clinical trials are intended, with the other available evidence, to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and physician labeling. Generally, two adequate and well-controlled Phase 3 trials are required by the FDA for approval of an NDA. Under certain circumstances, the FDA can conclude that one adequate and well-controlled clinical investigation plus confirmatory evidence is sufficient to establish effectiveness.

Post-approval trials, sometimes referred to as Phase 4 clinical trials or post-marketing studies, may be conducted after initial marketing approval. These trials are used to gain additional evidence from the treatment of study subjects in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting, or in some cases to confirm clinical benefit. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of NDA approval.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA all participating investigators no later than fifteen days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human volunteers, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor's initial receipt of the information.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing the drug product in commercial quantities in accordance with cGMP requirements. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

***Expanded Access***

Expanded access, sometimes called "compassionate use," is the use of investigational drug products outside of controlled clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. FDA regulations allow access to investigational products under an IND by the sponsor or the treating physician for treatment purposes on a case-by-case basis.

In addition, the Right to Try Act from 2018 provides, among other things, an additional mechanism for patients with a life-threatening condition who have exhausted approved treatments and are unable to participate in clinical trials to access certain investigational products that have completed a Phase 1 clinical trial, are the subject of an active IND, and are undergoing investigation in a clinical trial that is intended to form the primary basis of a claim of effectiveness in support of FDA approval. There is no obligation for a sponsor to make its investigational products available to eligible patients under the Right to Try Act.

***US Marketing Approval for Drugs***

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA package requesting approval to market the drug product for one or more indications. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt, and such decision could include a "refuse-to-file" decision by the FDA. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA. The FDA reviews an NDA to determine, among other things, whether the product is safe and effective for the indications sought and whether the facilities in which it is manufactured, processed, packaged, or held meet standards designed, including current good manufacturing practice, or cGMP, requirements, designed to assure and preserve the product's continued identity, strength, quality and purity. Under the goals and polices agreed to by the FDA under the Prescription Drug User Fee Act, as amended, or PDUFA, the FDA targets ten months, from the filing date, in which to complete its initial review of a new molecular entity NDA and respond to the applicant, and six months from the filing date of a new molecular entity NDA for priority review. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Further, under PDUFA, each NDA must be accompanied by a substantial user fee. For fiscal year 2023, the application fee for each application containing clinical data is $3,242,026. PDUFA also imposes an annual program fee for each approved prescription drug, which has been set at $393,933 for fiscal year 2023. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on applications for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides advice and recommendations to the FDA as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. Additionally, before approving an NDA, the FDA may inspect one or more select clinical trial sites involved in conducting pivotal studies to assure compliance with GCP and other requirements and the integrity of the clinical data submitted to the FDA. After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a Complete Response Letter. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. In issuing the Complete Response Letter, the FDA may require additional clinical or preclinical testing or recommend other actions, such as requests for additional information or clarification, that the applicant might take in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If the FDA issues an approval letter, the approval authorizes commercial marketing of the product with specific prescribing information for specific indication(s).

Even if the FDA approves a product, it may limit the approved indications for use, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies be conducted to further assess a product's safety and efficacy, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a Risk Evaluation and Mitigation Strategy, or REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs.

***Orphan Drug Designation and Exclusivity***

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is a disease or condition with either a patient population of fewer than 200,000 individuals in the US, or a patient population greater than 200,000 individuals in the US when there is no reasonable expectation that the cost of developing and making the product available in the US for the disease or condition will be recovered from sales of the product. Orphan drug designation must be requested before submitting a marketing application. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan products are eligible for certain incentives, including tax credits for qualified clinical testing and waiver of PDUFA application fees.

If a product that has orphan designation subsequently receives the first FDA approval for the use for which it has such designation, the product is entitled to a seven-year period of marketing exclusivity from the date of FDA approval during which the FDA may not approve any other applications to market the "same drug" for the same use, except in limited circumstances, such as a subsequent product's showing of "clinical superiority" over the product with orphan exclusivity or where the original applicant cannot produce sufficient quantities of product. The FDA defines "same drug" with respect to small molecule drugs as a drug that contains the same active moiety as a previously approved drug and is intended for the same use as the previously approved drug. Competitors, however, may receive approval of different therapeutic agents for the indication for which the orphan product has exclusivity or obtain approval for the same therapeutic agent for a different indication than that for which the orphan product has exclusivity. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. Further, orphan drug exclusive marketing rights in the US may be lost if the FDA later determines that the request for designation was materially defective or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition, or if the manufacturer chooses to provide consent to approval of other applications. In February 2022, we received orphan drug designation from the FDA for THE-630 for the treatment of gastrointestinal stromal tumors.

***Expedited Development and Review Programs for Drugs***

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

A new drug is eligible for Fast Track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition, or it has been otherwise designated as a qualified infectious disease product. Fast Track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed. Rolling review means that the FDA may review portions of the marketing application before the sponsor submits the complete application.

In addition, a new drug may be eligible for Breakthrough Therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug, alone or in combination with one or more other drugs, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy designation provides all the features of Fast Track designation, in addition to intensive guidance on an efficient product development program beginning as early as Phase 1 and FDA organizational commitment to expedited development.

Any drug product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review and approval process, including Priority Review and Accelerated Approval. A drug product is eligible for Priority Review, once an NDA is submitted, if the product that is the subject of the marketing application has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. Under Priority Review, the FDA's goal date to take action on the marketing application is six months compared to ten months for a standard review, running from the date of FDA's acceptance of the application for review in the case of a new molecular entity and otherwise running from the date of submission of the application to FDA.

The FDA may grant Accelerated Approval to a drug product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant Accelerated Approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

The Accelerated Approval pathway is contingent on a requirement that the sponsor conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the product. Periodic reports must be submitted to FDA on study progress. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA. In addition, the FDA requires, as a condition for Accelerated Approval, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the pre-approval review period. After the 120-day period has passed, all advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

Even if a drug product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval, though they may expedite the development or review process.

***Pediatric Study Plan and Pediatric Exclusivity***

Under the Pediatric Research Equity Act, as amended, or PREA, certain NDAs and certain NDA supplements must contain data that can be used to assess the safety and efficacy of the product candidate for the claimed indications in all relevant pediatric subpopulations to support dosing and administration for each pediatric subpopulation for which the product has been assessed to be safe and effective, and provide an assessment of the data gathered to support the safety and effectiveness of the product in the entire pediatric population. For a cancer drug directed at a molecular target, the pediatric testing requirement extends to pediatric cancers involving the molecular target even if different than the claimed adult cancer in the NDA. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to a drug for an indication for which orphan designation has been granted, except that PREA will apply to an original NDA for a new active ingredient that is orphan-designated if the drug is a molecularly targeted cancer product intended for the treatment of an adult cancer and is directed at a molecular target that the FDA determines to be substantially relevant to the growth or progression of a pediatric cancer.

A drug can also obtain pediatric market exclusivity in the US. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

***US Post-Approval Requirements for Drugs***

Drugs approved by the FDA are subject to continuing regulation by the FDA, including, among other things, requirements relating to manufacturing establishment registration and product listing, recordkeeping, periodic reporting, product sampling and distribution, reporting of adverse experiences with the product, field alerts regarding issues with distributed drug products, and promotion and advertising compliance, which include restrictions on promoting products for unapproved uses or patient populations (known as "off-label use"). Further, if there are any modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the development of additional data or preclinical studies and clinical trials.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, requirements for post-market studies or clinical trials to assess new safety risks, imposition of distribution or other restrictions under a REMS, or FDA withdrawal of product approval.

***US Patent Term Restoration and Marketing Exclusivity***

Depending upon the timing, duration, and specifics of FDA approval of our future product candidates, some of our US patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments.

Upon any approval of an NDA we receive, we may also be eligible to receive certain periods of regulatory exclusivity. For example, the FDCA provides a five-year period of non-patent marketing exclusivity within the US to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA, or a 505(b)(2) NDA, submitted by another company for another version of such drug that seeks to rely in whole or in part on the approved NDA with the exclusivity. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement for patents that the NDA holder has listed with the FDA.

***Regulation of Companion Diagnostics***

Companion diagnostics provide information that is essential for the safe and effective use of a corresponding therapeutic product. Companion diagnostics are regulated as medical devices by the FDA. In the US, the FDCA, and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption or FDA exercise of enforcement discretion applies, diagnostic tests generally require marketing clearance or approval from the FDA prior to commercialization. The two primary types of FDA marketing authorization applicable to a medical device are clearance of a premarket notification under section 510(k) of the FDCA, or 510(k), and approval of a premarket approval application, or PMA.

To obtain 510(k) clearance for a medical device, or for certain modifications to devices that have received 510(k) clearance, a manufacturer must submit a premarket notification demonstrating that the proposed device is substantially equivalent to a legally marketed predicate device, which is typically a previously

510(k)-cleared device. A proposed device is substantially equivalent to a predicate device if the subject device (1) has the same intended use as the predicate device and (2) either (a) has the same technological characteristics as the predicate device or (b) has different technological characteristics but does not raise different questions of safety and effectiveness than the predicate device and the submitted information demonstrates that the subject device is as safe and effective as the predicate device. If the FDA determines that the subject device is substantially equivalent to the predicate device, the subject device may be cleared for marketing. The 510(k) premarket notification pathway generally takes from three to twelve months from the date the application is completed, but can take longer.

A PMA must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the quality system regulation, or QSR, which requires manufacturers to follow design, testing, control, documentation, and other quality assurance procedures. FDA has committed to performance goals of reviewing original PMAs that are not referred to an Advisory Committee within 180 days and reviewing PMAs referred to an Advisory Committee within 320 days (excluding days when a request for additional information is pending with the applicant), although the process typically takes longer, and may require several years to complete. Once granted, PMA approval may be withdrawn by the FDA if compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or the device is determined to be unsafe or ineffective following initial marketing.

On August 6, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance document, for novel therapeutic products that depend on the use of a diagnostic test and where the diagnostic device could be essential for the safe and effective use of the corresponding therapeutic product, the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic, although the FDA recognizes that there may be cases when contemporaneous development may not be possible. However, in cases where a drug cannot be used safely or effectively without the companion diagnostic, the FDA's guidance indicates it will generally not approve the drug without the approval or clearance of the diagnostic device. The FDA also issued a draft guidance in July 2016 setting forth the principles for co-development of an in vitro companion diagnostic device with a therapeutic product. The draft guidance describes principles to guide the development and contemporaneous marketing authorization for the therapeutic product and its corresponding in vitro companion diagnostic.

Once cleared or approved, the companion diagnostic device must adhere to post-marketing requirements including the requirements of the FDA's QSR, establishment registration and device listing, adverse event and device malfunction reporting, reporting of recalls and corrections, along with product marketing requirements and limitations. Like drug makers, companion diagnostic makers are subject to unannounced FDA inspections at any time during which the FDA will conduct an audit of the product(s) and the company's facilities for compliance with its authorities.

***Other Regulatory Matters***

Manufacturing, sales, promotion and other activities of products following product approval, where applicable, or commercialization are also subject to regulation by numerous regulatory authorities in the US in addition to the FDA, which may include the Centers for Medicare & Medicaid Services, or CMS, other divisions of the US Department of Health and Human Services, or HHS, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments and governmental agencies.

***Healthcare Laws***

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers, and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we develop, market, sell and distribute any drugs for which we obtain marketing approval. In the US, these laws include federal and state anti-kickback, false claims (for example, False Claims Act), physician transparency, and patient data privacy (for example, the Health Insurance Portability and Accountability Act of 1996(HIPAA)) and security laws and regulations, including those described below. Comparable laws exist in other jurisdictions.

***Insurance Coverage and Reimbursement***

In the US and markets in other countries, patients who are prescribed treatments for their conditions and providers performing healthcare services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government healthcare programs such as Medicare and Medicaid, private health insurers, managed care organizations and other third-party payors, provide coverage, and establish adequate reimbursement levels for, the product. In the US, principal decisions about Medicare reimbursement for new products are typically made by CMS and regional contractors responsible for administering the Medicare program. CMS and these contractors decide whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree.

Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor's determination that use of a product is (1) a covered benefit under its health plan; (2) safe, effective and medically necessary; (3) appropriate for the specific patient; (4) cost-effective; and (5) neither experimental nor investigational. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Moreover, one third-party payor's determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product candidate. No uniform policy of coverage and reimbursement for products exists among third-party payors, and coverage and reimbursement levels for products can differ significantly from payor to payor.

Third-party payors are increasingly challenging the prices charged, examining the medical necessity, reviewing the cost-effectiveness of medical products and services, and imposing controls to manage costs. In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmaco-economic studies in order to demonstrate the cost effectiveness of the product, which will require additional expenditure above and beyond the costs required to obtain FDA or other comparable regulatory approvals. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication.

Moreover, the containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drug products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls or price increase penalties, restrictions on reimbursement and requirements for substitution of generic products. This interest has resulted in meaningful proposed and enacted reform measures affecting healthcare reimbursement and drug pricing, including the enactment in August 2022 of significant changes to potential Medicare drug product reimbursement, as well as manufacturer rebate and discount obligations, under the Inflation Reduction Act (IRA).

In addition, coverage and reimbursement for companion diagnostic tests is separate and apart from the coverage and reimbursement for their companion pharmaceutical products. Challenges to obtaining coverage and reimbursement similar to those applicable to pharmaceutical products will apply to companion diagnostics.

***Compliance with Other Federal and State Laws or Requirements; Changing Legal Requirements***

If any products that we may develop are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the US Poison Prevention Packaging Act. Manufacturing, labeling, packaging, distribution, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws, among other requirements to which we may be subject. The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive recordkeeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products, and state licensure.

***European Union Drug Development***

Similar to the US, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the Clinical Trials Directive, before a clinical trial can be initiated, it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority (NCA), and one or more Ethics Committees (ECs). Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. The Clinical Trials Regulation EU No 536/2014 entered into application on January 31, 2022 and is directly applicable, thus the rules governing clinical trials are further harmonized. The Clinical Trials Regulation provides for a transition period during which the Clinical Trials Directive continues to apply to certain trials. However, all trials conducted under the Clinical Trial Directive must be transitioned to conduct under the Clinical Trials Regulation by January 31, 2025, if still ongoing at that point.

***European Union Drug Review and Approval***

In the European Economic Area (EEA), which is comprised of the 27 Member States of the European Union and three European Free Trade Association States (Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization (MA). There are two types of marketing authorizations, a centralized MA and a national MA.

- The centralized MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use (CHMP), of the EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions, and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for

products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State (RMS). The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics (SmPC), and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Concerned Member States or CMS) for their approval. If the CMS raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the CMS).

Under the above described procedures, before granting the MA, EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. Similar to the US patent term-restoration, Supplementary Protection Certificates (SPCs) serve as an extension to a patent right in Europe for up to five years. SPCs apply to specific pharmaceutical products to offset the loss of patent protection due to the lengthy testing and clinical trials these products require prior to obtaining regulatory marketing approval. Alongside patent protection, there are a number of regulatory incentives offered (including SPC extensions, regulatory data protection and orphan market exclusivity, amongst others).

Outside the US, ensuring coverage and adequate payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to government control in many countries. Pricing negotiations with government authorities can extend well beyond the receipt of regulatory approval for a product and may require a clinical trial that compares the cost-effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

***Government Regulation of Personal Data Collection in the EU and UK***

In the event we conduct clinical trials in the European Union, we will be subject to additional privacy restrictions. The collection and use of personal health data in the EEA is governed by the General Data Protection Regulation, or the GDPR, which became effective on May 25, 2018. The GDPR applies to the processing of personal data by any company established in the EEA and to companies established outside the EEA to the extent they process personal data in connection with the offering of goods or services to data subjects in the EEA or the monitoring of the behavior of data subjects in the EEA. The GDPR enhances data protection obligations for data controllers of personal data, including stringent requirements relating to the consent of data subjects, expanded disclosures about how personal data is used, enhanced requirements for securing personal data, requirements to conduct privacy impact assessments for “high risk” processing, limitations on retention of personal data, mandatory data breach notification and “privacy by design” requirements, and creates direct obligations on service providers acting as processors. The GDPR also imposes strict rules on the transfer of personal data outside of the EEA to countries that do not ensure an adequate level of protection, like the US. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EEA member states, which may deviate slightly from the GDPR, may result, depending on the type of violation, in fines of up to 2% of a company’s global turnover for the preceding financial year, or €10 million, whichever is greater; or up to 4% of a company’s global turnover for the preceding financial year, or €20 million, whichever is greater. Moreover, the GDPR grants data subjects

the right to claim material and non-material damages resulting from infringement of the GDPR. Given the breadth and depth of changes in data protection obligations, maintaining compliance with the GDPR will require significant time, resources and expense, and we may be required to put in place additional controls and processes ensuring compliance with data protection rules. There has been increasing enforcement of the GDPR since it took effect in 2018, but less so in biopharmaceutical development, so we face uncertainty as to the exact interpretation of the requirements on any future trials and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the law. Further, the United Kingdom's decision to leave the European Union, means that it has in force its own legislation which is aligned with the GDPR, including the Data Protection Act 2018 and provisions of the GDPR incorporated into UK domestic law, or UK GDPR. The requirements are similar except that the United Kingdom is now regarded as a "third country" for the purposes of transfers of personal data from the EEA. Transfers continue to flow freely from the UK to the EEA following an adequacy decision from the European Commission adopted on June 28, 2021 and valid for four years, which may be renewed, if the European Commission finds that the UK continues to ensure an adequate level of protection.

Data protection authorities' enforcement and advisory activities differ across the EU, creating some uncertainty in the manner in which data protection authorities seek to enforce compliance with GDPR. Data protection authorities may both conduct random audits of companies doing business in the EU, and act on complaints filed by individuals who claim their rights have been violated. Enforcement uncertainty and the costs associated with ensuring GDPR compliance are onerous and may adversely affect our business, financial condition, results of operations and prospects.

Should we utilize third-party distributors, compliance with such foreign governmental regulations would generally be the responsibility of such distributors, who may be independent contractors over whom we have limited control.

**Employees and Human Capital**

As of February 28, 2023 we had 38 full-time and part-time employees, of which 15 have M.D. or Ph.D. degrees. Of our full-time and part-time employees, 25 were engaged in research and development activities and 13 were engaged in business development, finance and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, motivating and integrating our existing and future employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants, and directors through grants of stock-based compensation awards and payments of cash-based performance bonus awards, in order to increase stockholder value and the success of our company by motivating our employees to perform to the best of their abilities and achieve our objectives.

**Available Information**

We were initially formed on December 29, 2017 as Theseus Pharmaceuticals, Inc., a Delaware corporation. Our principal executive offices are located at 314 Main Street, Cambridge, Massachusetts 02142, and our telephone number is (857) 400-9491. We maintain an internet website at https://theseusrx.com/ and make available free of charge through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. You can review our electronically filed reports and other information that we file with the SEC on the SEC's website at http://www.sec.gov. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. In addition, we regularly use our website to post information regarding our business, product

development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled “Investor Relations,” as a source of information about us.

The information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report and should not be considered to be a part of this Annual Report. We have included our website address as an inactive textual reference only.

## ITEM 1A. Risk Factors

*You should consider carefully the risks described below, together with the other information contained in this Annual Report, including our financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations." If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and our stockholders may lose all or part of their investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of a number of factors, including the risks described below. See the section titled "Special Note Regarding Forward-Looking Statements."*

### RISK FACTORS

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

***Our limited operating history may make it difficult to evaluate our current business and likelihood of success and viability.***

We are a biopharmaceutical company with a limited operating history upon which investors can evaluate our business and prospects. We were incorporated in December 2017 and commenced significant operations in 2018, have never completed any clinical trials, have no products approved for commercial sale and have never generated any revenue. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. To date, we have devoted substantially all of our resources to research and development activities, including with respect to THE-630, our pan-variant KIT inhibitor, THE-349, our fourth-generation EGFR inhibitor, and our BCR-ABL and other discovery programs, business planning, establishing and maintaining our intellectual property portfolio, hiring personnel, raising capital and providing general and administrative support for these operations. We have not yet demonstrated our ability to successfully complete any clinical trials, obtain marketing approvals, manufacture the clinical or commercial supply of drug 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 investors to accurately predict our likelihood of success and viability than if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by biopharmaceutical companies in early clinical stages and operating in rapidly evolving fields. We also expect that, in the future, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. If we do not adequately address these risks and difficulties or successfully make such a transition, we may not be able to develop product candidates, raise capital, expand our business, or continue our operations.

***We have incurred significant net losses in each period since our inception, and we expect to continue to incur significant net losses for the foreseeable future.***

We have incurred significant net losses since our inception. Our net loss was $50.6 million and $27.3 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $112.2 million. We are still in the very early stages of development of our product candidates and expect to continue to incur significant expenses and increasing operating losses for the foreseeable future as our development programs advance. Our net losses we incur may fluctuate significantly from quarter to quarter and year to year.

Even if we obtain regulatory approval of and are successful in commercializing one or more of any product candidates, we expect that we will continue to incur substantial research and development and other expenses in order to discover and develop additional potential products. Because of the numerous risks and

uncertainties associated with developing and commercializing our product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

***We have never generated revenue from product sales and may never achieve or maintain profitability.***

We have no products approved for commercial sale. Our product candidates are in the early stage of development and we expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must succeed in developing, obtaining the necessary regulatory approvals for and eventually commercializing a product or products that generate significant revenue.

Our ability to generate revenue and achieve profitability depends significantly on our ability to be effective in a range of challenging activities, including:

- successfully and timely completing our ongoing and planned preclinical and clinical development of our product candidates, THE-630 and THE-349, and any other future product candidates and programs;
- obtaining regulatory approval for any product candidates we may develop;
- manufacturing, marketing and selling any products for which we may obtain regulatory approval;
- achieving market acceptance of any product candidates we may develop for which we obtain regulatory approval as a viable treatment option; and
- satisfying any post-marketing requirements.

See also "—Risks Related to the Discovery, Research and Development of Product Candidates."

We may never be successful in achieving our objectives and, even if we do, may never generate revenue that is significant or large enough to achieve profitability. Our failure to become and remain profitable would significantly decrease the value of our company and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business and continue our operations.

***We will need to obtain substantial additional funding. If we are unable to raise this capital when needed, we may be forced to delay, reduce or eliminate our product development programs or other operations.***

The development of product candidates, including conducting preclinical studies and clinical trials, is a very time-consuming, capital intensive and uncertain process that takes years to complete. We expect our expenses to increase substantially in the foreseeable future in connection with our ongoing activities, particularly as we continue the research and development of and initiate preclinical studies and clinical trials of product candidates. We will need substantial additional funds to expand our clinical, regulatory, quality and manufacturing capabilities. In addition, if we obtain marketing approval for product candidates, we expect to incur significant commercialization expenses related to marketing, sales, manufacturing and distribution.

As of December 31, 2022, we had $211.8 million in cash, cash equivalents, and marketable securities, including the net proceeds from our initial public offering completed in October 2021. Based on our current operating plan, we believe that our cash, cash equivalents, and marketable securities, in addition to the proceeds raised under sales of our common stock pursuant to our "at-the-market", or ATM, Program, in the first quarter of 2023, will be sufficient to fund our operations and capital expenses into the third quarter of 2025. This estimate is based on assumptions that may prove to be incorrect, and we could utilize our

available capital resources sooner than we currently expect, particularly given that the design and outcome of our ongoing and anticipated preclinical studies and clinical trials are highly uncertain.

Our existing cash, cash equivalents, and marketable securities will not be sufficient to fund our product candidates through regulatory approval, and we anticipate needing to raise additional capital to complete the development of and commercialize our product candidates and development programs, including through the potential use of our ATM Program. Our future capital requirements will depend on many factors, including:

- the scope, progress, success and costs of our drug discovery, preclinical development activities, laboratory testing and clinical trials for product candidates;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing development and commercial manufacturing activities for product candidates, if approved;
- the extent to which we acquire or in-license other product candidates and technologies;
- the timing and amount of any payments required to be made under the agreements governing acquired or in-licensed product candidates or technologies;
- the cost, timing and outcome of regulatory review of product candidates;
- the cost and timing of establishing sales and marketing capabilities, if any product candidate receives marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the impact of the COVID-19 pandemic or other external disruptions on our business, results of operations and financial position;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of product candidates;
- the costs associated with being a public company; and
- the cost associated with commercializing product candidates, if they receive marketing approval.

Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our research or drug development programs, clinical trials or future commercialization efforts.

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

Until such time, if ever, as we can generate substantial product revenue, we expect to obtain further funding through a combination of equity financings, debt financings, collaborations, licensing arrangements or other sources of financing, including potential sales of our common stock pursuant to our ATM Program, which may dilute our stockholders or restrict our operating activities. We do not have any committed external source of funds, and adequate additional financing 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, stockholders' ownership interests will be diluted, and the terms may include liquidation or other preferences that adversely affect our stockholders' rights. Debt financing or preferred equity financings may result in imposition of covenants, increased fixed payment obligations or other restrictions that may affect our business. If we raise additional funds through upfront payments or milestone payments pursuant to strategic collaborations with third parties, we may have to relinquish valuable rights to product candidates or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds 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. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of product candidates.

**Risks Related to the Discovery, Research and Development of Product Candidates**

***We are very early in our development efforts and are substantially dependent on THE-630, our pan-variant KIT product candidate for GIST, and THE-349, our fourth-generation EGFR product candidate, for NSCLC. If we are unable to advance any product candidates through clinical and preclinical development, obtain regulatory approval and ultimately commercialize such product candidates, or experience significant delays in doing so, our business will be materially harmed.***

Although we are enrolling patients in a Phase 1/2 dose escalation and expansion clinical trial of our most advanced product candidate, THE-630, all of our programs are still in the early stage of development. We currently generate no revenue from sales of any product, and we may never be able to develop or commercialize a marketable product. 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 eventual commercialization of THE-630, or THE-349.

The success of THE-630 and THE-349 will depend on several factors, including the following:

- successful and timely completion of preclinical studies;
- submission of INDs in the US and CTAs and/or comparable applications outside the US for regulatory authority review and agreement to proceed with our clinical trials;
- timely submission and clearance of INDs for our anticipated clinical trials;
- successful and timely initiation, enrollment and completion of clinical trials;
- maintaining and establishing relationships with contract research organizations, or CROs, and clinical trial sites for the clinical development of product candidates both in the US and internationally;
- the frequency and severity of adverse events in clinical trials;
- demonstrating efficacy, safety and tolerability profiles that are satisfactory to the FDA or any comparable foreign regulatory authorities for marketing approval;
- the timely receipt of marketing approvals from FDA and any comparable foreign regulatory authorities;
- the timely identification, development and approval of companion diagnostic tests, if required;
- the extent of any required post-marketing studies or other post-approval commitments to applicable regulatory authorities;

- the establishment and maintenance of supply arrangements with third-party drug product suppliers and manufacturers for clinical development and, if approved, commercialization of product candidates;

- obtaining and maintaining patent protection, trade secret protection and regulatory exclusivity, and the protection of our other intellectual property rights, both in the US and internationally;

- the availability of an approved product for evaluation as a combination therapy;

- successful commercialization following the receipt of any marketing approval;

- a continued acceptable safety profile following any marketing approval;

- acceptance of our products, if approved, by patients, the medical community and third-party payors;

- addressing any potential delays resulting from factors related to the COVID-19 pandemic; and

- our ability to compete with other therapies, including our ability to differentiate any product for which we receive marketing approval against other approved products within the same class of drugs.

We do not have complete control over many of these factors. If we are not successful with respect to 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 from our development programs, which would materially harm our business. If we do not receive marketing approvals for such product candidates, we may not be able to continue our operations. If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

***We may not be able to submit INDs for our EGFR inhibitor product candidate, THE-349, or for our BCR-ABL or other discovery programs, to commence clinical trials on the timelines we expect, and even if we are able to submit an IND, the FDA may not permit us to initiate clinical trials.***

Before we can initiate clinical trials in the US for product candidates, we must submit the results of preclinical testing to the FDA along with other information, including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol as part of an IND submission. We intend to submit an IND application for THE-349 to the FDA in the fourth quarter of 2023 and initiate a Phase 1/2 trial as soon as possible thereafter. In January 2023, we announced BCR-ABL as a target for our third development program. We expect to nominate a development candidate for this program by early 2024. However, we may not be able to submit such INDs, or any INDs we may submit for any of our other programs, on the timelines we expect, or at all.

We cannot be sure that submitting an IND will result in the FDA allowing clinical trials to begin or of the timelines to begin any such trials, or that, once begun, issues will not arise that will require us to suspend or terminate clinical trials. Any failure to submit INDs on the timelines we, our stockholders or securities analysts expect or to obtain regulatory approvals for our anticipated clinical trials may prevent us from initiating or completing our clinical trials or commercializing product candidates on a timely basis, if at all. Even if completed, any delays in commencing or completing our clinical trials will increase our costs, extend the time it takes to complete clinical development and jeopardize the commercial prospects of product candidates and our ability to commence product sales and generate revenue, if at all. Further, if we are unable to achieve our goals within the timeframes we announce, the price of our common stock could decline, and our stockholders may lose some or all of their investment.

In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. For example, if we make manufacturing or formulation changes to a product candidate, we may need to conduct additional studies to bridge that modified product candidate to earlier versions we have evaluated. Further, if one or more clinical trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of THE-630, THE-349 or any other product candidates that we may develop could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly. Any termination of any clinical trial of product candidates will harm our commercial prospects and our ability to generate revenue.

***We may not be successful in our efforts to identify, discover or develop potential product candidates.***

Our future operating results are dependent on our ability to successfully discover, develop, obtain regulatory approval for and commercialize product candidates from our research programs, in addition to THE-630 and THE-349. Research programs to identify new product candidates require substantial technical, financial and human resources.

Our approach to the discovery and design of small molecule tyrosine kinase inhibitor, or TKIs, relies on our PRA, a novel screening and characterization approach that incorporates two critical human serum proteins that can affect drug activity. While the results of preclinical studies have suggested that certain of our TKIs may have the ability to inhibit all major classes of activating and resistance mutations, we have not yet succeeded and may not succeed in demonstrating efficacy and safety of THE-630, THE-349, or any of our development programs in clinical trials or in obtaining marketing approval thereafter. If our approach to the discovery and design of product candidates does not lead to the development of product candidates that prove to be effective and safe for the targeted indication, this would adversely impact our business strategy and our financial position and share price and could potentially cause us to cease operations.

Even if identified, a development candidate can unexpectedly fail at any stage of development. The historical failure rate for development candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The success of other development candidates we may develop will depend on many factors, including those described elsewhere in this section.

***Our ongoing and anticipated preclinical studies and clinical trials may fail at any time, and because our product candidates, THE-630 and THE-349, are in a very early stage of development, there is a high risk of failure, and we may never succeed in developing marketable products.***

Before obtaining marketing approval from the FDA or other comparable foreign regulatory authorities for the sale of product candidates, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that such product candidates are both safe and effective for use in each target indication. Preclinical and clinical testing is expensive, difficult to design and implement and can take many years to complete, and its ultimate outcome is uncertain. Failure can occur at any time during the development processes, and, because our product candidates, THE-630 and THE-349, are in a very early stage of development, there is a high risk of failure and we may never succeed in developing products that receive marketing approval.

The commencement and completion of clinical trials, such as our Phase 1/2 dose escalation and expansion clinical trial for THE-630 that we initiated in the first quarter of 2022, can be delayed for a number of reasons, including delays related to:

- failure of product candidates in preclinical studies or clinical trials to demonstrate safety and efficacy;
- delays with IND-enabling studies or in analyzing the data collected from any completed clinical trials;

- negative or inconclusive clinical trial results that may require us to conduct additional clinical trials or abandon certain research and/or drug development programs;

- the number of study subjects required for clinical trials being larger than anticipated, enrollment in these clinical trials being slower than anticipated or participants dropping out of these clinical trials at a higher rate than anticipated, including as a result of actions taken by governments and individuals in response to the COVID-19 pandemic;

- subjects choosing an alternative treatment or other product candidates, or participating in competing clinical trials;

- lack of adequate funding to continue the clinical trial;

- subjects experiencing severe or unexpected drug-related adverse effects;

- any interruptions or delays in the supply of product candidates or other materials necessary to conduct preclinical or clinical trials of our product candidates, including due to supply chain interruptions caused by global political tensions or the COVID-19 pandemic;

- a facility manufacturing product candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of current good manufacturing practice, or cGMP, regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;

- any changes to the manufacturing process of product candidates that may be necessary or desired;

- any failure or delay in reaching an agreement with CROs and clinical trial sites;

- clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practices, or GCP, or regulatory requirements or other third parties not performing data collection or analysis in a timely or accurate manner;

- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other comparable foreign regulatory authorities for violations of applicable regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications;

- the effects of the ongoing COVID-19 global pandemic;

- one or more institutional review boards, or IRB, refusing to approve, suspending or terminating the trial at a clinical trial site, precluding enrollment of additional subjects, or withdrawing its approval of the trial; or

- changes in regulatory requirements and policies, which may require us to amend clinical trial protocols to comply with these changes and resubmit our clinical trial protocols to IRBs for reexamination.

If we are required to conduct additional preclinical studies, clinical trials or other testing of product candidates beyond those that are contemplated, if we are unable to successfully complete preclinical studies or clinical trials of product candidates or other testing in a timely manner, if the results of these studies, trials or tests are not positive or are only modestly positive or if there are safety concerns, we may incur unplanned costs, be delayed in seeking and obtaining marketing approval, if we receive such approval at all, receive more limited

or restrictive marketing approval, be subject to additional post-marketing testing requirements or have the drug removed from the market after obtaining marketing approval.

***We have limited experience as a company in conducting clinical trials.***

Although we have initiated a Phase 1/2 dose escalation and dose expansion clinical trial for the evaluation of THE-630 in patients with advanced GIST whose disease has developed resistance to prior KIT-targeting therapies, we have no experience as a company in conducting clinical trials to completion. In part because of this lack of experience as a company and our limited infrastructure, we cannot be certain that our ongoing preclinical studies and clinical trial will be completed on time or that our planned preclinical studies and clinical trials will begin or be completed on time, if at all. Large-scale clinical trials would require significant additional financial and management resources and reliance on third-party clinical investigators, CROs, and consultants. Relying on third-party clinical investigators, CROs and consultants may force us to encounter delays that are outside of our control. We may be unable to identify and contract with sufficient investigators, CROs and consultants on a timely basis or at all. There can be no assurance that we will be able to negotiate and enter into any necessary services agreement with CROs on terms that are acceptable to us on a timely basis or at all.

***The outcome of preclinical testing and early clinical trials may not be predictive of the success of subsequent clinical trials.***

Although we initiated a Phase 1/2 dose escalation and expansion clinical trial of THE-630, all of our programs are still in the early stage of development, including our product candidate THE-349 and our BCR-ABL and other discovery programs. The results of preclinical studies may not be predictive of the results of later preclinical studies or clinical trials, and the results of any early-stage clinical trials may not be predictive of the results of later clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Our future clinical trials may not ultimately be successful or support further clinical development of any product candidates we may develop. There is a high failure rate for product candidates proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving encouraging results in earlier studies. Any such setbacks in our clinical development could materially harm our business and results of operations.

***The design or our execution of our clinical trials may not support marketing approval.***

The design or execution of a clinical trial can determine whether its results will support marketing approval, and flaws in the design or execution of a clinical trial may not become apparent until the clinical trial is well advanced and significant resources have been expended.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dose and dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Assessments of safety and efficacy can therefore vary widely for a particular patient, and from patient to patient and site to site within a clinical trial. As a result, we do not know whether any clinical trials we conduct will demonstrate consistent or adequate efficacy and safety to obtain marketing approval to market THE-630, THE-349 and any additional product candidates that we may develop.

Additionally, even if the FDA or a comparable foreign regulatory authority agrees with the design and implementation of the clinical trials set forth in an IND, such as our IND for THE-630, or comparable foreign regulatory submission, there is no guarantee such regulatory authority will not change its requirements in the

future. The FDA and comparable foreign regulatory authorities have substantial discretion in the product approval process and in determining when or whether to approve product candidates. For example, as more product candidates within a particular class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change. Moreover, data obtained from clinical trials are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do. Regulators may require us to conduct additional clinical trials or preclinical studies due to negative or inconclusive results. Any changes in requirements for the approval of product candidates made by these regulatory authorities may occur even after they have reviewed and provided comments or advice on a protocol for a planned clinical trial, including a registrational trial, and irrespective of whether product candidates achieve their primary endpoints in such trials.

Any of these regulatory authorities may also approve a product candidate for fewer or more limited indications than we request, or with other limitations, or may grant approval contingent on the performance of costly post-marketing clinical trials. The FDA or comparable foreign regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of product candidates, if approved.

***We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial, managerial and research and development resources, we must prioritize our research programs and will need to focus product candidates on the potential treatment of certain indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may also relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Any such event could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

The pharmaceutical and biotechnology industries, particularly the field of oncology, are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. We have competitors both in the US and internationally, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, emerging and start-up companies, universities and other research institutions.

Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. There are several approved therapies for the treatment of conditions for which we are attempting or may attempt to develop product candidates. In addition, we believe that a significant number of product candidates are currently under development, and may become commercially available in the future. We also compete to recruit and retain qualified scientific and management personnel, which could negatively affect our level of expertise and our ability to execute our business plan. As a result, our potential commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects or are more convenient than any products that we may develop.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than our product candidates or that would render any product candidates that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do.

We also face competition more broadly across the oncology market for cost-effective and reimbursable cancer treatments. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While product candidates, if any are approved, may compete with these existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, product candidates may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or other specific branded products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any product candidates that we successfully introduce to the market may pose challenges. Additionally, product candidates may need to compete with drugs physicians use off-label to treat the indications for which we seek approval. This may make it difficult for us to replace existing therapies with our product candidates and any additional product candidates that we may develop. Moreover, many companies are developing new oncology therapeutics, and we cannot predict what the standard of care will be as product candidates progress through clinical development.

If we are unable to compete effectively, our opportunity to generate revenue from the sale of any product candidates we may develop, if approved, could be adversely affected.

***Interim, topline and preliminary data from our preclinical studies and clinical trials that we announce or publish from time to time may change as more 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 publicly disclose preliminary, interim or topline data from our preclinical studies and clinical trials. These updates are based on a preliminary analysis of then-available data. These data should be viewed with caution as they may differ from future results of the same studies or trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. For example, we may report responses in certain patients that are unconfirmed at the time and which do not ultimately result in confirmed responses to treatment after follow-up evaluations. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. Certain data may also be subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. If the preliminary, interim or topline data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, any product candidates may be harmed. Adverse differences between preliminary, interim or topline data and final data, including that of our competitors, may also cause the price of our common stock to fluctuate or decline.

***Product candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs.***

We, the FDA or other comparable foreign regulatory authorities or an IRB may suspend or terminate clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable safety risks or adverse side effects. For example, some potential therapeutics that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development.

While we have not yet completed clinical trials for our product candidates, it is likely that there will be side effects associated with their use and the use of any other additional product candidates that we may develop, as is typically the case with oncology drugs. Results of our studies or trials could reveal a high and unacceptable severity and prevalence of these or other side effects or adverse events. In addition, product candidates may be studied in combination with other therapies, which may exacerbate adverse events associated with the therapy. Patients treated with product candidates may also be undergoing surgical, radiation and chemotherapy treatments, which can cause side effects or adverse events that are unrelated to product candidate but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses. For example, it is expected that some of the patients enrolled in our clinical trials will die or experience major clinical events either during the course of or after participating in such trials for non-treatment related reasons. Moreover, product candidates may be used in populations for which safety concerns may be particularly scrutinized by regulatory agencies.

If product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs, we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Drug-related side effects could also result in potential product liability claims.

Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Further, if product candidates obtain marketing approval, toxicities associated with such product candidates previously not seen during clinical testing may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional contraindications, warnings and precautions being added to the drug label, significant restrictions on the use of the product or the withdrawal of the product from the market. We cannot predict whether our product candidates and any additional product candidates that we may develop will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on preclinical studies or early-stage clinical trials.

Any of these occurrences may prevent us from obtaining or maintaining regulatory approvals or achieving or maintaining market acceptance of the affected product candidate and, accordingly, may harm our business, financial condition and prospects significantly.

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

Identifying and qualifying study subjects to participate in clinical trials of product candidates is critical to our success. The timing of initiation and completion of our clinical trials depends in part on the speed at which we can recruit study subjects to participate in testing product candidates. We may not be able to initiate or continue clinical trials for product candidates, such as our Phase 1/2 dose escalation and expansion clinical trial for THE-630, if we are unable to locate and enroll a sufficient number of eligible study subjects to participate in these clinical trials to their conclusion as required by the FDA or other comparable foreign

regulatory authorities. In addition, if others develop products for the treatment of similar diseases, we would potentially compete with them for the enrollment in rare patient populations, which may adversely impact the rate of patient enrollment in and the timely completion of our current and planned clinical trials. Any negative results or perceived negative results in clinical trials of our product candidates may make it difficult or impossible to recruit or retain patients in other clinical trials of the same product candidate. Insufficient patient enrollment may be a function of other factors, including the size and nature of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the timing and magnitude of disease symptom presentation, the availability of effective treatments for the relevant disease, and the eligibility criteria for the clinical trial. Our inability to identify and enroll a sufficient number of eligible patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials or development program. The ongoing COVID-19 pandemic has and is expected to continue to have an impact on our ability to enroll and retain patients in our clinical trials. Delays in patient enrollment in the future as a result of these and other factors may result in increased costs or may affect the timing or outcome of our clinical trials, which could prevent us from completing these trials and adversely affect our ability to advance the development of our product candidates.

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

As product candidates progress through preclinical and clinical trials to marketing approval and commercialization, it is common that various aspects of the development program are altered along the way in an effort to optimize yield and manufacturing batch size, minimize costs and achieve consistent quality and results. For example, we may introduce an alternative formulation of one or more product candidates during the course of our clinical trials. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause product candidates to perform differently and affect the results of clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of product candidates and jeopardize our ability to commercialize product candidates, if approved.

**Risks Related to the Manufacturing, Commercialization and Marketing of Product Candidates**

***The manufacture of drugs is complex, and our third-party manufacturers may encounter difficulties in production, which may delay or prevent our ability to provide adequate supply of product candidates for clinical trials or our products for patients, if approved.***

Manufacturing drugs, especially in large quantities, is complex and may require the use of innovative technologies. Each lot of an approved drug product must undergo thorough testing for identity, strength, quality, purity and potency. Manufacturing drugs requires facilities specifically designed for and validated for this purpose, as well as sophisticated quality assurance and quality control procedures. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our manufacturer, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. The use of biologically derived ingredients can also lead to allegations of harm, including infections or allergic reactions, or closure of product facilities due to possible contamination. If our third-party manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization as a result of these challenges, or otherwise, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

***We have never commercialized a product candidate as a company before and currently lack the necessary expertise, personnel and resources to successfully commercialize any products on our own or together with suitable collaborators.***

We have never commercialized a product candidate as a company. For product candidates for which we retain commercialization rights and marketing approval, we will have to develop our own sales, marketing and supply organization or outsource these activities to a third party. We may also license certain rights with respect to product candidates to collaborators, and, if so, we will rely on the assistance and guidance of those collaborators. Establishing an internal sales or marketing team with technical expertise and supporting distribution capabilities to commercialize product candidates will be expensive and time-consuming and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could adversely impact the commercialization of any product candidates that we obtain approval to market if we do not have arrangements in place with third parties to provide such services on our behalf. Alternatively, if we 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 our own sales force and distribution systems or in lieu of our own sales force and distribution systems, we will be required to negotiate and enter into arrangements with such third parties relating to the proposed collaboration and such arrangements may prove to be less profitable than commercializing the product on our own. 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 product candidates that receive regulatory approval, or any such commercialization may experience delays or limitations. If we are unable to successfully commercialize our approved product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may incur significant additional losses.

***The market opportunities for any product candidates we develop, if approved, may be limited to certain smaller patient subsets and may be smaller than we estimate them to be.***

When cancer is detected early (referred to as localized disease), conventional treatments, which include chemotherapy, hormone therapy, surgery and radiation therapy and/or selected targeted therapies, may be adequate to cure the patient in many cases. However, if cancer has spread to other areas (advanced or metastatic disease), initial cancer treatments may not be sufficient and other cancer therapies may be considered. Cancer therapies are sometimes characterized by line of therapy (for example, first-, second-, third-, fourth- or fifth-line). The FDA and other comparable foreign regulatory authorities often approve cancer therapies for a particular line of treatment. Typically, drug approvals are initially granted for use in later lines of treatment. With additional evidence of significant efficacy and safety from clinical trials, pharmaceutical and biotechnology companies can seek, and sometimes gain, approval for use in earlier lines of treatment.

We plan to initially seek approval of THE-630, THE-349 and, in most instances, any additional product candidates that we may develop where prior therapies have had limited clinical benefit or lost their effectiveness. For those product candidates that prove to be sufficiently safe and effective, if any, we would expect to seek approval as earlier lines of therapy. For example, one population will be GIST patients who have already received four prior lines of therapy, or fifth-line GIST. Depending on the clinical data observed in the Phase 1/2 trial, we intend to evaluate THE-630 in second-line GIST. There is no guarantee that THE-630 or any product candidates we may develop in the future, even if approved in later lines of therapy, would be approved for an earlier line of therapy, and prior to any such approvals we may have to conduct additional clinical trials that may be costly, time-consuming and subject to risk.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive a particular line of therapy and who have the potential to benefit from treatment with product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, which could include scientific literature, surveys of clinics or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of the cancers that we are targeting. The potentially addressable patient population for product

candidates may be limited or may not be amenable to treatment with product candidates, particularly if product candidates are only approved for later lines of treatment. Consequently, even if product candidates are approved, the number of patients that may be eligible for treatment with product candidates may turn out to be much lower than expected. In addition, we have not conducted market research to determine how treating physicians would expect to prescribe a product that is approved for multiple tumor types if there are different lines of approved therapies for each such tumor type.

***Product candidates, if approved, may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.***

Even if product candidates ultimately receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, third-party payors and others in the medical community. The degree of market acceptance of any product candidates that may be approved in the future will depend on a number of factors, including:

- the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments;
- the indications for which a product candidate is approved;
- restrictions on the use of product candidates in the labeling approved by regulatory authorities, such as boxed warnings or contraindications in labeling, or a risk evaluation and mitigation strategy, or REMS, if any, which may not be required of alternative treatments and competitor products;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of product candidates, if approved, in relation to alternative treatments;
- the availability of coverage and adequate reimbursement by third-party payors, including government authorities;
- the availability of an approved product for evaluation as a combination therapy;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and undergo required diagnostic screening to determine treatment eligibility and of physicians to prescribe these therapies and diagnostic tests;
- the effectiveness of sales and marketing efforts;
- unfavorable publicity relating to product candidates; and
- the approval of other new therapies for the same indications.

If any product candidates are approved but do not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate or derive sufficient revenue from that product candidate, and our financial results could be negatively impacted.

***Any product candidates we develop may become subject to unfavorable third-party coverage and reimbursement practices.***

The availability and extent of coverage and adequate reimbursement by third-party payors, including government health care programs, private health insurers, managed care organizations and other third-party payors is essential for most patients to be able to afford expensive treatments. Sales of any product

candidates that receive marketing approval will depend substantially, both in the US and internationally, on the extent to which the costs of such product candidates will be covered and reimbursed by third-party payors. If coverage is not available, or is available only in limited circumstances, we may not be able to successfully commercialize product candidates.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is (1) a covered benefit under its health plan; (2) safe, effective and medically necessary; (3) appropriate for the specific patient; (4) cost-effective; and (5) neither experimental nor investigational. For example, in order to obtain reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. Additionally, eligibility for coverage does not imply that any drug will be paid for 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 not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services.

Moreover, in the US, principal decisions about Medicare reimbursement for new products are typically made by or on behalf of the Centers for Medicare & Medicaid Services, or CMS, an agency within the US Department of Health and Human Services, or HHS. CMS and regional contractors responsible for administering the Medicare program decide whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow these decisions regarding coverage and reimbursement to a substantial degree. However, one third-party payor's determination to provide coverage for a product candidate does not ensure that other payors will also provide coverage for the product candidate. No uniform policy of coverage and reimbursement for products exists among third-party payors, and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often time-consuming and costly. This process may require us to provide scientific and clinical support for the use of our products to each third-party payor separately, with no assurance that coverage and adequate reimbursement will be available consistently or obtained in the first instance. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the US and have not been approved for reimbursement in certain European countries.

Third-party payors are increasingly examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third-party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies to demonstrate the cost effectiveness of our products. Notwithstanding the results of these studies, product candidates may not be considered medically necessary or cost effective. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be.

In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics. Further, if any companion diagnostic provider is unable to obtain reimbursement or is inadequately reimbursed, that may limit the availability of such companion diagnostic, which would negatively impact prescriptions for product candidates, if approved.

If we are unable to establish or sustain coverage and adequate reimbursement for any product candidates from third-party payors, the adoption of those products and sales revenue will be adversely affected, which, in

turn, could adversely affect the ability to market or sell those product candidates, if approved. Coverage policies and third-party payor reimbursement rates may change at any time. Any of these could have a material and adverse effect on our business, financial condition, results of operations and prospects.

***Downward pressure on healthcare costs may negatively affect the coverage and pricing of product candidates.***

The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. Legislative or regulatory requirements related to pricing and reimbursement may limit our ability to recoup our investment in one or more product candidates and therefore affect such product candidate's commercial viability, if approved. Moreover, third-party payors are increasingly requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We expect to experience pricing pressures in connection with the commercialization of any product candidates, which could have a material and adverse effect on our business, financial condition, results of operations and prospects.

***A variety of risks associated with marketing product candidates internationally could materially adversely affect our business.***

We may seek regulatory approval of product candidates outside of the US and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements and reimbursement regimes in foreign countries, such as the lack of pathways for accelerated drug approval, may result in foreign regulatory approvals taking longer and being more costly than obtaining approval in the US;
- foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials or our interpretation of data from nonclinical studies or clinical trials;
- approval policies or regulations of foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval;
- impact of the COVID-19 pandemic on our ability to produce product candidates and conduct clinical trials in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with legal requirements applicable to privacy, data protection, information security and other matters;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;

- complexities associated with managing multiple payor reimbursement regimes and government payors in foreign countries;

- workforce uncertainty in countries where labor unrest is more common than in the US;

- potential liability under the Foreign Corrupt Practices Act or comparable foreign regulations;

- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the US;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

- business interruptions resulting from regional or larger scale conflicts or geo-political actions, including war or other military conflicts, and terrorism, trade policies, sanctions, treaties and tariffs.

These and other risks associated with international operations may materially adversely affect our ability to attain or maintain profitable operations, our product development efforts or our potential clinical trials.

**Risks Related to Regulatory Approval Process and Other Healthcare Compliance Matters**

***We may be unable to obtain US or foreign regulatory approval and, as a result, may be unable to commercialize product candidates.***

We have not submitted for, or obtained, regulatory approval for any drug product candidate, and it is possible that no product candidates will ever obtain regulatory approval.

Drug product candidates are and will continue to be subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, and distribution of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process must be successfully completed in the US and in many foreign jurisdictions before a new drug can be approved for marketing in each jurisdiction. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays.

Moreover, the standards that the FDA and its foreign counterparts use when evaluating clinical trial data can, and often do, change during drug development, which makes it difficult to predict with any certainty how they will be applied. We may also encounter unexpected delays or increased costs due to new government regulations, including future legislation or administrative action, or changes in applicable FDA or any other regulatory policy during the period of drug development, clinical trials and regulatory review and approval. Accordingly, the time required to obtain approvals from the FDA or any other regulatory authorities is unpredictable and will take many years, depending upon the type, complexity and novelty of the product candidate. We cannot provide any assurance that any product candidate we may develop will progress through required clinical testing and obtain the regulatory approvals necessary for us to begin selling them.

Regulatory authorities have substantial discretion in the approval process. Applications for product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;

- the FDA or other comparable foreign regulatory authorities may determine that product candidates are not safe and effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;

- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;

- the FDA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data;

- we may be unable to demonstrate to the FDA or other comparable foreign regulatory authorities that our product candidate's risk-benefit ratio for its proposed indication is acceptable;

- the FDA or other comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and

- the approval policies or regulations of the FDA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Any delay or failure in seeking or obtaining required approvals would have a material and adverse effect on our ability to generate revenue from any particular product candidates we are developing and for which we are seeking approval. Furthermore, any regulatory approval to market a drug may be approved for a narrower patient population than we originally requested or subject to significant limitations on the approved uses or indications for which we may market, promote and advertise the drug or the labeling or other restrictions. In addition, the FDA has the authority to require a REMS as part of approving an NDA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. These requirements or restrictions might include limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may significantly limit the size of the market for the drug and affect reimbursement by third-party payors.

There are also numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization. The foreign regulatory approval process varies among countries, and generally includes all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval.

***We may develop our current or future product candidates in combination with other therapies, which would expose us to additional risks.***

We may develop our current or future product candidates in combination with one or more currently approved cancer therapies or therapies in development. Even if any of our current or future product candidates were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or other comparable foreign regulatory authorities could revoke approval of the therapy used in combination with any product candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies. In addition, it is possible that existing therapies with which product candidates are approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for product candidates or our own products being removed from the market or being less successful commercially.

We may also evaluate our current or future product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA or other comparable foreign regulatory authorities. We will not be able to market any product candidate in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval.

If the FDA or other comparable foreign regulatory authorities do not approve or withdraw their approval of these other therapies, or if safety, efficacy, commercial adoption, manufacturing or supply issues arise with the therapies we choose to evaluate in combination with any of our current or future product candidates, we may be unable to obtain approval of or successfully market any one or all of the current or future product candidates we develop. Additionally, if the third-party providers of therapies or therapies in development used in combination with our current or future product candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our current or future product candidates, or if the cost of combination therapies are prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, operations and growth prospects.

***The FDA and other comparable foreign regulatory authorities may not accept data from trials conducted in locations outside of their jurisdiction.***

We anticipate we will conduct clinical trials of THE-630, THE-349 and any additional product candidates that we may develop both in and outside the US. The acceptance of study data by the FDA or other comparable foreign regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. In cases where data from US clinical trials are intended to serve as the basis for marketing approval in the foreign countries outside the US, the standards for clinical trials and approval may be different. Similarly, in cases where clinical trial data from outside the US are intended to serve as the basis for marketing approval in the US, the standards for clinical trials and approvals may be different. There can be no assurance that the FDA or foreign regulatory authority would accept data from trials conducted outside of its applicable jurisdiction. If the FDA or other comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

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

Obtaining and maintaining regulatory approval of product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the clinical trials, manufacturing, marketing and promotion and reimbursement of the product candidate in those jurisdictions. However, a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the US, including that additional preclinical studies or clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the US, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to governmental approval.

Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any collaborator fails to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our potential product candidates will be harmed.

***Even if product candidates receive regulatory approval, they will be subject to significant post-marketing regulatory requirements and oversight.***

Any regulatory approvals that we may receive for product candidates will require the submission of reports to regulatory authorities and on-going surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements and regulatory inspection. In addition, if the FDA or other comparable foreign regulatory authorities approve product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, as well as on-going compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. In addition, our contract manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other comparable foreign regulatory authorities for compliance with cGMP regulations and standards. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

Later discovery of previously unknown problems with any approved products, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with FDA and other comparable foreign regulatory requirements may subject our company to administrative or judicially imposed sanctions, including:

- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on the products, manufacturers or manufacturing process;
- warning or untitled letters;
- civil and criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- product seizures, detentions or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production;
- imposition of restrictions on operations, including costly new manufacturing requirements;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS, which may include distribution or use restrictions; and
- requirements to conduct additional post-market clinical trials to assess the safety of the product.

The FDA and any other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of product candidates or impose additional requirements post-approval. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the US or abroad. Compliance with these post-marketing requirements may result in significant costs. 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. The occurrence of any event or penalty described above may inhibit our ability to commercialize product candidates, if approved, and generate revenue.

***The FDA and other comparable foreign regulatory agencies actively enforce the laws and regulations governing advertising and promotion, including those prohibiting the promotion of off-label uses.***

The FDA and other comparable foreign regulatory agencies strictly regulate the promotion and advertisement of prescription drug products, such as our products, if approved. In particular, a product may not be promoted in the US for uses that are not approved by the FDA as reflected in the product's approved labeling, or in other jurisdictions for uses that differ from the labeling or uses approved by the applicable regulatory agencies. While physicians may prescribe products for off-label uses, the FDA and any other regulatory agencies actively enforce laws and regulations that prohibit the promotion of off-label uses by manufacturers, including promotional communications made by companies' sales force with respect to off-label uses that are not consistent with the approved labeling. If we are found to have promoted such off-label uses, we may become subject to significant liability. The US federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The US federal government and state governments have also required that drug manufacturers enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

***If we are required by the FDA or other comparable foreign regulatory authority to obtain approval of a companion diagnostic test in connection with approval of any product candidates or a group of therapeutic products, and we do not obtain or we face delays in developing and obtaining approval of a diagnostic test, we may not be able to commercialize the product candidate and our ability to generate revenue would be materially impaired.***

If we are required by the FDA or other comparable foreign regulatory authority to obtain approval of a companion diagnostic test in connection with approval of any product candidates, such companion diagnostic test would be used during our more advanced phase clinical trials as well as in connection with the commercialization of product candidates. Companion diagnostics are regulated as medical devices by FDA and, unless an exemption applies, require premarket clearance or approval by FDA. The two primary types of FDA marketing authorization applicable to a medical device are clearance of a premarket notification under section 510(k) of the FDCA, or 510(k), and approval of a premarket approval application, or PMA. According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared at the same time the product candidate is approved. To date, the FDA has required PMA approval for the vast majority of companion diagnostic tests for cancer therapies. Various foreign regulatory authorities also regulate *in vitro* companion diagnostics as medical devices and, under those regulatory frameworks, will likely require the conduct of clinical trials or performance studies to demonstrate the safety and effectiveness of our current diagnostics and any future diagnostics we may develop, which we expect will require separate regulatory clearance or approval prior to commercialization.

The approval of a companion diagnostic as part of the therapeutic product's labeling may limit the use of the therapeutic product to only those patients who express certain biomarkers or the specific genomic alteration

that the companion diagnostic was developed to detect. If the FDA or other comparable foreign regulatory authority requires approval of a companion diagnostic for any product candidates, whether before or concurrently with approval of the product candidate, we and our collaborators, may encounter difficulties in developing and obtaining approval for these companion diagnostics. Any delay or failure by us or third-party collaborators to develop or obtain regulatory approval of a companion diagnostic could cause or contribute to delayed enrollment of our clinical trials, may prevent us from initiating a pivotal trial or may delay or prevent approval or continued marketing of our related product candidates.

Further, in April 2020, the FDA issued new guidance on developing and labeling companion diagnostics for a specific group of oncology therapeutic products, including recommendations to support a broader labeling claim rather than individual therapeutic products. We will continue to evaluate the impact of this guidance on our companion diagnostic development and strategy. This guidance and future issuances from the FDA and other comparable foreign regulatory authorities may impact our development of a companion diagnostic for product candidates and result in delays in regulatory approval. We may be encouraged to conduct additional studies to support a broader labeling claim. Also, to the extent other approved diagnostics are able to broaden their labeling claims to include our approved drug products, we may decide to abandon our companion diagnostic development plans or we may not be able to compete effectively upon approval, which could adversely impact our ability to generate revenue from the sale of our approved products and our business operations.

To be successful in developing, validating, obtaining approval of and commercializing a companion diagnostic, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. We have no prior experience with medical device or diagnostic test development. If we choose to develop and seek FDA approval for companion diagnostic tests on our own, we will require additional personnel. Additionally, we may rely on third parties for the design, development and manufacture of companion diagnostic tests for product candidates that may require such tests. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our collaborators in developing and obtaining approval for these companion diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our collaborators may encounter difficulties in developing, obtaining regulatory approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to product candidates themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. In addition, a diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of product candidates.

If we are unable to successfully develop companion diagnostics for product candidates, or experience delays in doing so, the development of product candidates may be adversely affected, product candidates may not obtain marketing approval, and we may not realize the full commercial potential of any product candidates that obtain marketing approval. As a result, our business, results of operations and financial condition could be materially harmed.

***Where appropriate, we plan to seek approval from the FDA or other comparable foreign regulatory authorities through the use of an accelerated approval pathway. If we are unable to obtain agreement from the FDA or other comparable foreign regulatory authorities to pursue accelerated approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA or other comparable foreign regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA or such other comparable foreign regulatory authorities may seek to withdraw accelerated approval.***

Where possible, we plan to pursue accelerated development strategies in areas of high unmet need. We may seek an accelerated approval pathway for one or more product candidates from the FDA or other comparable foreign regulatory authorities. Under the accelerated approval provisions in the Federal Food, Drug, and Cosmetic Act, and the FDA's implementing regulations and guidance for the industry, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit, as well as a requirement that all promotional materials be submitted to FDA before dissemination within prescribed timeframes. If a sponsor's post-approval studies fail to confirm the drug's clinical benefit, the sponsor fails to conduct such studies at all, or other evidence demonstrates that the product is not shown to be safe or effective under the conditions of use, the FDA may withdraw its approval of the drug using expedited procedures.

Prior to seeking accelerated approval, we will seek feedback from the FDA or other comparable foreign regulatory authorities and will otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent feedback from the FDA or other comparable foreign regulatory authorities, we will continue to pursue or apply for accelerated approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation (for example, Fast Track designation, Breakthrough Therapy designation), there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

***We may seek Fast Track designation from the FDA for one or more product candidates. Even if one or more product candidates receive Fast Track designation, we may be unable to obtain or maintain the benefits associated with the Fast Track designation.***

Fast Track designation is designed to facilitate the development and expedite the review of therapies for serious conditions and fill an unmet medical need. Programs with Fast Track designation may benefit from early and frequent communications with the FDA, potential priority review and the ability to submit a rolling application for regulatory review. Fast Track designation applies to both the product candidate and the specific indication for which it is being studied. If any product candidates receive Fast Track designation but do not continue to meet the criteria for Fast Track designation, or if our clinical trials are delayed, suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply, we will not receive the benefits associated with the Fast Track program. Furthermore, Fast Track designation does not change the standards for approval. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures.

If we decide to apply for Fast Track designation, we must submit a request to FDA for evaluation. Even if we believe that a product candidate meets the criteria for this designation, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a Fast Track designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if any product candidate qualifies for Fast Track designation, the FDA may later decide that the product candidates no longer meet the conditions for qualification and withdraw the designation or decide that the time period for FDA review or approval will not be shortened.

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

We may seek Breakthrough Therapy designation for one or more of our current or future product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

Designation as a Breakthrough Therapy is largely within the discretion of the FDA. Accordingly, even if we believe that a product candidate meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to candidate products considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by the FDA. In addition, even if one or more product candidates are designated as breakthrough therapies, the FDA may later decide that the product no longer meets the conditions for qualification and revoke the designation.

***While we received orphan drug designation from the FDA for THE-630 for the treatment of gastrointestinal stromal tumors, we may not be able to obtain orphan drug designation for THE-630 for other indications or other product candidates, or obtain or maintain orphan drug exclusivity if obtained and, even if we do, that exclusivity may not prevent the FDA or other comparable foreign regulatory authorities, from approving all competing products.***

Regulatory authorities in some jurisdictions, including the US and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is a drug intended to treat a rare disease or condition, which is

generally defined as a patient population of fewer than 200,000 individuals annually in the US, or a patient population greater than 200,000 in the US where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the US. Our target indications may include diseases with large patient populations or may include orphan indications.

In the US, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax credits and user-fee exemptions. In addition, if a product candidate that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product candidate is entitled to orphan drug exclusivity. Orphan drug exclusivity in the US provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances. In the EU, orphan exclusivity prevents marketing authorization applications being accepted for similar products for the orphan indication for a period of 10 years. This period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation.

We have received orphan drug designation from the FDA for THE-630 for the treatment of gastrointestinal stromal tumors. However, there can be no assurances that we will be able to obtain orphan designations for THE-630 for other indications or other product candidates in the US or any other jurisdictions. Even if we obtain orphan drug designation for a product candidate, we may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the US may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to ensure that we will be able to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process or entitles the product candidate to priority review. Similar rules apply in the EU.

***We may face difficulties from changes to current regulations and future legislation. Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.***

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of 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 US or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

Even if product candidates receive marketing approval, changes to laws and regulations may affect the commercialization of and revenue generated by our products. In the US and other markets, there have been, and we expect there will continue to be, a number of legislative and regulatory changes that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the ACA, was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and continues to significantly impact the US pharmaceutical industry.

Certain provisions have been subject to judicial and Congressional challenges, as well as efforts by a past US presidential administration to repeal or replace certain aspects of the ACA. The Tax Cuts and Jobs Act of 2017, or the TCJA, for example, included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate.” The ACA has been challenged numerous times in various court cases, including challenges before the US Supreme Court. In the most recent case (decided in June 2021) the Supreme Court held that the individual plaintiffs and states lacked standing to challenge the constitutionality of the ACA.

Other legislative changes have been proposed and adopted in the US since the ACA was enacted. These changes included reductions of Medicare payments to providers of up to 2%, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2030 unless additional congressional action is taken. (These reductions were temporarily suspended due to COVID-19 pandemic; the full suspension expired on in March 31, 2022. From April 1 to June 30, 2022, the reduction was 1%, and the full 2% reduction was reinstated on July 1, 2022). Additionally, in January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. It is possible that new laws that would result in additional reductions in Medicare and other healthcare funding, may be enacted, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations.

Further, there has been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in numerous Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient assistance programs, and reform government program reimbursement methodologies for drug products. At the federal level, former President Trump used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders, and policy initiatives. Similarly, the Biden administration has identified drug pricing as a priority. On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug’s average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

On August 16, 2022, President Biden signed the Inflation Reduction Act (IRA) into law, which sets forth meaningful changes to drug product reimbursement by Medicare. Among other actions, the IRA permits HHS to engage in price-capped negotiation to set the price of certain drugs and biologics reimbursed under Medicare Part B and Part D. The IRA contains statutory exclusions to the negotiation program, including for certain orphan designated drugs for which the only approved indication (or indications) is for the orphan disease or condition. Should our product candidates be approved and covered by Medicare Part B or Part D, and fail to fall within a statutory exclusion, such as that for an orphan drug, those products could, after a period of time, be selected for negotiation and become subject to prices representing a significant discount from average prices to wholesalers and direct purchasers. The IRA also establishes a rebate obligation for drug manufacturers that increase prices of Medicare Part B and Part D covered drugs at a rate greater than the rate of inflation. The inflation rebates may require us to pay rebates if we increased the cost of a covered Medicare Part B or Part D approved product faster 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 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. Our cost-sharing responsibility for any approved product covered by Medicare Part D could be significantly greater under the newly designed Part D benefit structure compared to the pre-IRA benefit design. Additionally, manufacturers that fail to comply with certain provisions of the IRA may be subject to penalties, including civil monetary penalties. The IRA is anticipated to have significant effects on the pharmaceutical industry and may reduce the prices we can charge and reimbursement we can receive for our products, among other effects.

In addition, at the state level, individual states have increasingly proposed or adopted legislation and regulations related to pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that additional state and federal healthcare reform measures will be adopted in the future. Such reform measures may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. We are, however, unable to predict the future course of federal or state healthcare legislation in the US directed at broadening the availability of healthcare and containing or lowering the cost of healthcare, particularly in light of the new presidential administration. These and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain coverage and reimbursement for a product;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

***Inadequate funding for the FDA and other US government agencies or other comparable foreign regulatory authorities, COVID-19 and other factors could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.***

The ability of the FDA and other US government agencies or other comparable foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result.

In addition, government funding of government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. For example, in recent years, including in 2018 and 2019, the US government shut down several times and certain regulatory agencies, such as the FDA, had to furlough critical employees and stop critical activities.

Separately, since March 2020 when foreign and domestic inspections were largely placed on hold due to the COVID-19 pandemic, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections and resumed inspections in China and India in early 2021. In April 2021, the FDA issued guidance for industry formally announcing plans to employ remote interactive evaluations, using risk management methods, to meet user fee

commitments and goal dates, and in May 2021 announced plans to continue progress toward resuming standard operational levels. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be appropriate, the agency has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the US may adopt similar restrictions or other policy measures on inspections in response to the COVID-19 pandemic and may experience delays in their regulatory activities. As recently as late 2021, when COVID-19 infection surged due to the highly transmissible omicron variant, FDA again paused routine inspections. While the Agency resumed routine inspections again relatively quickly in February 2022, the ongoing pandemic may continue to cause periodic interruptions in FDA's ability to conduct inspections and further exacerbate the backlog of inspections.

Disruptions at the FDA and other comparable foreign regulatory authority may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, or if global health concerns continue to prevent or delay the FDA or other regulatory authorities from conducting business as usual or conducting inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

***Our relationships with healthcare professionals, clinical investigators, clinical trial sites, CROs and third-party payors in connection with our current and future business activities may be subject to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, government price reporting, and health information privacy and security laws, the noncompliance of which could expose us to significant losses, including, among other things, criminal sanctions, civil penalties, contractual damages, exclusion from governmental healthcare programs, reputational harm, administrative burdens and diminished profits and future earnings.***

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, clinical investigators, CROs, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, as well as market, sell and distribute product candidates for which we obtain marketing approval.

The laws that may affect our ability to operate include, but are not limited to: (i) the federal Anti-Kickback Statute; (ii) federal civil and criminal false claims law; (iii) HIPAA, relating to schemes to defraud any healthcare benefit program; (iv) HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization; (v) the federal Physician Payments Sunshine Act, created under the ACA and its implementing regulations, relating to reporting obligations to HHS in respect of information related to payments or other transfers of value made to physicians and teaching hospitals; (vi) federal consumer protection and unfair competition laws; and (vii) analogous state and foreign laws and regulations.

Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, 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. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment, especially in light of the lack of applicable precedent and regulations. Ensuring that our business arrangements with third parties comply with applicable healthcare and data privacy laws and regulations, as well as responding to investigations by government authorities, can be time- and resource-consuming and can divert management's attention from the business.

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private actions brought by individual whistleblowers in the name of the government, debarment or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

***Our employees, independent contractors, consultants, collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.***

We are exposed to the risk that our employees, independent contractors, consultants, collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (1) the Federal Food, Drug and Cosmetic Act, FDA regulations or those of comparable foreign regulatory authorities, (2) GCP or cGMP, (3) federal and state health and data privacy, security, fraud and abuse, government price reporting, transparency reporting requirements, and other healthcare laws and regulations in the US and abroad, (4) sexual harassment and other workplace misconduct, or (5) laws that require the true, complete and accurate reporting of clinical information or data. In particular, research, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties 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.

We have adopted a code of conduct and have contracts in place with third parties, but it is not always possible to identify and deter misconduct by these parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations.

**Risks Related to Employee Matters, Managing Our Growth and Other Risks Related to Our Business**

***Our business could be adversely affected by the effects of health epidemics, including the evolving effects of the COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of potential clinical trial sites or other business operations.***

Health epidemics in regions where we have concentrations of potential clinical trial sites or other business operations could adversely affect our business, including by causing significant disruption in the operations of third parties upon whom we rely. For example, the COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting employees, patients, communities and business operations, as well as the US economy and financial markets. Several of our third-party suppliers and contractors are located in countries and regions that have been negatively impacted by the COVID-19 global pandemic. In March 2020, the US government imposed bans and restrictions on travel between the US, Asia and certain other continents and countries and other countries have restricted travel to and from the US.

In addition, our preclinical studies and clinical trials may be affected by the COVID-19 pandemic, including as a result of:

- delays or difficulties in enrolling and retaining patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in receiving authorizations from regulatory authorities to initiate our clinical trials;
- diversion of healthcare resources away from the conduct of clinical trials;
- the risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- the risk that we are unable to enroll participants in our clinical trials in adequate numbers;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of product candidates or other materials necessary to conduct preclinical or clinical trials of our product candidates, from our contract manufacturing organizations or other third-party suppliers due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- interruptions in preclinical studies and clinical trials due to restricted or limited operations at our contractors' facilities;
- 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;
- changes in local regulations as part of a response to the COVID-19 pandemic, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;

- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; and

- interruption or delays to our sourced identification, discovery and clinical activities.

Furthermore, while the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, the pandemic could continue to produce significant and prolonged disruption of or volatility in global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the COVID-19 pandemic, the lack of efficacy of vaccines or lack of vaccine availability could materially affect our business and the value of our common stock. In addition, to the extent the evolving effects of the COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described elsewhere in this "Risk Factors" section.

***Our success is highly dependent on our ability to attract, hire and retain highly skilled executive officers and employees.***

We currently have a small team focused on research and development of small molecule TKIs. To succeed, we must recruit, hire, retain, manage and motivate qualified clinical, scientific, technical and management personnel, and we face significant competition for experienced personnel. We are highly dependent on the principal members of our management and scientific and medical staff, including our founders. The loss of one or more of such persons could be detrimental to us if we cannot recruit suitable replacements in a timely manner. In particular, our research and development approach, including our PRA, was developed in part over years of our management team's experience in developing approved therapeutics at ARIAD. The loss of any of these personnel could result in delays in our product development efforts and have a material adverse effect on our financial condition, results of operations and prospects.

Moreover, if we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. We could in the future have difficulty attracting and retaining experienced personnel and may be required to expend significant financial resources in our employee recruitment and retention efforts. Many of the pharmaceutical and biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide higher compensation, more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize product candidates will be limited and the potential for successfully growing our business will be harmed.

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

As of February 28, 2023, we had 38 full-time and part-time employees, including 25 employees engaged in research and development. In order to successfully implement our development and clinical trial plans and strategies, and as we transition into operating as a public company, we expect to need significant additional managerial, operational, sales, marketing, financial and other personnel. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining, retaining and motivating our current and additional employees;

- managing our internal development efforts effectively, including the preclinical, clinical, FDA and other comparable foreign regulatory agencies' review process for THE-630, THE-349, and any other programs, while complying with any contractual obligations to contractors and other third parties;

- managing increasing operational and managerial complexity; and

- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to successfully develop and, if approved, commercialize product candidates developed from THE-630 and THE-349 and any other programs will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of research, clinical development, manufacturing and regulatory approval. In particular, we do not currently operate our own laboratory facilities, and we rely completely on the services of independent contractors and consultants for the conduct of preclinical studies and clinical trials. There can be no assurance that the services of independent 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 third-party service providers is compromised for any reason, our preclinical studies and clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval for any product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing third-party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and/or engaging additional third-party service providers, we may not be able to successfully implement the tasks necessary to further develop and commercialize THE-630 and THE-349 and any of our other product candidates and, accordingly, may not achieve our research, development and commercialization goals.

***Our internal computer systems, or those of any of our CROs, manufacturers, other contractors or consultants or collaborators, may fail or suffer actual or suspected security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations, and potentially significant delays in our delivery to market.***

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 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, other contractors (including sites performing our anticipated clinical trials) and consultants who have access to our confidential information. Our internal information technology systems and infrastructure are also vulnerable to damage from natural disasters, terrorism, war or other military conflict, telecommunication and electrical failures. System failures or outages, including any potential disruptions due to significantly increased global demand on certain cloud-based systems during the 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. Such failures could materially adversely affect our operating results and financial condition.

Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our business, financial condition, results of operations and prospects. Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems and external processing and storage systems (for example, cloud), and those of our third-party CROs, other contractors and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war or other military conflict and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners, and/or other third parties, or from cyber-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 lead to the loss, destruction, alteration or dissemination of, or damage to, our data. 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 COVID-19 pandemic increased the attack surface available for exploitation, as more companies and individuals work online and work remotely, and as such, the risk of a cybersecurity incident potentially occurring, and our investment in risk mitigations against such an incident, is increasing. For example, there has been an increase in phishing and spam emails as well as social engineering attempts from “hackers” hoping to use the recent COVID-19 pandemic to their advantage. In addition, due to the conflict involving Russia and Ukraine, there is an increased likelihood that continuation or escalation of tensions could result in cyberattacks that could either directly or indirectly impact our operations.

We may not be able to anticipate all types of security threats, nor may we be able to 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. While we have not experienced any such system failure, accident or security breach to date, we cannot assure our stockholders 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, 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, other contractors and consultants, it could result in a material disruption of our programs and the development of product candidates could be delayed. In addition, the loss of data from preclinical studies or clinical trial data 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, 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, data (including trade secrets or other confidential information, intellectual property, proprietary business information, and personal information).

We rely on third parties for various operations, including the manufacture of our products and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. Any breach in our or our third-party providers’ information technology systems could lead to the unauthorized access, disclosure and use of non-public information, including protected health information and other personally identifiable information which is protected by HIPAA, and other laws. Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, damage to

our reputation and the further development and commercialization of our products could be delayed. If we or our third-party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third-party providers could have difficulty preventing, detecting and controlling such cyberattacks and any such attacks could result in losses described above as well as disputes with physicians, participants and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business.

Any security incident or similar event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to financial exposure related to investigation of the incident (including cost of forensic examinations), subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information (including under HIPAA), which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business. Moreover, if the information technology systems of our third-party CROs, 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.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption in or, failure or security breach of our systems or third-party systems where information important to our business operations or commercial development is stored. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

Accordingly, significant breakdowns or breaches in systems or other cyber incidents that cause loss, destruction, unavailability, alteration or dissemination of, or damage to, our data could have a material adverse effect upon our reputation, business, operations or financial condition.

***Our business entails a significant risk of product liability and if we are unable to obtain sufficient insurance coverage such inability could have an adverse effect on our business and financial condition.***

Our business exposes us 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, such claims could result in an investigation by the FDA or any other regulatory authority of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs. FDA or any other regulatory authority investigations could potentially lead to 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, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources and substantial monetary awards to trial participants or patients. We currently have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels prior to advancing product candidates into clinical trials or marketing any product candidates, if approved. 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 an adverse effect on our business and financial condition.

***We may not be able to utilize a significant portion of our net operating loss carryforwards.***

We have generated, and expect to continue to generate in the future, significant federal and state net operating loss, or NOL, carryforwards. As of December 31, 2022, we had $47.0 million and $49.5 million in federal and state NOL carryforwards, respectively. We do not anticipate generating revenue from sales of product candidates for the foreseeable future, if ever, and we may never achieve profitability. These NOL carryforwards could expire unused and be unavailable to offset future income tax liabilities because of their limited duration or because of restrictions under US tax law. The state NOL carryforwards will begin to expire in 2037. Additionally, under the TCJA, as modified by the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, although federal NOL carryforwards incurred in taxable years beginning after December 31, 2017 and in future taxable years may be carried forward indefinitely, the deductibility of such federal NOL carryforwards incurred in taxable years beginning after December 31, 2020 is limited. In particular, the deductibility of such federal NOL carryforwards may be limited to 80% of current year taxable income for tax years beginning after December 31, 2020. In addition, at the state level, there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. It is uncertain how various states will respond to the TCJA and CARES Act.

In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation’s ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. The amount of the annual limitation is determined based on the value of a company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The completion of our initial public offering in October 2021, together with private placements and other transactions that have occurred since our inception, may trigger such an ownership change pursuant to Section 382 of the Code. We have not yet completed a Section 382 analysis. We may experience ownership changes as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs or our ability to use our NOL carryforwards is otherwise materially limited, it would harm our future operating results by effectively increasing our future tax obligations. We have a full valuation allowance for deferred tax assets including NOLs.

**Risks Related to Intellectual Property**

***We depend on intellectual property licensed from ARIAD, the termination of which could result in the loss of significant rights, which would harm our business.***

We are dependent on technology, patents, know-how and proprietary materials, both our own and licensed from ARIAD. We entered into the ARIAD License Agreement in June 2018, pursuant to which we acquired an exclusive, transferable (subject to certain restrictions), sublicensable (subject to certain conditions), worldwide license, under certain of ARIAD’s patent rights, know-how and compounds and a certain ARIAD chemical library, to develop, use, manufacture, market and commercialize certain compounds, and products that contain such compounds, that are therapeutically useful for the treatment of diseases and disorders in humans, including with respect to KIT, a type of receptor tyrosine kinase and tumor marker.

Any termination of this license could result in the loss of significant rights and will restrict our ability to develop and commercialize our pan-variant KIT inhibitor product candidates, including our most advanced product candidate, THE-630. For example, ARIAD may terminate the ARIAD License Agreement (1) for our uncured material breach of such agreement, (2) if we, or any of our affiliates or sublicensees, commence, and do not stop after receiving notice from ARIAD, any interference or opposition proceeding in relation to, challenges to the validity or enforceability of, or opposition to any extension of or the grant of a supplementary protection

certificate with respect to, any ARIAD patent or patent application licensed under this agreement, or (3) in the event of our bankruptcy. Moreover, if we or ARIAD fails to adequately protect this intellectual property, our ability to commercialize THE-630 may be impaired. See "—Risks Related to Intellectual Property—Our rights to develop and commercialize our technology and product candidates may be subject, in part, to the terms and conditions of licenses granted to us by others" and "—Risks Related to Intellectual Property—If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business."

***If we and our licensors and collaborators, if any, are unable to obtain and maintain sufficient patent and other intellectual property protection for product candidates and technology, our competitors could develop and commercialize products and technology similar or identical to ours, and we may not be able to compete effectively in our market or successfully commercialize any product candidates we may develop.***

Our commercial success depends in part on our ability and the ability of our licensors and collaborators, if any, to obtain, maintain, enforce and defend patents and other intellectual property rights with respect to product candidates and technology and to operate our business without infringing, misappropriating, or otherwise violating the intellectual property rights of others. If we and our licensors and our collaborators, if any, are unable to obtain and maintain sufficient intellectual property protection for our product candidates and any additional product candidates that we may develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors and other third parties could develop and commercialize product candidates similar or identical to ours, and our ability and the ability of our collaborators to successfully commercialize product candidates that we and our collaborators may pursue may be impaired.

To establish our proprietary position, we have filed patent applications in the US related to our novel product candidates that are important to our business, and we have exclusively licensed certain patent applications from ARIAD; we may in the future also license or purchase issued patents or pending patent applications filed by others. Given the very early stage of development of our product candidates and development programs, our patent portfolio is similarly at a very early stage. In particular, as of December 31, 2022, we had exclusively licensed one issued US patent and one pending US application relating to THE-630, we owned one pending PCT application relating to THE-630, and we owned one pending US non-provisional patent application, one pending US provisional patent application, and two pending PCT patent applications relating to THE-349. Accordingly, our current patent rights provide us with limited legal right to prevent third parties from competing with us in any way. If we do not obtain additional meaningful patent coverage for product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment, competitors may be able to erode or negate any competitive advantage we may have, which would likely harm our business and ability to achieve profitability. US provisional patent applications are not eligible to become issued patents until, among other things, we file a non-provisional patent application within 12 months of filing of one or more of our related provisional patent applications. With regard to such US provisional patent applications, if we do not timely file any non-provisional patent applications, we may lose our priority date with respect to our provisional patent applications and any patent protection on the inventions disclosed in our provisional patent applications. 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. If we are unable to secure or maintain patent protection with respect to product candidates, our business, financial condition, results of operations, and prospects could be materially harmed.

We cannot be certain that the claims in US patent applications (including provisional and non-provisional), corresponding international patent applications and patent applications in certain foreign territories, or those of our licensors and collaborators, will be considered patentable by the US Patent and Trademark Office, or the USPTO, courts in the US or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our future issued patents will not be found invalid or unenforceable if challenged. Moreover,

the patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we, any licensors or any collaborators will be successful in protecting product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;

- patent applications may not result in any patents being issued;

- patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;

- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates;

- there may be significant pressure on the US government and international governmental bodies to limit the scope of patent protection both inside and outside the US for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and

- countries other than the US may have patent laws less favorable to patentees than those upheld by US courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or the patent applications of our licensors and collaborators will result in patents being issued or that issued patents will afford sufficient protection against competitors with similar technology.

The patent prosecution process is also expensive and time-consuming, and we and our licensors and collaborators may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is possible that we or our licensors and collaborators will fail to identify important patentable aspects of our research and development efforts in time to obtain appropriate or any patent protection or fail to file patent applications covering inventions made in the course of development and commercialization activities before a competitor or another third party files a patent application covering, or publishes information disclosing, a similar, independently-developed invention. Such competitor's or other third party's patent application may pose obstacles to our ability to obtain patent protection or limit the scope of the patent protection we or our licensors and collaborators may obtain. In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the US and most other countries are confidential for a period of time after filing or until issuance, we may not be certain that we or our licensors are the first to either (1) file any patent application related to product candidates or (2) invent any of the inventions claimed in the patents or patent

applications. Similarly, publications of discoveries in the scientific and scholarly literature often lag behind the actual discoveries, and patent applications in the US and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Consequently, we cannot be certain that we or our licensors and collaborators were the first to make the inventions claimed in our owned or in-licensed patent rights and patent applications or were the first to file for patent protection on the inventions claimed in our pending patent applications. Further, 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.

The degree of future protection for our and our licensors' proprietary rights is uncertain. Only limited protection may be available. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts, as described further throughout "—Risks Related to Intellectual Property." As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours, and may not adequately protect our rights or permit us to gain or keep any competitive advantage. These uncertainties and/or limitations in our ability to properly protect the intellectual property rights relating to product candidates could have a material adverse effect on our financial condition and results of operations.

***If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected.***

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications and those of our licensors and collaborators may not result in patents being issued that protect product candidates or which effectively prevent others from commercializing competitive product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own or in-license in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-license may be challenged or circumvented by third parties or may be narrowed or invalidated as a result of challenges by third parties. Consequently, we do not know whether product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents or the patents of our licensors and collaborators by developing similar or alternative technologies or products in a non-infringing manner, which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents or the patents of our licensors may be challenged in the courts or patent offices in the US and abroad. We may be subject to a third-party pre-issuance submission of prior art to the USPTO or third-party observations at the European Patent Office, or become involved in opposition, derivation, revocation, reexamination, post-grant review, or PGR, and *inter partes* review, or IPR, or other similar proceedings challenging our owned patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, our patents or the patents of our licensors may become subject to post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our priority of invention or other features of patentability with respect to our patents and patent applications and those of our licensors. Such challenges may result in loss of patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and

products, or limit the duration of the patent protection of product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our patents and patent applications or the patents and patent applications of our licensors is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

***Intellectual property rights do not necessarily address all potential threats to our competitive advantage.***

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to any product candidates we may develop or utilize similar technology but that are not covered by the claims of our patents or the patents that we license or may own in the future;
- we or our licensors might not have been the first to make the inventions covered by an issued patent or pending patent application that we license or may own in the future;
- we or our licensors or collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending owned or licensed patent applications or those that we may own or license in the future will not lead to issued patents;
- issued patents that we own or license may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may have an adverse effect on our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

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

***Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.***

Our commercial success depends significantly on avoiding infringement of the patents and proprietary rights of third parties. Numerous third-party US and foreign issued patents and pending patent applications exist in

the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of product candidates. There is a substantial amount of litigation, both within and outside the US, involving patent and other intellectual property rights in the pharmaceutical and biotechnology industries, including patent infringement lawsuits, oppositions, reexaminations, IPR proceedings and PGR proceedings before the USPTO and/or corresponding foreign patent offices. Accordingly, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties.

As the pharmaceutical and biotechnology industries expand and more patents are issued, the risk increases that product candidates may be subject to claims of infringement of the patent rights of third parties. Patent applications are maintained as confidential for a certain period of time, until the relevant application is published. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. There is also no assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our products that may be approved in the future, or impair our competitive position. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Thus, we may be unaware of third-party patents that may be infringed by commercialization of any product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology.

Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation that may cause negative publicity;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing any product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- subject us to significant liability to third parties; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non-exclusive, which could result in our competitors gaining access to the same technology.

Although no third party has asserted a claim of patent infringement against us as of the date of this Annual Report, it is possible that a third party may assert a claim of patent infringement directed at any product candidates in the future. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to product candidates, treatment indications, or processes could subject us to significant liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our strategic partners or collaborators were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual

property. In addition, we cannot be certain that we could redesign product candidates, treatment indications, or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing product candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing product candidates and technology.

Even if resolved in our favor, litigation or other legal proceedings could cause us to incur significant expenses, distract our technical and management personnel from their normal responsibilities, delay development of product candidates, subject us to significant uncertainties and harm our reputation, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. See "—Risks Related to Intellectual Property—Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities" and "—Risks Related to Intellectual Property—Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline."

***Our rights to develop and commercialize our technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.***

We have licensed, and may in the future license, patent and other intellectual property rights from other parties. We may enter into additional license agreements in the future with others to advance our existing or future research or allow commercialization of our existing or future product candidates. These licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. We may also need to devote substantial time and attention to ensuring that we successfully integrate these transactions into our existing operations and are compliant with our obligations under these agreements, which may divert management's time and attention away from our research and development programs or other day-to-day activities.

In addition, subject to the terms of any such license agreements, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. Accordingly, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such patents or patent applications, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our future product candidates that are subject of such licensed rights could be adversely affected.

Our licensors may rely on third-party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in-license. If other third parties have ownership rights to our future in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

It is possible that we may be unable to obtain licenses at a reasonable cost or on reasonable terms, if 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 redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly.

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

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 patents and other rights to third parties;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- our right to transfer or assign the license;
- the inventorship and 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
- the priority of invention of patented technology.

In addition, the agreements under which we license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. In the event of any disagreement about the interpretation of these provisions, our management may need to devote a disproportionate amount of its attention to resolving these disagreements. Such disruptions may cause delays in our research and development programs and other business objectives. Additionally, the resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we license in the future prevent or impair our ability to maintain our licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

In spite of our best efforts, our licensors might conclude that we materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

***We may not be successful in obtaining or maintaining necessary rights to product candidates through acquisitions and in-licenses.***

Because our development programs may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive

area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment 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. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***We may be involved in lawsuits to protect or enforce our patents or our licensors' patents, which could be expensive, time consuming and unsuccessful. Further, our issued patents or our licensors' patents could be found invalid or unenforceable if challenged in court.***

Competitors and other third parties may infringe or otherwise violate our patents or other intellectual property or the patents or other intellectual property of our licensors. In addition, our patents or the patents of our licensors may become involved in inventorship or priority disputes. 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. To counter infringement or other unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Our ability to enforce patent rights also depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents or that our patents are invalid or unenforceable. In a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology. An adverse result in any litigation proceeding could put one or more of our owned or licensed patents at risk of being invalidated, held unenforceable or interpreted narrowly. We may find it impractical or undesirable to enforce our intellectual property against some third parties.

If we or licensors were to initiate legal proceedings against a third party to enforce a patent directed to our product candidates or any additional product candidates that we may develop, the defendant could counterclaim that our patent or that of our licensor is invalid or unenforceable. In patent litigation in the US, 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, including lack of novelty, obviousness, non-enablement or insufficient written description. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution.

Third parties may also raise similar claims before the USPTO or an equivalent foreign body, even outside the context of litigation. Potential proceedings include re-examination, PGR, IPR, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (for example, opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer cover our technology or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability 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 the applicable product candidates or technology covered by the patent rendered invalid or unenforceable.

Some of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent 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, misappropriating or otherwise violating our intellectual property.

Even if resolved in our favor, litigation or other legal proceedings could cause us to incur significant expenses, distract our technical and management personnel from their normal responsibilities, delay development of product candidates, subject us to significant uncertainties and harm our reputation, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

***Intellectual property litigation could cause us to spend substantial resources, distract our personnel from their normal responsibilities and subject us to significant uncertainties.***

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. 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. Moreover, 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.

In addition, the uncertainties associated with litigation could compromise our ability to raise the funds necessary to initiate or continue our preclinical studies and clinical trials, continue our internal research programs, in-license needed technology or other product candidates or enter into development collaborations that would help us commercialize product candidates, if approved. If the breadth or strength of protection provided by our patents and patent applications or the patents and patent applications of our licensors is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Accordingly, these uncertainties could compromise our ability to compete in the marketplace. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. These uncertainties could cause the price of shares of our common stock to decline, as well as have a material adverse effect on our business, financial condition, results of operations and prospects.

***Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline.***

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings or developments in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing product candidates, approved products, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

***Derivation proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party.***

Derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. 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. Our defense of derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our development programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring product candidates to market.

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

Obtaining and enforcing patents in the pharmaceutical and biotechnology industries is inherently uncertain, due in part to ongoing changes in the patent laws. Changes in either the patent laws or in the interpretations of patent laws in the US and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. In the US, depending on decisions by Congress, the federal courts, and the USPTO, the laws and regulations governing patents, and interpretation thereof, could change in unpredictable ways that could weaken our and our licensors' or collaborators' ability to obtain new patents or to enforce existing or future patents. Moreover, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. For example, the US Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Therefore, there is increased uncertainty with regard to our and our licensors' or collaborators' ability to obtain patents in the future, as well as uncertainty with respect to the value of patents once obtained.

In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' or collaborators' patent applications and the enforcement or defense of our or our licensors' or collaborators' issued patents. For example, in the US, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, which was signed into law in September 2011, includes a number of significant changes to US patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the US transitioned in March 2013 to a "first inventor to file" system in which, assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application.

The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including PGR, IPR, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in US federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

The USPTO has developed regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, particularly the first inventor-to-file provisions. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the

operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents, including for the reasons described above. Similarly, statutory or judicial changes to the patent laws of other countries may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Any of these could have a material adverse effect on our business, financial condition, results of operations and prospects.

***We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing product candidates. While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning this intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to product candidates. Even if resolved in our favor, litigation or other legal proceedings could cause us to incur significant expenses, distract our technical and management personnel from their normal responsibilities, delay development of product candidates, subject us to significant uncertainties and harm our reputation, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Patents have a limited lifespan. In the US, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest US non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented product and practicing our own patented technology. 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.

***If we or our licensors do not obtain patent term extension for product candidates, our business may be materially harmed.***

Depending upon the timing, duration and specifics of FDA marketing approval of product candidates, one or more of our US patents or those of our licensors may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA approved product as compensation for the 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 and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of product candidates. However, we may not be granted an extension because of, for example, 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. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

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

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

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

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 those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of the applicable patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and 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 the USPTO and various foreign patent offices at various points over the lifetime of our patents and/or applications and those of our licensors. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official communications within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. While an inadvertent lapse can in some cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in irrevocable abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we or our licensors or collaborators fail to maintain the patents and patent applications covering product candidates, our competitors might be able to enter the market with similar or identical products or technology, which would harm our business, financial condition, results of operations and prospects.

***If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.***

We use and intend to use registered or unregistered trademarks or trade names to brand and market ourselves and our products. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

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

We rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and 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 inside and outside the US are less willing or unwilling to protect trade secrets.

Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced, and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of

our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

***We may be subject to claims that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets.***

We have entered into and may in the future enter into non-disclosure and confidentiality agreements to protect the proprietary positions of third parties, such as outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, and other third parties. We may become subject to litigation where a third party asserts that we or our employees inadvertently or otherwise breached the agreements and used or disclosed trade secrets or other information proprietary to the third parties. Failure to successfully defend against any such claim could subject us to significant liability for monetary damages or prevent or delay our developmental and commercialization efforts, which could adversely affect our business. Even if resolved in our favor, litigation or other legal proceedings could cause us to incur significant expenses, distract our technical and management personnel from their normal responsibilities, delay development of product candidates, subject us to significant uncertainties and harm our reputation, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

***We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.***

Many of our employees were previously employed at other biotechnology or pharmaceutical companies and our consultants and advisors may work for other biotechnology or pharmaceutical companies in addition to us. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any of these individuals' former or concurrent employers or clients. We may also be subject to claims that patents and applications we have filed to protect inventions of our employees, consultants and advisors, even those related to one or more product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims.

If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if resolved in our favor, litigation or other legal proceedings could cause us to incur significant expenses, distract our technical and management personnel from their normal responsibilities, delay development of product candidates, subject us to significant uncertainties and harm our reputation, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

***The patent protection and patent prosecution for some product candidates may be dependent on third parties.***

While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to product candidates, there may be times when the filing and prosecution activities for patents and patent applications relating to product candidates are controlled by our licensors or collaboration partners. If any of our licensors or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

**Risks Related to Our Reliance on Third Parties**

***We rely on third parties to conduct our preclinical studies and clinical trial, and plan to rely on third parties to conduct any future preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.***

We do not have the ability to independently conduct all aspects of our preclinical studies or clinical trials ourselves. We utilize and depend upon third-party investigators and collaborators, such as medical institutions, CROs, clinical trial sites and CMOs, to conduct and support our preclinical studies and clinical trial under agreements with us and plan to continue to do so for future preclinical studies and any clinical trials we may initiate. These third parties have had and will continue to have a significant role in the conduct of our ongoing and anticipated preclinical studies and clinical trials and the subsequent collection and analysis of data.

These third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we have limited ability to control the amount or timing of resources that any such third party will devote to our preclinical studies or our clinical trials. The third parties we rely on for these services may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting preclinical studies, clinical trials or other drug development activities, which could affect their performance on our behalf. Some of these third parties may terminate their engagements with us at any time. We also expect to have to negotiate budgets and contracts with CROs, clinical trial sites and CMOs and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs. If we need to enter into alternative arrangements with, or replace or add any third parties, it would involve substantial cost and require extensive management time and focus, or involve a transition period, and may delay our drug development activities, as well as materially impact our ability to meet our desired clinical development timelines.

Our heavy reliance on these third parties for such drug development activities will reduce our control over these activities. As a result, we will have less direct control over the conduct, timing and completion of preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCP standards, regulations for conducting, recording and reporting the results of clinical trials to assure that data and reported results are reliable and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs or any clinical trial sites fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials substantially comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under current cGMP regulations and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of study subject, may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

There is no guarantee that any 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 subjects enrolled in such clinical trial unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible.

Accordingly, 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, or if these third parties need to be replaced, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize product candidates. As a result, our financial results and the commercial prospects for product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

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

We do not currently have the infrastructure or internal capability to manufacture supplies of product candidates for use in development and commercialization.

We rely, and expect to continue to rely, on third-party manufacturers for the production of product candidates for preclinical studies and clinical trials under the guidance of members of our organization, including for our Phase 1/2 dose escalation and expansion clinical trial for THE-630. We do not have long-term supply agreements, and we purchase our required drug product on a purchase order basis, which means that aside from any binding purchase orders we have from time to time, our supplier could cease supplying to us or change the terms on which it is willing to continue supplying to us at any time. Even if we are able to replace any raw materials or other materials with an alternative, such alternatives may cost more, result in lower yields or not be as suitable for our purposes. In addition, some of the materials that we use to manufacture product candidates are complex materials, which may be more difficult to substitute. In addition, the ongoing COVID-19 pandemic may result in disruptions to the operations or an extended shutdown of certain businesses, which could include certain of our third-party manufacturers. Current or future supply chain interruptions that could be exacerbated by global political tensions, such as the situation in Ukraine, could negatively impact our ability to further develop our product candidates or to manufacture supplies of product candidates for use in development and commercialization, which could negatively impact our timelines and prospects. If we were to experience an unexpected loss of supply of any product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing preclinical studies and clinical trials, which could result in delays and additional regulatory submissions.

If we obtain marketing approval for any product candidates, given that our limited existing supply arrangements do not extend to commercial supply, we will need to establish one or more agreements with third parties to develop and scale up the drug manufacturing process. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Our product candidates and any additional product candidates that we may develop may compete with other product candidates and products for access to manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Even if we are able to establish agreements with third-party manufacturers, they may be unable to successfully increase the manufacturing capacity for any product candidates in a timely or cost-effective

manner, or at all. In addition, quality issues may arise during scale-up or commercial activities. Reliance on third-party manufacturers also entails additional risks, including:

- the failure of the third party to manufacture product candidates according to our schedule and specifications, or at all, including if our third-party contractors give greater priority to the supply of other products over product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;

- the reduction or termination of production or deliveries by suppliers, or the raising or prices or renegotiation of terms;

- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;

- the breach by the third-party contractors of our agreements with them;

- the failure of third-party contractors to comply with applicable regulatory requirements, including cGMPs;

- the breach by the third-party contractors of our agreements with them;

- the failure of the third party to manufacture product candidates according to our specifications;

- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;

- clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and

- the misappropriation of our proprietary information, including our trade secrets and know-how.

Our current and anticipated future dependence upon others for the manufacture of product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

***Our manufacturing process needs to comply with FDA regulations relating to the quality and reliability of such processes. Any failure to comply with relevant regulations could result in delays in or termination of our clinical programs and suspension or withdrawal of any regulatory approvals.***

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the US. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other comparable foreign regulatory authorities, they will not be able to secure and/or maintain marketing approval for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or other comparable foreign regulatory authority does not approve these facilities for the manufacture of product candidates or if it withdraws any such approval in the future, we will need to find alternative manufacturing facilities, and those new facilities would need to be inspected and approved by FDA or other comparable foreign regulatory authority prior to commencing manufacturing, which would significantly impact our ability to develop, obtain marketing approval for or market product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could

significantly and adversely affect supplies of product candidates or drugs and harm our business and results of operations.

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

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

***If we decide to establish collaborations, but are not able to establish those collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.***

Our drug development programs and the potential commercialization of product candidates will require substantial additional cash to fund expenses. Although we have not entered into any collaborations to date, we may seek to selectively form collaborations to expand our capabilities, potentially accelerate research and development activities and provide for commercialization activities by third parties. Any of these relationships may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business.

We face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Whether we reach a definitive agreement for a collaboration depends, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of preclinical studies or clinical trials, the likelihood of approval by the FDA or other comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of intellectual property and industry and market conditions generally. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. Further, we may not be successful in our efforts to establish a collaboration or other alternative arrangements for product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view them as having the requisite potential to demonstrate safety and efficacy.

In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential collaborators. Even if we are successful in entering into a collaboration, the terms and conditions of that collaboration may restrict us from entering into future agreements on certain terms with potential collaborators.

If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other research programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to

increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

***If conflicts arise between us and our collaborators or strategic partners, these parties may act in a manner adverse to us and could limit our ability to implement our strategies.***

If conflicts arise between any corporate or academic collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Collaborators or strategic partners may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for product candidates. Our collaborators or strategic partners may preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, or fail to devote sufficient resources to the development and commercialization of products. Any of these developments could harm our product development efforts.

***We may not realize the benefits of any acquisitions, in-license or other collaborations or strategic alliances that we enter into.***

We have entered into the ARIAD License Agreement, and in the future we may seek and form strategic alliances, create joint ventures or collaborations, or enter into acquisitions or additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any additional product candidates that we may develop.

These transactions can entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. We may agree to and be bound by negative covenants which may limit our development and commercial opportunities. As a result, if we enter into collaboration agreements, strategic partnerships or license our products, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business.

We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction or such other benefits that led us to enter into the arrangement. Failure to realize the benefits of any collaborations or strategic alliances may further cause us to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any planned sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we will need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop product candidates or bring them to market and generate product sales revenue, which would harm our business prospects, financial condition and results of operations.

**Risks Related to Our Common Stock**

***The market price of our common stock has been, and will likely continue to be, volatile and may fluctuate substantially or may decline regardless of our operating performance and our stockholders may not be able to resell shares of common stock at or above the price paid for such shares.***

Prior to the listing of our common stock, there was no market for shares of our common stock, and we cannot assure our stockholders that an active trading market for our shares will continue to develop or be sustained. Since our initial public offering, the market price of our common stock has experienced volatility. Our stockholders may not be able to resell those shares at or above the price paid for such shares. The market price of our common stock may fluctuate significantly in response to numerous factors, many of which are beyond our control, including:

- overall performance of the equity markets;
- our operating performance and the performance of other similar companies;
- results from any clinical trials with our current and future product candidates or those of our competitors;
- changes in recommendations by securities analysts that elect to follow our common stock;
- regulatory or legal developments in the US and other countries;
- the level of expenses related to future product candidates or clinical development programs;
- our failure to achieve product development goals in the timeframe we announce;
- announcements of acquisitions, strategic alliances or significant agreements by us or by our competitors;
- recruitment or departure of key personnel;
- the economy as a whole and market conditions in our industry, including conditions resulting from the COVID-19 pandemic;
- trading activity by a limited number of stockholders who together hold a significant amount of our outstanding common stock;
- the expiration of market standoff or contractual lock-up agreements;
- the size of our market float; and
- any other factors discussed in this Annual Report.

In addition, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many biotechnology companies. Stock prices of many biotechnology companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies.

***Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.***

The price of our common stock could decline if there are substantial sales of our common stock, particularly sales by our directors, executive officers and significant stockholders, or if there is a large number of shares of our common stock available for sale and the market perceives that sales will occur. As of March 1, 2023, we had 43,561,124 shares of our common stock outstanding.

Substantially all of our outstanding shares of common stock issued prior to our initial public offering were restricted from resale as a result of securities laws or market standoff and lock-up agreements. Shares subject to market standoff and lock-up agreements became available to be sold on April 5, 2022. Sales of a substantial number of such shares or the perception that such sales may occur, could cause our market price to fall or make it more difficult for our stockholders to sell common stock at a time and price that such stockholder deems appropriate.

On November 3, 2022, we filed our Shelf Registration Statement which included a prospectus for our ATM Program pursuant to which we may sell from time to time up to an aggregate of $100.0 million of shares of our common stock. As of December 31, 2022, no shares have been issued and sold pursuant to the ATM Program. Sales of common stock, debt securities or other equity securities by us may represent a significant percentage of our common stock currently outstanding. If we sell, or the market perceives that we intend to sell, substantial amounts of our common stock under the Shelf Registration Statement or otherwise, the market price of our common stock could decline significantly.

We also registered 9,494,003 shares of common stock that we have issued and may issue under our employee equity plans and will file additional registration statements on Form S-8 to register additional shares pursuant to the “evergreen” provisions under our equity compensation plans. Accordingly, these shares are available for sale in the open market, subject to Rule 144 volume limitations applicable to affiliates, and subject to any vesting restrictions and lock-up agreements applicable to these shares.

In addition, certain of our employees, executive officers, and directors may enter into Rule 10b5-1 trading plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 trading plan, a broker executes trades pursuant to parameters established by the employee, director, or officer when entering into the plan, without further direction from the employee, officer, or director. A Rule 10b5-1 trading plan may be amended or terminated in some circumstances. Our employees, executive officers, and directors also may buy or sell additional shares outside of a Rule 10b5-1 trading plan when they are not in possession of material, nonpublic information.

The market price of the shares of our common stock could decline as a result of the sale of a substantial number of shares in the public market or the perception in the market that the holders of a large number of shares intend to sell their shares.

***If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could result in sanctions or other penalties that would harm our business and the trading price of our common stock may decline.***

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of the Nasdaq Global Select Market, or Nasdaq. Commencing with our fiscal year ending December 31, 2022, we must perform system and process design evaluation and testing of the effectiveness of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. 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, including through hiring additional financial and accounting personnel, 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 will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts.

We may in the future discover material weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are unable to successfully remediate any future material weaknesses in our internal control over financial reporting, 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 the SEC, or other regulatory authorities.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls over financial reporting, we may not be able to produce timely and accurate financial statements. If that were to happen, our investors could lose confidence in our reported financial information, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, including equivalent foreign authorities.

***We are an "emerging growth company" as defined in the JOBS Act and a "smaller reporting company" as defined in the Exchange Act, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.***

We are an "emerging growth company" as defined in the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;

- not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act in the assessment of our internal control over financial reporting;

- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;

- reduced disclosure obligations regarding executive compensation; and

- not being required to hold a non-binding advisory vote on executive compensation or obtain stockholder approval of any golden parachute payments not previously approved.

In addition, as an emerging growth company, the JOBS Act allows us to delay adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies. We have elected to use this extended transition period under the JOBS Act. As a result, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies, which may make comparison of our financials to those of other public companies more difficult.

We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) December 31, 2026, the last day of the fiscal year following the fifth anniversary of the completion of our initial public offering in October 2021, (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.235 billion, (3) the date on which we are deemed to be a large accelerated filer, which means, among other things, the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Even after we no longer qualify as an emerging growth company, we may still qualify as a “smaller reporting company,” as defined in the Exchange Act, which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

***We do not intend to pay dividends for the foreseeable future.***

We have never declared nor paid cash dividends on our capital stock. We currently intend to retain any future earnings to finance the operation and expansion of our business, and we do not expect to declare or pay any dividends in the foreseeable future. Consequently, stockholders must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investment.

***The concentration of our stock ownership will likely limit our stockholders’ ability to influence corporate matters, including the ability to influence the outcome of director elections and other matters requiring stockholder approval.***

As of March 1, 2023, our executive officers, directors and the holders of more than 5% of our outstanding capital stock, in the aggregate, hold voting power over approximately 58% of our outstanding common stock. As a result, these stockholders, acting together, will have significant influence over all matters that require approval by our stockholders, including the election of directors and approval of significant corporate transactions. Corporate actions might be taken even if other stockholders oppose them. This concentration of ownership might also have the effect of delaying or preventing a change of control of our company that other stockholders may view as beneficial.

***Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make a merger, tender offer or proxy contest difficult, thereby depressing the trading price of our common stock.***

Our status as a Delaware corporation and the anti-takeover provisions of the Delaware General Corporation Law may discourage, delay or prevent a change in control by prohibiting us from engaging in a business combination with an interested stockholder for a period of three years after the person becomes an interested stockholder, even if a change of control would be beneficial to our existing stockholders. In addition, our

amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may make the acquisition of our company more difficult, including the following:

- a classified board of directors with three-year staggered terms, which could delay the ability of stockholders to change the membership of a majority of our board of directors;

- the ability of our board of directors to issue shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;

- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of our board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;

- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;

- the requirement that a special meeting of stockholders may be called only by a majority vote of our entire board of directors, the chairman of our board of directors or our chief executive officer, which could delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors;

- the requirement for the affirmative vote of holders of at least 66 2/3% of the voting power of all of the then-outstanding shares of the voting stock, voting together as a single class, to amend the provisions of our amended and restated certificate of incorporation relating to the management of our business or our amended and restated bylaws, which may inhibit the ability of an acquiror to effect such amendments to facilitate an unsolicited takeover attempt; and

- advance notice procedures with which stockholders must comply to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

In addition, as a Delaware corporation, we are subject to Section 203 of the Delaware General Corporation Law. These provisions may prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a certain period of time. A Delaware corporation may opt out of this provision by express provision in its original certificate of incorporation or by amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have not opted out of this provision.

These and other provisions in our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by our then-current board of directors, including delay or impede a merger, tender offer or proxy contest involving our company. The existence of these provisions could negatively affect the price of our common stock and limit opportunities for our stockholders to realize value in a corporate transaction.

***Our amended and restated certificate of incorporation designates the Court of Chancery of the State of Delaware and federal court within the State of Delaware as the exclusive forum for certain types of actions and proceedings that our stockholders may initiate, which could limit a stockholder's ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.***

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the Court of Chancery of the State of Delaware and federal court within the State of Delaware will be exclusive forums for any:

- derivative action or proceeding brought on our behalf;
- action asserting a claim of breach of a fiduciary duty owed by any current or former director, officer, stockholder or other employee of the Corporation to the Corporation or the Corporation's stockholders;
- any action arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or bylaws (as the foregoing may be amended, modified, supplement, and/or restated from time to time);
- any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or
- any action asserting a claim governed by the internal affairs doctrine.

We refer to this as the Delaware Forum Provision. This choice of forum provision does not apply to actions brought to enforce a duty or liability created under the Exchange Act. Our amended and restated certificate of incorporation also provides that the federal district courts of the US are the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision. We intend for this provision to apply to any complaints asserting a cause of action under the Securities Act despite the fact that Section 22 of the Securities Act creates concurrent jurisdiction for the federal and state courts over all actions brought to enforce any duty or liability created by the Securities Act or the rules and regulations promulgated thereunder. There is uncertainty as to whether a court would enforce such a provision with respect to claims under the Securities Act, and our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above.

We recognize that the Delaware Forum Provision and the Federal Forum Provision may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, the forum selection clauses in our certificate of incorporation may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court and other states courts have upheld the validity of federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found inapplicable to, or unenforceable, we may incur additional costs associated with resolving such matters The Federal Forum provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid The Court of Chancery of the State of Delaware and the federal district courts of the US may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

**General Risks**

***We could be subject to securities class action litigation.***

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

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

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

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

could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

***Requirements associated with being a public company will increase our costs significantly, as well as divert significant company resources and management attention.***

We are subject to the reporting requirements of the Exchange Act, the other rules and regulations of the SEC relating to public companies and the rules of Nasdaq. Compliance with the various reporting and other requirements applicable to public companies requires considerable time and attention of management. We cannot assure our stockholders that we will satisfy our obligations as a public company on a timely basis.

In addition, as a public company, it may be more difficult or more costly for us to obtain certain types of insurance, including directors' and officers' liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified personnel to serve on our board of directors, our board committees or as executive officers.

***If securities or industry analysts do not continue to publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.***

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If securities or industry analysts cease coverage of us, or only very few such analysts cover us, the trading price for our common stock would be negatively affected. If one or more of the analysts who covers us downgrades our common stock or publishes inaccurate or unfavorable research about our business, our common stock price would likely decline. If one or more of these analysts cease coverage of us or fails to publish reports on us regularly, demand for our common stock could decrease, which might cause our common stock price and trading volume to decline.

***Data collection, use, transfer and processing activities are governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.***

We are, and may increasingly become, subject to various laws and regulations, as well as contractual obligations and mandatory industry standards relating to privacy and security in the jurisdictions in which we operate. The regulatory environment related to data privacy and security is increasingly rigorous, with new and constantly changing requirements applicable to our business, and enforcement practices are likely to remain uncertain for the foreseeable future. These laws and regulations may be interpreted and applied differently over time and from jurisdiction to jurisdiction, and it is possible that they will be interpreted and applied in ways that may have a material adverse effect on our business, financial condition, results of operations and prospects.

In the US, various federal and state regulators, including governmental agencies like the Federal Trade Commission, have adopted, or are considering adopting, laws and regulations concerning personal information privacy and data security. Certain state laws may be more stringent or broader in scope, or offer greater individual rights, with respect to personal information than federal, international or other state laws, and such laws may differ from each other, all of which may complicate compliance efforts. For example, the California Consumer Privacy Act of 2018, or the CCPA, which increases privacy rights for California residents and imposes obligations on companies that process their personal information and meet certain revenue or volume processing thresholds, came into effect on January 1, 2020, and was further amended by the California Privacy Rights Act, or the CPRA, on November 3, 2020. Among other things, the CCPA requires covered companies to provide new disclosures to California residents and provide such residents new data protection and privacy rights, including the ability to opt-out of certain sales of personal information. The CPRA significantly modifies the CCPA by expanding residents' rights with respect to certain personal information and creates a new state agency to oversee implementation and enforcement efforts. Many of the CPRA's provisions will become effective on January 1, 2023. The CCPA provides for civil penalties for

violations, as well as a private right of action for certain data breaches. This private right of action may increase the likelihood of, and risks associated with, data breach litigation, including class action litigation. In addition, laws in all 50 US states require businesses to provide notice to individuals if certain of their personal information has been disclosed as a result of a qualifying data breach.

Moreover, the CCPA has prompted a number of proposals for new federal and state-level privacy legislation. Specifically, in 2023, state consumer privacy laws similar to the CCPA and CPRA enter into force in Connecticut, Colorado, Utah and Virginia, State laws and regulations are not necessarily preempted by federal laws and regulations, such as HIPAA, particularly if a state affords greater protection to individuals than federal law. Where state laws are more protective, we have to comply with the stricter provisions. In addition to fines and penalties imposed upon violators, some of these state laws also afford private rights of action to individuals who believe their personal information has been misused. The interplay of federal and state laws may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and data we receive, use and share, potentially exposing us to additional expense, adverse publicity and liability. Legal requirements relating to the collection, storage, handling, and transfer of personal information and personal data continue to evolve and may result in increased public scrutiny and escalating levels of enforcement, sanctions and increased costs of compliance. This legislation may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies.

Internationally, data protection and privacy laws, regulations and standards in many jurisdictions apply broadly to the collection, use, retention, security, disclosure, transfer or other processing of personal data. For example, the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018, is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including imposing special requirements in respect of the processing of health and other sensitive data. Specifically, the GDPR enhances data protection obligations for data controllers of personal data, including, for example, requirements to establish a legal basis for processing, stringent standards for obtaining consent from individuals to process their personal data, robust disclosures to individuals about how personal data is used, a strengthened individual data rights regime (including rights of access and deletion in certain circumstances), strict rules regarding the transfer of personal data out of the European Economic Area, including to the US, requirements to implement safeguards to protect the security and confidentiality of personal data that requires the adoption of administrative, physical and technical safeguards, mandatory data breach notification, limitations on retention and secondary use of personal data, and obligations to take certain measures when engaging third party processors in connection with the processing of personal data. The GDPR also creates direct obligations on service providers acting as processors. EU member states are tasked under the GDPR to enact, and have enacted, certain implementing legislation that adds to and/or further interprets the GDPR requirements and potentially extends our obligations and potential liability for failing to meet such obligations. Failure to comply with the requirements of the GDPR and the related national data protection laws of the European Union Member States may result in potential fines of up to €20 million or 4% of annual global revenues, whichever is greater, and other administrative penalties. The GDPR also confers a private right of action on data subjects and nonprofit organizations, acting subject to a mandate granted by the data subject, to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. In addition, further to the UK's exit from the EU on January 31, 2020, the GDPR ceased to apply in the UK at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law, referred to as the UK GDPR. The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher.

Certain legal regimes outside of the US, including in the United Kingdom and under the GDPR, prohibit the transfer of personal data to the US unless certain measures are in place, including, for example, executing Standard Contractual Clauses, or a derogation applies. However, certain EU court decisions cast doubt on the ability to use the European Commission's Standard Contractual Clauses to lawfully transfer personal data to the US and other third countries. Use of the Standard Contractual Clauses must be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals, and additional supplementary technical, organizational and/or contractual measures and/or contractual provisions may need to be put in place. On December 13, 2022, the European Commission published a draft adequacy decision on the EU-US Data Privacy Framework or the Framework, the successor to the EU-US Privacy Shield Framework that was invalidated by the Court of Justice of the European Union's July 2020 decision in the so-called Schrems II case (Case C-311/18). If approved, the Framework will allow US companies to self-certify to the US Department Commerce their compliance with a set of agreed privacy principles in order to freely receive EU personal data. However, data subjects, civil liberties groups, and data protection authorities may challenge the Framework, which could lead to further scrutiny by the courts. There is no guarantee that any transfer mechanism upon which we rely will be deemed to be valid by the relevant authorities, or that mechanisms that are currently deemed to be valid will remain valid in the future. This uncertainty, and its eventual resolution, may increase our costs of compliance, impede our ability to transfer data and conduct our business and harm our business or results of operations. Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of operating our business.

Compliance with US and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Any actual or alleged failure to comply with US or international laws and regulations relating to privacy, data protection, and data security could result in governmental investigations, proceedings and enforcement actions (which could include civil or criminal penalties), private litigation or adverse publicity, harm to our reputation, and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information or impose other obligations or restrictions in connection with our use, retention and other processing of information, and we may otherwise face contractual restrictions applicable to our use, retention, and other processing of information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

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

The rules dealing with US federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the US Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, the TCJA was enacted in 2017 and made significant changes to corporate taxation, including the reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses from taxable years beginning after December 31, 2017 to 80% of current year taxable income and the elimination of net operating loss carrybacks generated in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), and the modification or repeal of many business deductions and credits, including a reduction of the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as "orphan drugs."

Additionally, on March 27, 2020, former President Trump signed into law the CARES Act, which, among other things, suspends the 80% limitation on the deduction for net operating losses in taxable years beginning before January 1, 2021, permits a 5-year carryback of net operating losses arising in taxable years beginning after December 31, 2017 and before January 1, 2021, and generally caps the limitation on the deduction for net interest expense at 50% of adjusted taxable income for taxable years beginning in 2019 and 2020.

Beginning in 2022, the TCJA amended Section 174 and now requires US-based and non-U.S-based research and experimental (R&E) expenditures to be capitalized and amortized over a period of five or 15 years, respectively, for amounts paid in tax years starting after December 31, 2021. Prior to the TCJA amendment, Section 174 allowed taxpayers to immediately deduct R&E expenditures in the year paid or incurred. The Company has applied this required change in accounting method beginning in 2022 and the computation may be adjusted pending future IRS guidance.

The presidential and congressional elections in the US could also result in significant changes in, and uncertainty with respect to, tax legislation, regulation and government policy directly affecting us and our business. For example, the US government may enact significant changes to the taxation of business entities including, among others, a permanent increase in the corporate income tax rate, an increase in the tax rate applicable to the global intangible low-taxed income and elimination of certain exemptions, and the imposition of minimum taxes or surtaxes on certain types of income. The likelihood of these changes being enacted or implemented is unclear.

It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be promulgated or issued under existing or new tax laws, which could result in an increase in our or our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

## ITEM 1B. Unresolved Staff Comments

None.

## ITEM 2. Properties

Our corporate headquarters are located in Cambridge, Massachusetts, where we lease approximately 7,351 square feet of office space. Pursuant to the lease agreement, the lease term commenced in March 2022 and the initial term of the lease is seven years, with a one-time option right to extend the term five additional years, subject to an increase in rent in accordance with the terms of the lease agreement. We believe that this space will be sufficient for our needs for the foreseeable future. To meet the future needs of our business, however, we may lease additional or alternate space, and we believe suitable additional or alternative space will be available in the future on commercially reasonable terms.

## ITEM 3. Legal Proceedings

We are from time to time subject to litigation and other legal proceedings. We believe that there are no pending lawsuits or claims that, individually or in the aggregate, may have a material effect on our business, financial condition or operating results.

## ITEM 4. Mine Safety Disclosures

None.

# PART II

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

Our common stock has been publicly traded on the Nasdaq Global Select Market under the symbol "THRX" since our initial public offering, or IPO, on October 6, 2021. Prior to this date, there was no public market for our common stock.

### Holders of Common Stock

As of March 1, 2023, there were approximately 8 holders of record of our common stock. The actual number of stockholders 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 and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

### Dividend Policy

We have never declared or paid any cash dividends on our common stock and do not anticipate paying cash dividends in the foreseeable future.

### Securities Authorized for Issuance under Equity Compensation Plans

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

**Recent Sales of Unregistered Securities**

None.

**Use of Proceeds from Initial Public Offering**

On October 12, 2021, we closed the IPO, in which we sold 10,000,200 shares of our common stock at a public offering price of $16.00 per share. On October 25, 2021, the Underwriters (as defined below) exercised their option to purchase an additional 1,171,990 shares of our common stock at the public offering price of $16.00 per share. After deducting underwriting discounts, commissions and offering expenses, the aggregate net offering proceeds raised in the IPO were approximately $162.5 million. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-259549), which was declared effective by the SEC on October 6, 2021, and a Registration Statement on Form S-1 MEF (File No. 333-260102) filed pursuant to Rule 462(b) of the Securities Act. No payments for such offering expenses were made directly or indirectly to (i) any of our officers or directors or their associates, (ii) any persons owning 10% or more of any class of our equity securities or (iii) any of our affiliates.

Jefferies LLC, SVB Leerink LLC and Cantor Fitzgerald & Co. acted as joint book-running managers, and Wedbush Securities Inc. acted as lead manager for the offering, or collectively, the Underwriters.

There has been no material change in the planned use of proceeds from our IPO from that described in the final prospectus filed with the SEC on October 7, 2021.

**Purchases of Equity Securities by the Issuer and Affiliated Purchases**

None.

**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 together with our consolidated financial statements and related notes and other financial information included elsewhere in this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. See "Special Note Regarding Forward-Looking Statements" and "Risk Factors" for a discussion of forward-looking statements and important factors that could cause actual results to differ materially from the results described in or implied by these forward-looking statements.*

**Overview**

We are a clinical-stage biopharmaceutical company focused on improving the lives of cancer patients through the discovery, development, and commercialization of transformative targeted therapies. Our development programs are designed to address drug resistance mutations in key driver oncogenes, which are mutated genes that cause cancer. Resistance mutations limit the efficacy of existing targeted therapies by rendering tumor cells unresponsive to drugs, and therefore present a critical challenge in cancer treatment today. Our initial focus is on developing the next generation of TKIs and is rooted in the critical role that tyrosine kinases play in the development of cancer. Despite the commercial success of approved TKIs, the development of drug resistance is a persistent limitation, narrowing the number of effective treatment options available to patients as they progress through subsequent lines of therapy.

Our goal is to develop “pan-variant” kinase inhibitors-inhibitors that target all major cancer causing and drug resistance mutations in clinically significant protein kinases. We believe that truly pan-variant inhibitors are required to effectively inhibit the heterogeneous mix of resistance mutations found in patients, and may also suppress the emergence of new mutations when used in earlier lines of therapy. To develop such inhibitors, we deploy our novel PRA, a highly differentiated cell-based method for testing TKIs that we believe is predictive for “pan-ness”. We also employ structure-guided drug design, and, coupled with our PRA, we believe our approach has the potential to optimize molecules for pan-variant activity while maintaining selectivity and tolerability.

Our most advanced product candidate, THE-630, is a pan-variant inhibitor of all major classes of activating and resistance mutations of the KIT kinase for the treatment of GIST, a type of cancer most often characterized by oncogenic activation of KIT. GIST is the most common sarcoma of the gastrointestinal tract and often initiates in the stomach or small intestines. We are currently enrolling patients in a Phase 1/2 dose escalation and dose expansion clinical trial for the evaluation of THE-630 in patients with advanced GIST whose disease has developed resistance to prior KIT-targeting therapies. As of December 31, 2022, we were treating patients in cohort 5 of dose escalation, with all seven planned Phase 1 sites in the US open and enrolling patients. We expect to present initial data from the Phase 1 dose escalation portion of the clinical trial at an academic meeting in the second quarter of 2023, and to report additional data from the dose escalation study at an academic meeting in the fourth quarter of 2023. The primary objective of the Phase 1 dose escalation portion of the study are to evaluate the safety profile of THE-630, including the determination of an RP2D in GIST patients who have received imatinib and at least one other TKI. Secondary objectives include determining the PK profile of THE-630, and to characterize preliminary evidence of antitumor activity of THE-630. Once an RP2D is determined, the study will transition into the Phase 2 portion consisting of three expansion cohorts in patients with second-line GIST, third or fourth-line GIST, and fifth (or greater) line GIST. The Phase 2 dose expansion portion is expected to include sites in the US and Europe. The FDA has granted orphan drug designation to THE-630 for the treatment of GIST.

Our second product candidate is THE-349, a fourth-generation EGFR inhibitor for the treatment of NSCLC. THE-349 is designed to address on-target treatment resistance to existing EGFR inhibitors by targeting the common activating mutations in exons 19 and 21 alone or in combination with the most frequently observed resistance mutations, T790M and C797X. Preclinical characterization of THE-349 as central nervous system, or CNS active, and mutant-selective inhibitor with potent activity against single-, double-, and triple-mutant EGFR variants, including T790M and C797X, was shared in a poster presentation at the 34th ENA Symposium in Barcelona on October 26-28, 2022. We have initiated IND-enabling studies, and expect to file an IND application for this product candidate with the FDA in the fourth quarter of 2023. We plan to pursue initial clinical development as monotherapy in patients with C797X-mediated resistance after treatment with osimertinib, or another third-generation inhibitor, and then, assuming positive clinical data and subject to discussions with the FDA, expand into evaluation of combination treatment with other relevant modalities and, if clinical data support, target a broader second-line patient population to address the unmet need of patients who have been previously treated with osimertinib, but progress with either on-target or off-target resistance.

Our third program is a next-generation BCR-ABL TKI that we are designing to be potent, selective, and pan-variant—features that we believe would balance safety and efficacy—for patients with relapsed/refractory CML and Ph+ ALL. We expect to nominate a development candidate for this program by early 2024, with the goal of pursuing clinical development in patients with CML who have been previously treated with a second-generation TKI or have the T315I mutation, and in combination therapy for newly diagnosed patients with Ph+ ALL.

Since our inception in December 2017, our operations have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and performing research and development activities, including with respect to THE-630 and THE-349. 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 through the sale and issuance of our preferred stock and common stock including the net proceeds from the underwriters’ partial exercise of their option to purchase additional shares in our IPO and

the sale and issuance of our common stock pursuant to our ATM Program in the first quarter of 2023. Upon the closing of the IPO, each outstanding share of our preferred stock automatically converted into one share of common stock.

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 one or more product candidates. Our net losses for the years ended December 31, 2022 and 2021 were $50.6 million and $27.3 million, respectively. As of December 31, 2022, we had an accumulated deficit of $112.2 million. We expect to continue to incur significant and increasing losses for the foreseeable future. We expect that our expenses and capital requirements will increase substantially in connection with our ongoing activities, particularly if and as we:

- advance the clinical development of THE-630;
- advance THE-349, our BCR-ABL program and other compounds we may develop in the future from discovery through preclinical development and clinical trials;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- obtain, expand, maintain, defend and enforce our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- establish agreements with CROs, and CMOs; and
- add operational, legal, compliance, financial and management information systems and personnel to support our research, product development and future commercialization efforts, as well as to support our operations as a public company.

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 a combination of equity offerings, debt financings or other capital sources, which could include collaborations, strategic alliances or 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.

Because of the numerous risks and uncertainties associated with development of targeted oncology therapies, 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. We will need to generate significant revenue to achieve profitability, and we may never do so. 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.

As of December 31, 2022, we had cash, cash equivalents, and marketable securities of $211.8 million. Based on our current operating plan, we believe that our existing cash, cash equivalents, and marketable securities, in addition to the proceeds raised through sales of our common stock pursuant to our ATM Program in the first quarter of 2023, will be sufficient to fund our operations and capital expenses into the third quarter of 2025. 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 section titled "—Liquidity and Capital Resources."

**Impact of COVID-19 on Our Business**

The COVID-19 pandemic continues to evolve, and we will continue to monitor the COVID-19 situation, including the resurgence of cases relating to the spread of new variants. The extent of the impact of the COVID-19 pandemic on our 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 our CMOs, CROs, and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is uncertain and subject to change. To the extent possible, we are conducting business as usual. We will continue to actively monitor the rapidly evolving situation related to COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with whom we do business. At this point, the extent to which the COVID-19 pandemic may affect our business, operations and development timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain and is subject to change.

**Initial Public Offering**

On October 6, 2021, our Registration Statement on Form S-1 (File No. 333-259549) relating to our IPO was declared effective by the SEC, and we filed a Registration Statement on Form S-1 MEF (File No. 333-260102) pursuant to Rule 462(b) of the Securities Act. Pursuant to the Registration Statements and in connection with the IPO, we issued and sold an aggregate of 11,172,190 shares of common stock (inclusive of 1,171,990 shares pursuant to the partial exercise of the underwriters' option to purchase additional shares) at a price of $16.00 per share for aggregate cash proceeds of $162.5 million, net of underwriting discounts and commissions and offering costs payable by us. Upon closing of the IPO, all outstanding shares of our preferred stock automatically converted into an aggregate of 25,475,905 shares of common stock.

**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 product candidates, THE-630, THE-349, and our BCR-ABL program or any other 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 Expenses*

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

- salaries, benefits, stock-based compensation and other related costs for individuals involved in research and development activities;
- external research and development expenses incurred under agreements with CROs and consultants that conduct our preclinical studies and other scientific development services;
- costs incurred under agreements with CMOs for manufacturing material for our preclinical studies and planned clinical trials; and
- costs related to compliance with regulatory requirements.

We expense research and development costs as incurred. We recognize external 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 external 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 consolidated financial statements as prepaid expenses or accrued expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

A significant portion of our research and development costs have been external costs, which we track after a clinical product candidate has been identified. We utilize third-party contractors for our research and development activities and CMOs for our manufacturing activities and we do not have our own laboratory or manufacturing facilities. Therefore, we have no material facilities expenses attributed to research and development. Our internal research and development costs are primarily personnel-related costs and other indirect costs.

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 advance clinical development of our product candidates, THE-630, THE-349, our BCR-ABL program, and continue to discover and develop additional product candidates, expand our headcount and maintain, expand and enforce our intellectual property portfolio. If any 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.

The successful development of our current product candidates, THE-630 and THE-349, and our BCR-ABL program or 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 THE-630, THE-349, our BCR-ABL program and 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 current or future product candidate, if approved. This is due to the numerous risks and uncertainties associated with product development, including the uncertainty of:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to maintain our current research and development programs and to establish new programs;
- successful patient enrollment in, and the initiation and completion of, clinical trials;
- the successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- our ability to establish new licensing or collaboration arrangements;
- the performance of our future collaborators, if any;
- our ability to establish arrangements with third-party manufacturers for the clinical supply of our product candidates and commercial supply of products that receive marketing approval, if any;
- development and timely delivery of commercial-grade drug formulations that can be used in our planned clinical trials and for commercialization;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- commercializing product candidates, if approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

Any changes in the outcome of any of these variables with respect to the development of THE-630, THE-349, our BCR-ABL program, or any other future product candidates in clinical and preclinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA 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 FDA's acceptance and clearance of an IND application, 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.

*General and Administrative Expenses*

General and administrative expenses consist primarily of personnel-related expenses, including salaries, benefits, and stock-based compensation expenses for personnel in executive, finance, accounting, human resources 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 anticipate that our general and administrative expenses will increase in the 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 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 candidates 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.

We do not believe that inflation has had a material effect on our business. However, if our costs, in particular costs related to clinical trial expenses, preclinical expenses and/or employee-related expenses, were to become subject to significant inflationary pressures, it may adversely impact our business, operating results and financial condition.

***Other Income, Net***

Other income, net primarily consists of interest income, which is earned on cash equivalents that generate interest on a monthly basis, and short-term and long-term marketable securities.

**Results of Operations**

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

| | YEAR ENDED DECEMBER 31, | | |
|---|---|---|---|
| | 2022 | 2021 | CHANGE |
| Operating expenses: | | | |
| Research and development | $ 35,698 | $ 18,328 | $ 17,370 |
| General and administrative | 18,388 | 9,008 | 9,380 |
| Total operating expenses | 54,086 | 27,336 | 26,750 |
| Loss from operations | (54,086) | (27,336) | (26,750) |
| Other income, net | 3,478 | 28 | 3,450 |
| Total other income, net | 3,478 | 28 | 3,450 |
| Net loss | $ (50,608) | $ (27,308) | $ (23,300) |

*Research and Development Expenses*

The following table summarizes our research and development expenses for the years ended December 31, 2022 and 2021 (in thousands):

| | YEAR ENDED DECEMBER 31, | | |
|---|---|---|---|
| | 2022 | 2021 | CHANGE |
| Direct research and development expenses by program: | | | |
| Pan-variant KIT inhibitor (THE-630) | $ 7,965 | $ 9,006 | $ (1,041) |
| Fourth-generation EGFR inhibitor (THE-349) | 6,569 | 1,740 | 4,829 |
| Discovery programs | 3,959 | 1,132 | 2,827 |
| Unallocated research and development expenses: | | | |
| Personnel-related (including stock-based compensation) | 15,517 | 5,922 | 9,595 |
| Other | 1,688 | 528 | 1,160 |
| Total research and development expenses | $ 35,698 | $ 18,328 | $ 17,370 |

Research and development expenses were $35.7 million for the year ended December 31, 2022 compared to $18.3 million for the year ended December 31, 2021. The increase in research and development expenses was primarily attributable to the following:

- a $1.0 million decrease in costs related to THE-630, primarily driven by a decrease in IND-enabling costs of $6.3 million and clinical start-up costs of $1.9 million in 2021, partially offset by an increase of clinical costs of $3.2 million, manufacturing costs of $3.9 million and other development costs of $0.1 million as we advanced THE-630 in the Phase 1 portion of the ongoing Phase 1/2 clinical trial;

- a $4.8 million increase in costs related to THE-349, primarily driven by an increase in contract research expenses of $2.6 million as we completed lead optimization, and manufacturing costs of $2.2 million;

- a $2.8 million increase in costs related to progress on our discovery programs, including an increase in contract research expenses of $3.1 million, partially offset by a decrease in the use of outside independent consultants of $0.3 million;

- a $9.6 million increase in employee costs consisting of $4.4 million of stock-based compensation expense, and an increase in salary and benefit related expense of $5.2 million driven by an increase in headcount; and

- a $1.2 million increase in unallocated research and development expenses primarily from an increase of $0.5 million in facilities, $0.5 million of IT costs and $0.2 million of other office and employee travel expenses.

*General and Administrative Expenses*

The following table summarizes our general and administrative expenses for the years ended December 31, 2022 and 2021 (in thousands):

| | YEAR ENDED DECEMBER 31, | | |
|---|---|---|---|
| | 2022 | 2021 | CHANGE |
| Personnel-related expenses (including stock-based compensation) | $ 10,364 | $ 4,744 | $ 5,620 |
| Facilities and supplies | 585 | 113 | 472 |
| Legal and professional fees | 3,911 | 2,481 | 1,430 |
| Other expenses | 3,528 | 1,670 | 1,858 |
| | $ 18,388 | $ 9,008 | $ 9,380 |

General and administrative expenses were $18.4 million for the year ended December 31, 2022, compared to $9.0 million for the year ended December 31, 2021. The increase in general and administrative expenses was primarily attributable to the following:

- a $5.6 million increase in personnel-related costs primarily due to an increase in headcount, including an increase in stock-based compensation expense of $2.7 million, and an increase in salary and benefit related expense of $3.5 million, partially offset by a decrease in recruiting expense of $0.5 million;
- a $1.4 million increase in legal and professional fees, primarily due to increased legal and audit expenses and other costs associated with operating as a growing public company; and
- a $1.9 million increase in other expenses primarily due to increased insurance expense.

*Total Other Income, Net*

Total other income, net, was $3.5 million for the year ended December 31, 2022, and consisted of interest income of $2.8 million, and amortization and accretion in marketable securities earned of $0.7 million. During the year ended December 31, 2021, total other income, net, of $28,000 was recorded.

**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. As of December 31, 2022, we had cash, cash equivalents, and marketable securities of $211.8 million.

We have funded our operations primarily from sales of our preferred stock and common stock, including the net proceeds received from the underwriters' partial exercise of their over-allotment option in our IPO.

On November 3, 2022, we filed a shelf registration statement on Form S-3 (File No. 333-268125), with the SEC, which was declared effective on November 10, 2022, or the Shelf Registration Statement, in relation to the registration of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof for the purposes of selling, from time to time, our common stock, debt securities or other equity securities in one or more offerings. The Shelf Registration Statement also included a prospectus for "an at-the-market" program pursuant to which we may sell from time to time up to an aggregate of $100.0 million of

shares of our common stock, under a Sales Agreement with Cantor Fitzgerald & Co., as Sales Agent. We will pay to the Sales Agent cash commissions of up to 3.0 percent of the aggregate gross proceeds of sales of common stock under the Sales Agreement.

***Cash Flows***

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

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Net cash used in operating activities | $ (32,945) | $ (27,193) |
| Net cash used in investing activities | (117,294) | — |
| Net cash provided by financing activities | 182 | 263,777 |
| Net (decrease) increase in cash | $ (150,057) | $ 236,584 |

*Net Cash Used in Operating Activities*

During the year ended December 31, 2022, net cash used in operating activities was $32.9 million, primarily due to our net loss of $50.6 million, uses of cash for our operating lease liability of $0.7 million, prepaid expenses and other current assets of $0.8 million, and amortization and accretion of marketable securities of $0.7 million, partially offset by $11.4 million of stock-based compensation expense, a $4.0 million change in accounts payable, a $1.2 million change in other assets, a $0.4 million change in non-cash operating lease expense, and a $3.0 million change in accrued expenses and other current liabilities.

During the year ended December 31, 2021, net cash used in operating activities was $27.2 million, primarily due to our net loss of $27.3 million and uses of cash for prepaid expenses and other current assets of $3.2 million and other assets of $2.5 million, partially offset by $4.4 million of stock-based compensation expense, and a $1.6 million change in accrued expenses and other current liabilities.

*Net Cash Provided by Investing Activities*

During the year ended December 31, 2022, net cash used in investing activities was $117.3 million, resulting from our net purchases and sales of $116.8 million of marketable securities, and purchases of property and equipment of $0.5 million. No cash was provided by or used in investing activities for the year ended December 31, 2021.

*Net Cash Provided by Financing Activities*

During the year ended December 31, 2022, net cash provided by financing activities was $0.2 million, resulting entirely from proceeds received from the issuance of common stock under our employee stock purchase plan.

During the year ended December 31, 2021, net cash provided by financing activities was $263.8 million, resulting from proceeds of $99.9 million received from the issuance and sale of shares of our Series B Preferred Stock, net of issuance costs, $1.4 million in proceeds from the early exercise of stock options, and net proceeds of $162.5 million received in connection with the IPO.

***Funding Requirements***

We expect our expenses to increase substantially in connection with our ongoing research and development activities, particularly as we continue research and development and advance our THE-630 clinical trial and

advance the preclinical development of our other programs, including THE-349 and our BCR-ABL program. Furthermore, we expect to continue to incur additional costs associated with operating as a public company including increased costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs and investor and public relations costs. As a result, we expect to incur substantial operating losses and negative operating cash flows for the foreseeable future.

Based on our current operating plan, we believe that our cash, cash equivalents, and marketable securities of $211.8 million as of December 31, 2022, in addition to the proceeds raised from sales of our common stock pursuant to our ATM Program in the first quarter of 2023, will be sufficient to fund our operations and capital expenses into the third quarter of 2025. 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 scope, rate of progress, success and costs of our drug discovery, preclinical development activities, laboratory testing and clinical trials for product candidates;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing development and commercial manufacturing activities for product candidates, if approved;
- the extent to which we acquire or in-license other product candidates and technologies;
- the timing and amount of any payments required to be made under the agreements governing acquired or in-licensed product candidates or technologies;
- the cost, timing and outcome of regulatory review of product candidates;
- the cost and timing of establishing sales and marketing capabilities, if any product candidate receives marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the impact of the COVID-19 pandemic or other external disruptions on our business, results of operations and financial position;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of product candidates;
- the costs associated with being a public company; and
- the cost associated with commercializing product candidates, if they receive marketing approval.

A change in the outcome of any of these or other variables with respect to the development of THE-630 or THE-349 or any product or development candidate 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.

**Contractual Obligations**

We did not have during the periods presented, and we do not currently have, any material contractual obligations, other than as described below. Refer to Note 9 in our consolidated financial statements included elsewhere in this Annual Report for further details.

***License Agreement***

We may incur contingent royalty payments that we are required to make under the ARIAD License Agreement, pursuant to which we have in-licensed certain intellectual property used to develop THE-630. Due to the uncertainty of the achievement and timing of the events requiring payment under the ARIAD License Agreement, the amounts to be paid by us are not fixed or determinable at this time. We are required to pay ARIAD royalties on all sales of licensed products, with such royalty percentages in the low- to mid-single digits of sales. We have not paid any royalties to date as we have no products commercially approved for sale.

***Lease***

On September 16, 2021, we entered into an operating lease agreement for 7,351 rentable square feet of office space located in Cambridge, Massachusetts. The premises required additional build-out at the time the lease agreement was entered into. The lease commenced in March 2022 when the space was made available for use. Upon lease commencement, we recorded a ROU asset of $4.7 million and a corresponding lease liability of $4.7 million. The lease has a term of seven years, expiring in March 2029, with a one-time option right to extend the term five additional years, subject to an increase in rent in accordance with the terms of the lease agreement. The option to extend the lease term is not reflected in the ROU asset and lease liability as it is not reasonably certain of being exercised. Lease payments are paid monthly. The initial annual base rent is approximately $0.8 million, subject to a 3% annual rent increase, plus an allocation of our proportionate share of building operating costs such as maintenance, utilities, and insurance that are treated as variable costs and excluded from the measurement of the lease. Pursuant to the terms of the lease agreement, we provided a security deposit in the form of a letter of credit in the amount of approximately $0.4 million upon signing, which is recognized as restricted cash within other assets on the consolidated balance sheets.

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

## Critical Accounting Policies and Significant Judgments and Estimates

This management's discussion and analysis is based on our consolidated financial statements, which have been prepared in accordance with US generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make judgments and estimates 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 reported periods. We base our estimates on historical experience, known trends and events, and various other factors that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

While our accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report, we believe that the following accounting policies used in the preparation of our consolidated financial statements require the most significant judgments and estimates.

### *Accrued Research and Development Expenses*

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued 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 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 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.

### *Tranche Rights and Anti-dilution Rights*

The initial fair value of the Tranche Rights recognized in connection with our issuance of our Series A Preferred Stock in June 2018 and the Anti-dilution Rights issued to ARIAD in June 2018 were determined based on significant inputs not observable in the market, which represent Level 3 measurements within the fair value hierarchy. The initial fair values of the obligations were estimated based on the results of valuations performed in connection with the initial issuance of our Series A Preferred Stock. These obligations were

remeasured prior to the issuance of subsequent tranches and anti-dilution shares and at each subsequent reporting period.

Each Tranche Right and Anti-dilution Right was valued as a forward contract. The values were determined using a probability-weighted present value calculation. In determining the fair values, estimates and assumptions impacting fair value included the future value of our Series A Preferred Stock, risk free interest rates, estimated years to liquidity and probability of each milestone being achieved. We determined the per share future value of the shares of Series A Preferred Stock by back-solving to the initial proceeds of the Series A Preferred Stock financing. We remeasured each Tranche Right and Anti-dilution Right at each reporting period and prior to settlement. The purchase price of the Series A Preferred Stock at initial issuance, and all subsequent issuances, was higher than the fair value of our common stock.

***Stock-Based Compensation***

We measure stock-based compensation expense in accordance with ASC 718, *Compensation — Stock Compensation (ASC 718),* which requires that all stock-based awards granted to employees and non-employees, including stock options, restricted stock awards, and restricted stock units, be recognized in the consolidated statement of operations and comprehensive loss based on their grant date fair values. We estimate the fair value of stock options using the Black-Scholes option-pricing model. The fair values of restricted stock awards and restricted stock units are based on the fair value of our common stock on the date of grant. The grant date fair value of stock-based awards is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the award. We recognize forfeitures as they occur.

We estimate the fair value of stock options using the Black-Scholes option-pricing model which uses the following inputs: the fair value of our common stock, the expected term of our stock options, the expected volatility of our common stock, the risk-free interest rate for a period that approximates the expected term of our stock options, and our expected dividend yield. Certain assumptions used in our Black-Scholes option-pricing model represent management's best estimates and involve a number of variables, uncertainties and assumptions and the application of management's judgment, as they are inherently subjective. If any assumptions change, our stock-based compensation expense could be materially different in the future.

These subjective assumptions are estimated as follows:

- Fair value of common stock – The closing price of our common stock on the Nasdaq Global Select Market as reported on the date of grant.

- Expected term – The expected term represents the period that stock-based awards are expected to be outstanding. We use the "simplified" method to calculate the expected term for awards that qualify as "plain-vanilla", which deems the expected term to be the midpoint between the vesting date and the contractual life of the stock-based awards.

- Expected volatility – Due to the lack of a public market for our common stock and a lack of company-specific historical and implied volatility data, we have based our computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to us, including stage of product development, life science industry focus, length of trading history and similar vesting provisions. The historical volatility data is calculated based on a period of time commensurate with the expected term assumption. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation.

- Risk-free interest rate – The risk-free interest rate is based on the US Treasury yield in effect at the time of grant for zero-coupon US Treasury notes with maturities approximately equal to the expected term of the awards.

- Expected dividend yield – The expected dividend yield is assumed to be zero as we have never paid cash dividends on our common stock and have no plans to pay cash dividends on our common stock in the visible future.

**Emerging Growth Company Status**

In April 2012, the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company", or an EGC, may take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for new or revised accounting standards during the period in which we remain an emerging growth company; however, we may adopt certain new or revised accounting standards early.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than $1.235 billion in annual revenue; (2) the date we qualify as a "large accelerated filer," with at least $700.0 million of equity securities held by non-affiliates; (3) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (4) December 31, 2026, the last day of the fiscal year ending after the fifth anniversary of our IPO.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our common stock held by non-affiliates is more than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100.0 million during the most recently completed fiscal year and our common stock held by non-affiliates is more than $700.0 million measured on the last business day of our second fiscal quarter.

**Recently Issued Accounting Pronouncements**

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report.

**ITEM 7A. Quantitative and Qualitative Disclosures About Market Risks**

We are a smaller reporting company, as defined in Rule 12b-2 under the Exchange Act, for this reporting period and are not required to provide the information required under this item.

## ITEM 8. Consolidated Financial Statements and Supplementary Data

### Index to Consolidated Financial Statements

## Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Theseus Pharmaceuticals, Inc.

### Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Theseus Pharmaceuticals, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (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 "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at 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 U.S. generally accepted accounting principles.

### 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/ Ernst & Young LLP

We have served as the Company's auditor since 2021.
Boston, Massachusetts
March 9, 2023

**Theseus Pharmaceuticals, Inc.**
**Consolidated Balance Sheets**

(in thousands, except share and per share data)

| | DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 94,605 | $ 244,662 |
| Short-term marketable securities | 103,374 | — |
| Prepaid expenses and other current assets | 4,137 | 3,309 |
| Total current assets | 202,116 | 247,971 |
| Property and equipment, net | 416 | 11 |
| Operating lease right-of-use asset | 4,334 | — |
| Long-term marketable securities | 13,817 | — |
| Other assets | 1,764 | 2,947 |
| Total assets | $ 222,447 | $ 250,929 |
| **Liabilities and Stockholders' Equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 4,973 | $ 1,002 |
| Accrued expenses and other current liabilities | 5,414 | 2,678 |
| Operating lease liability, current portion | 743 | — |
| Total current liabilities | 11,130 | 3,680 |
| Operating lease liability, net of current portion | 3,236 | — |
| Restricted stock liability, net of current portion | 466 | 815 |
| Total liabilities | 14,832 | 4,495 |
| Commitments and contingencies (Note 9) | | |
| Stockholders' equity: | | |
| Preferred stock, $0.0001 par value; 50,000,000 shares authorized as of December 31, 2022 and December 31, 2021; 0 shares issued and outstanding as of December 31, 2022 and December 31, 2021 | — | — |
| Common stock, $0.0001 par value; 500,000,000 shares authorized as of December 31, 2022 and December 31, 2021; 38,734,446 and 38,702,650 shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively | 4 | 4 |
| Additional paid-in capital | 320,183 | 308,008 |
| Accumulated deficit | (112,186) | (61,578) |
| Accumulated other comprehensive loss | (386) | — |
| Total stockholders' equity | 207,615 | 246,434 |
| Total liabilities and stockholders' equity | $ 222,447 | $ 250,929 |

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

**Theseus Pharmaceuticals, Inc.**
**Consolidated Statements of Operations and Comprehensive Loss**

(in thousands, except share and per share data)

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Operating expenses: | | |
| Research and development | $ 35,698 | $ 18,328 |
| General and administrative | 18,388 | 9,008 |
| Total operating expenses | 54,086 | 27,336 |
| Loss from operations | (54,086) | (27,336) |
| Other income, net | 3,478 | 28 |
| Total other income, net | 3,478 | 28 |
| Net loss | $ (50,608) | $ (27,308) |
| Net loss attributable to common stockholders—basic and diluted | $ (50,608) | $ (27,308) |
| Weighted-average common stock outstanding—basic and diluted | 38,490,104 | 9,631,818 |
| Net loss per share attributable to common stockholders—basic and diluted | $ (1.31) | $ (2.84) |
| | | |
| Comprehensive loss: | | |
| Net loss | $ (50,608) | $ (27,308) |
| Other comprehensive loss: | | |
| Unrealized loss on marketable securities | (386) | — |
| Total comprehensive loss | $ (50,994) | $ (27,308) |

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

**Theseus Pharmaceuticals, Inc.**
**Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)**

(in thousands, except share data)

| | REDEEMABLE CONVERTIBLE PREFERRED STOCK | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | SERIES A $0.0001 PAR VALUE | | SERIES B $0.0001 PAR VALUE | | COMMON STOCK $0.0001 PAR VALUE | | ADDITIONAL PAID-IN CAPITAL | ACCUMULATED OTHER COMPREHENSIVE LOSS | ACCUMULATED DEFICIT | TOTAL STOCKHOLDERS' EQUITY (DEFICIT) |
| | SHARES | AMOUNT | SHARES | AMOUNT | SHARES | AMOUNT | | | | |
| Balance at December 31, 2020 | 16,734,179 | $ 41,289 | — | $ — | 882,789 | $ — | $ — | $ — | $ (34,270) | (34,270) |
| Issuance of Series B redeemable convertible preferred stock, net of issuance costs of $208 | — | — | 8,741,726 | 99,892 | — | — | — | — | — | — |
| Conversion of redeemable convertible preferred stock into common stock | (16,734,179) | (41,289) | (8,741,726) | (99,892) | 25,475,905 | 3 | 141,178 | — | — | 141,181 |
| Issuance of common stock upon closing of initial public offering, net of issuance costs of $16,285 | | | | | 11,172,190 | 1 | 162,469 | — | — | 162,470 |
| Vesting of restricted stock | — | — | — | — | 341,720 | — | — | — | — | — |
| Stock-based compensation | — | — | — | — | — | — | 4,361 | — | — | 4,361 |
| Net loss | — | — | — | — | — | — | — | — | (27,308) | (27,308) |
| Balance at December 31, 2021 | — | $ — | — | $ — | 37,872,604 | $ 4 | $ 308,008 | $ — | $ (61,578) | $ 246,434 |
| Vesting of restricted stock | — | — | — | — | 374,084 | — | — | — | — | — |
| Vesting of early exercised options | — | — | — | — | 144,137 | — | 581 | — | — | 581 |
| Stock-based compensation | — | — | — | — | — | — | 11,412 | — | — | 11,412 |
| Issuance of common stock under employee stock purchase plan | — | — | — | — | 31,796 | — | 182 | — | — | 182 |
| Unrealized loss on marketable securities | — | — | — | — | — | — | — | (386) | — | (386) |
| Net loss | — | — | — | — | — | — | — | — | (50,608) | (50,608) |
| Balance at December 31, 2022 | — | $ — | — | $ — | 38,422,621 | $ 4 | $ 320,183 | $ (386) | $ (112,186) | $ 207,615 |

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

**Theseus Pharmaceuticals, Inc.**
**Consolidated Statements of Cash Flows**

(in thousands)

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| **Cash flows from operating activities:** | | |
| Net loss | $ (50,608) | $ (27,308) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation expense | 50 | 2 |
| Stock-based compensation expense | 11,412 | 4,361 |
| Amortization and accretion of marketable securities | (655) | — |
| Non-cash interest income | (83) | — |
| Non-cash operating lease expense | 388 | — |
| Changes in operating assets and liabilities: | | |
| Prepaid expenses and other current assets | (829) | (3,196) |
| Other assets | 1,184 | (2,525) |
| Accounts payable | 3,971 | (150) |
| Accrued expenses and other current liabilities | 2,968 | 1,623 |
| Operating lease liability | (743) | — |
| Net cash used in operating activities | (32,945) | (27,193) |
| **Cash flows from investing activities:** | | |
| Purchases of short-term and long-term marketable securities | (191,439) | — |
| Sales and maturities of short-term and long-term marketable securities | 74,600 | — |
| Purchases of property and equipment | (455) | — |
| Net cash used in investing activities | (117,294) | — |
| **Cash flows from financing activities:** | | |
| Proceeds from initial public offering, net of underwriting discounts and commissions of $12,513 | — | 166,242 |
| Payment of initial public offering costs | — | (3,752) |
| Proceeds from issuance of Series B redeemable convertible preferred stock, net of issuance costs of $208 | — | 99,892 |
| Proceeds from early exercise of options | — | 1,395 |
| Proceeds from issuance of common stock under employee stock purchase plan | 182 | — |
| Net cash provided by financing activities | 182 | 263,777 |
| Net (decrease) increase in cash and cash equivalents | (150,057) | 236,584 |
| Cash and cash equivalents at beginning of year | 245,041 | 8,457 |
| Cash and cash equivalents at end of period | $ 94,984 | $ 245,041 |
| **Supplemental disclosure of cash flows:** | | |
| Conversion of redeemable convertible preferred stock into common stock | $ — | $ 141,181 |
| Purchases of property and equipment in accounts payable | $ — | $ 12 |
| Deferred financing costs in accounts payable | $ — | $ 19 |
| Vesting of early exercised options | $ 581 | $ — |
| Obtaining a right-of-use asset in exchange for an operating lease liability | $ 4,721 | $ — |

The following table provides a reconciliation of the cash, cash equivalents, and restricted cash balances as of each of the dates shown below:

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Cash and cash equivalents | $ 94,605 | $ 244,662 |
| Restricted cash (included in other assets) | 379 | 379 |
| Total cash, cash equivalents, and restricted cash | $ 94,984 | $ 245,041 |

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

**Theseus Pharmaceuticals, Inc.**

**Notes to Consolidated financial statements**

## 1. Nature of the Business

Theseus Pharmaceuticals, Inc. ("Theseus" or the "Company") is a clinical biopharmaceutical company focused on improving the lives of cancer patients through the discovery, development and commercialization of transformative targeted therapies. The Company was incorporated in December 2017 under the laws of the State of Delaware, and its principal offices are in Cambridge, Massachusetts.

### *Reverse Stock Split*

On September 27, 2021, the Company effected a one-for-1.32286 reverse stock split of shares of the Company's common stock and convertible preferred stock. All of the share and per share amounts included in the accompanying consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital. Shares of common stock underlying outstanding stock options were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased in accordance with the terms of the appropriate securities agreements. Stockholders entitled to fractional shares as a result of the reverse stock split received a cash payment in lieu of receiving fractional shares.

### *Initial Public Offering*

On October 12, 2021, the Company closed the initial public offering ("IPO"), in which it sold 10,000,200 shares of common stock at a public offering price of $16.00 per share. On October 25, 2021, the underwriters partially exercised their option to purchase an additional 1,171,990 shares of common stock at the public offering price of $16.00 per share. After deducting underwriting discounts, commissions and offering expenses, the aggregate net offering proceeds raised in the IPO were approximately $162.5 million. Upon the closing of the IPO, all of the Company's outstanding shares of redeemable convertible preferred stock automatically converted into an aggregate of 25,475,905 shares of common stock.

In connection with the closing of the IPO, the Company amended and restated its certificate of incorporation to among other things: (a) authorize 500,000,000 shares of voting common stock; (b) eliminate all references to the previously existing series of redeemable convertible preferred stock; and (c) authorize 50,000,000 shares of preferred stock that may be issued from time to time by the Company's board of directors (the "Board") in one or more series.

### *Basis of Presentation*

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("US GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative US GAAP as found in the ASC and as amended by Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

### *Liquidity*

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. The Company's development programs will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities.

Because of the numerous risks and uncertainties associated with product development, the Company is unable to predict the timing or amount of increased expenses or when or if the Company will be able to achieve or maintain profitability. Even if the Company is able to generate revenue from product sales, the Company may not become profitable. If the Company fails to become profitable or is unable to sustain profitability on a continuing basis, then the Company may be unable to continue its operations at planned levels and be forced to reduce or terminate its operations. The Company expects to incur substantial operating losses and negative cash flows from operations for the foreseeable future.

In accordance with Accounting Standards Codification ("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 that the consolidated financial statements are issued. As of December 31, 2022, the Company had an accumulated deficit of $112.2 million. During the year ended December 31, 2022, the Company incurred a loss of $50.6 million and utilized $32.9 million of cash in operations. The Company expects to continue to generate operating losses in the foreseeable future. The Company expects that its cash, cash equivalents, and marketable securities of $211.8 million at December 31, 2022 will be sufficient to fund its operating expenses and capital expenditure requirements for at least the next twelve months from issuance of the accompanying consolidated financial statements.

## 2. Summary of Significant Accounting Policies

### *Principles of Consolidation*

The accompanying consolidated financial statements include the accounts of Theseus Pharmaceuticals, Inc. and Theseus Securities Corporation, which is a Massachusetts subsidiary. All intercompany transactions and balances have been eliminated in consolidation.

### *Use of Estimates*

The preparation of consolidated financial statements in conformity with US 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 periods. Estimates and judgments are based on historical information and other market-specific or various relevant assumptions, including in certain circumstances, future projections, that management believes to be reasonable under the circumstances. Actual results could differ materially from estimates. Significant estimates and assumptions are used for, but not limited to, the accruals for research and development expenses, the incremental borrowing rate for determining the operating lease right-of-use ("ROU") asset and lease liabilities, and for periods prior to the completion of the IPO, the determination of fair value of equity instruments, and the fair value of the preferred stock tranche rights and the anti-dilution right, and stock-based compensation expense.

### *Concentration of Credit Risk*

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents, and marketable securities. Periodically, the Company maintains deposits in accredited financial institutions in excess of federally insured limits. The Company deposits its cash in financial institutions that it believes have high credit quality and have not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships. Such deposits have and will continue to exceed federally insured limits. The Company has not experienced any losses on its cash deposits. The Company's short-term and long-term marketable securities are invested in high grade securities with limited concentration in any one issuer, and as a result, the Company believes represent minimal credit risk.

***Fair Value of Financial Instruments***

The Company categorizes its assets and liabilities measured at fair value in accordance with ASC Topic 820, *Fair Value Measurement* ("ASC 820"), the authoritative accounting guidance that establishes a consistent framework for measuring fair value, and expands disclosures for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is defined as the exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, ASC 820 establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

- Level 1—Unadjusted quoted prices in active markets that are accessible at the measurement date for identical assets or liabilities;

- Level 2—Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liability; or

- Level 3—Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

***Cash and Cash Equivalents***

Cash includes cash in readily available checking accounts. Cash is carried at cost, which approximates its fair value. The Company considers all highly liquid marketable securities with original maturities of three months or less at the date of purchase to be cash equivalents. Cash equivalents are carried at fair market value based on quoted prices for identical assets.

***Restricted Cash***

Restricted cash consists of a restricted cash deposit of $0.4 million which serves as collateral for a letter of credit issued to the landlord of the Company's leased facility for a security deposit upon entering into the lease in September 2021. The Company classified this amount as restricted cash in the accompanying consolidated balance sheet within other assets as of December 31, 2022 and 2021.

***Marketable Securities***

All marketable securities have been classified as "available-for-sale" and are carried at fair value as determined based upon quoted market prices or pricing models for similar securities at period end. Marketable securities with contractual maturities less than 12 months at the balance sheet date are considered short-term marketable securities. Those marketable securities with contractual maturities 12 months or greater at the balance sheet date are considered long-term marketable securities. Dividend and interest income are recognized in the Company's consolidated statements of operations and comprehensive loss when earned. Realized gains and losses are included in earnings and are derived using the specific identification method for determining the cost of securities sold. Unrealized gains and losses are reported as a component of accumulated other comprehensive income (loss). The cost of the Company's available-for-sale debt securities is adjusted for amortization of premium and accretion of discounts to maturity. The Company reviews its portfolio of available-for-sale debt securities, using both quantitative and qualitative factors, to determine if declines in fair value below cost have resulted from a credit-related loss or other factors. If the decline in fair value is due to credit-related factors, a loss is recognized in statements of operations, whereas if the decline in fair value is not due to credit-related factors, the loss is recorded in other comprehensive income (loss).

***Property and Equipment, net***

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets as follows:

| | Estimated Useful Life (Years) |
|---|---|
| Office equipment | 5 years |
| Computer equipment and software | 3 years |
| Furniture and fixtures | 7 years |
| Leasehold improvements | Lesser of asset useful life or lease term |

Costs for capital assets not yet placed into service are capitalized as construction-in-progress and are depreciated once placed into service. When an item is sold or retired, the costs and related accumulated depreciation are eliminated, and the resulting gain or loss, if any, is included in the consolidated statement of operations. Repairs and maintenance costs are expensed as incurred.

***Leases***

Effective on January 1, 2021, the Company accounts for leases in accordance with ASC Topic 842, *Leases* ("ASC 842"). 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 Company, as operating or finance leases and records a ROU asset and a lease liability on the consolidated balance sheet for all real-estate leases with an initial lease term of greater than 12 months. Leases with a lease term of 12 months or less are not recorded on the balance sheet, but payments are recognized as expense on a straight-line basis over the lease term.

A lease qualifies as a finance lease if any of the following criteria are met at the inception of the lease: (i) there is a transfer of ownership of the leased asset to the Company by the end of the lease term, (ii) the Company holds an option to purchase the leased asset that it is reasonably certain to exercise, (iii) the lease term is for a major part of the remaining economic life of the leased asset, (iv) the present value of the sum of lease payments equals or exceeds substantially all of the fair value of the leased asset, or (v) the nature of the leased asset is specialized to the point that it is expected to provide the lessor no alternative use at the end of the lease term. All other leases are recorded as operating leases.

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 all real estate asset classes, the Company combines the lease and non-lease components of fixed costs in its lease arrangements as a single lease component. Variable costs, such as utilities or maintenance costs, are not included in the measurement of ROU assets and lease liabilities, but rather are expensed when the event determining the amount of variable consideration to be paid occurs.

Finance and operating 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 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. Finance lease assets are amortized to depreciation expense using the straight-line method over the shorter of the useful life of the related asset or the lease term. Finance lease payments are bifurcated into (i) a portion that is recorded as interest expense and (ii) a portion that reduces the finance liability associated with the lease.

***Impairment of Long-lived Assets***

Long-lived assets consist of property and equipment. The Company reviews the recoverability of its long-lived assets, including the related useful lives, whenever events or changes in circumstances indicate that the carrying amount of a long-lived asset might not be recoverable, based on undiscounted cash flows. If such assets are considered to be impaired, an impairment loss is recognized and is measured as the amount by which the carrying amount of the assets exceed their estimated fair value, which is measured based on the projected discounted future net cash flows arising from the assets. There were no impairments for the years ended December 31, 2022 and 2021.

***Accrued Research and Development Costs***

The Company records accrued liabilities for estimated costs of research and development activities conducted by service providers for sponsored research, preclinical studies and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced and includes these costs in accrued expenses in the accompanying consolidated balance sheets and within research and development expense in the accompanying statements of operations.

The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with service providers. The Company makes judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued costs and actual costs incurred since its inception.

***Deferred Issuance Costs***

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred issuance costs until such financings are consummated. After consummation of such an equity financing, these costs are recorded as a reduction of the proceeds generated as a result of the offering. Should the planned equity financing be abandoned, the deferred issuance costs, currently recorded within other assets, will be expensed immediately as a charge to operating expenses in the statements of operations and comprehensive loss. On October 6, 2021, the Company completed its IPO. Accordingly, the Company recognized deferred issuance costs of $3.8 million as a reduction from the gross proceeds associated with the closing of the IPO through additional paid-in capital in the accompanying consolidated balance sheet as of December 31, 2021.

***Research and Development Costs***

Research and development costs are expensed as incurred. Research and development costs consist of direct and indirect internal costs related to specific projects as well as fees paid to other entities that conduct certain research and development activities on the Company’s behalf.

***Patent Costs***

The Company expenses all costs as incurred in connection with patent applications, including direct application fees, and the legal and consulting expenses related to making such applications, and such costs are included in general and administrative expenses within the Company’s statements of operations.

***Stock-based Compensation***

The Company's stock-based compensation plan grants awards to employees and non-employees that may include stock options, restricted stock awards, restricted stock units, and other stock-based awards, and recognizes the expense in the consolidated statement of operations and comprehensive loss based on their grant date fair values. The fair values of stock options are estimated on the date of grant using the Black-Scholes option-pricing model. The fair values of restricted stock awards and restricted stock units are based on the fair value of the Company's common stock on the date of grant. The estimated grant date fair value of stock-based awards is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the award. The Company has performance-based vesting conditions in some of its awards, and all performance-based milestones have been met or waived as of December 31, 2021. The Company accounts for awards granted to non-employees using the same treatment as awards granted to employees. The Company recognizes forfeitures as they occur.

Estimating the fair value of stock options using the Black-Scholes option-pricing model requires the input of subjective assumptions including: the fair value of common stock, the expected term of stock options, the expected volatility of common stock, the risk-free interest rate for a period that approximates the expected term of stock options, and expected dividend yield. The fair value is the closing price of the Company's common stock on the Nasdaq Global Select Market as reported on the date of grant. The expected term is estimated using the "simplified" method for awards that qualify as "plain-vanilla", which deems the expected term to be the midpoint between the vesting date and the contractual life of the stock-based awards. For expected volatility, the Company based its computation on the historical volatility of a representative group of public companies with similar characteristics, including stage of product development, life science industry focus, length of trading history and similar vesting provisions. The risk-free interest rate is based on the US Treasury yield in effect at the time of grant for zero-coupon US Treasury notes with maturities approximately equal to the expected term of the awards. The expected dividend yield is assumed to be zero as the Company has never paid cash dividends on its common stock and has no plans to pay cash dividends on common stock in the visible future.

Certain assumptions used in the Black-Scholes option-pricing model represent management's best estimates and involve a number of variables, uncertainties and assumptions and the application of management's judgment, as they are inherently subjective. If any assumptions change, the Company's stock-based compensation expense could be materially different in the future.

The Company's equity incentive plan allows for but does not require the inclusion of early exercise provisions in individual awards. The unvested shares of any restricted stock awards are held in escrow as the stock award vests or until award holder termination, whichever occurs first. In the event of a termination, the Company has the right of repurchase, at its option, the portion of unvested stock awards from the terminated award holder at their original issuance price. For all unvested stock option awards for which the award recipient has transferred cash to the Company prior to the vesting date, a liability is established related to the cash received for the unvested portion of the stock awards, which represents the Company's obligation if all award holders were to be terminated.

Prior to the Company's IPO, the estimated fair value of its common stock was determined by the Board of Directors as of the date of each option grant, with input from management, considering the most recently available third-party valuations of common stock and the Board's assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. Historically, these independent third-party valuations of the Company's equity instruments were performed contemporaneously with identified value inflection points.

These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation* (the "Practice Aid"). The Practice Aid identifies various

available methods for allocating the enterprise value across classes of series of capital stock in determining the fair value of the Company's common stock at each valuation date.

The Company issues rights to employees to purchase common stock under the Theseus Pharmaceuticals, Inc. 2021 Employee Stock Purchase Plan (the "ESPP"). The purchase price of common stock under the Company's ESPP is equal to 85% of the lesser of (i) the fair market value per share of common stock on the first trading day of an offering period and (ii) the fair market value per share of common stock on the purchase date. The fair value of the discounted purchases made under the ESPP is calculated using the Black-Scholes option-pricing model. The fair value of the look-back provision plus the 15% discount is recognized as compensation expense over the 180-day purchase period.

***Net Loss Per Share***

The Company follows the two-class method when computing net loss allocable to common securities per share as the Company has issued shares that meet the definition of participating securities, see Note 13 for additional information. During periods of loss, there is no allocation required under the two-class method since the participating securities do not have a contractual obligation to fund the losses of the Company.

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock and potentially dilutive securities outstanding during the period determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share calculation, diluted net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding after giving consideration to the dilutive effect of convertible preferred stock, restricted common stock, restricted stock units and stock options that are outstanding during the period. The Company has generated a net loss in all periods presented, therefore the basic and diluted net loss per share attributable to common stockholders are the same as the inclusion of the potentially dilutive securities would be anti-dilutive.

***Redeemable Convertible Preferred Stock***

Prior to the Company's IPO, the Company's redeemable convertible preferred stock was classified as temporary equity in the consolidated balance sheets and excluded from stockholders' equity (deficit) as the potential redemption of such stock was outside the Company's control. Upon the completion of the Company's IPO on October 6, 2021, all outstanding shares of the Company's redeemable convertible preferred stock converted into shares of the Company's common stock.

***Income Taxes***

Income taxes for the Company are recorded in accordance with ASC Topic 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Under this method, deferred income tax assets and liabilities are recognized based on future income tax consequences attributable to differences between the financial statement carrying amount of existing assets and liabilities, and their respective income tax basis. Deferred income tax assets and liabilities are measured using enacted income tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect of changes in income tax rates on deferred income tax assets and liabilities is recognized as income or expense in the period of the change provided that the future realization of any income tax benefits is more likely than not.

The Company provides reserves for potential payments of tax to various tax authorities related to uncertain tax positions. The tax benefits recorded are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is "more likely than not" to be realized following resolution of any uncertainty related to the tax benefit, assuming that the matter in question will be raised by

the tax authorities. The Company's policy is to recognize interest and penalties accrued on any uncertain tax positions, if any, as a component of income tax expense in its statements of operations and comprehensive loss.

***Comprehensive Loss***

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders, including unrealized gains and losses on marketable securities. For the year ended December 31, 2022, the unrealized losses on marketable securities represent the only component of other comprehensive loss that is excluded from the reported net loss. For the year ended December 31, 2021, there were no differences between net loss and comprehensive loss.

***Segments***

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the chief operating decision maker ("CODM") in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its chief executive officer. The Company has determined it operates in a single operating segment and has one reportable segment. All long-lived assets of the Company reside in the US.

***Recently Issued Accounting Pronouncements***

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

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326)—Measurement of Credit Losses on Financial Instruments*, which has been subsequently amended ("ASU 2016-13"). ASU 2016-13 significantly changes the impairment model for most financial assets and certain other instruments. ASU 2016-13 will require immediate recognition of estimated credit losses expected to occur over the remaining life of many financial assets, which will generally result in earlier recognition of allowances for credit losses on trade receivables, loans and other financial instruments. ASU 2016-13 is effective for the Company's fiscal year beginning after December 15, 2022 and subsequent interim periods. The adoption of this standard is not expected to have a material impact on the Company's consolidated financial statements and related disclosures.

**3. Fair Value of Financial Assets and Liabilities**

The carrying values of other current assets, accounts payable, and accrued expenses approximate their fair values due to the short-term nature of these instruments. The Company's marketable securities, which may include both short-term and long-term marketable securities consisting of high-quality, marketable debt instruments of corporations, are measured at fair value in accordance with the fair value hierarchy.

Assets measured at fair value on a recurring basis as of December 31, 2022 are as follows (in thousands):

| | FAIR VALUE MEASUREMENTS AT DECEMBER 31, 2022 | | | |
|---|---|---|---|---|
| | LEVEL 1 | LEVEL 2 | LEVEL 3 | TOTAL |
| Cash equivalents: | | | | |
| Money market funds | $ 6,846 | $ — | $ — | $ 6,846 |
| Commercial paper | — | 3,989 | — | 3,989 |
| Marketable Securities: | | | | |
| Commercial paper | — | 25,187 | — | 25,187 |
| Corporate debt securities | — | 45,673 | — | 45,673 |
| Asset-backed securities | — | 13,574 | — | 13,574 |
| Government securities | — | 32,757 | — | 32,757 |
| Total financial assets | $ 6,846 | $ 121,180 | $ — | $ 128,026 |

As of the year ended December 31, 2021, there were no assets or liabilities measured at fair value. During the year ended December 31, 2022, there were no transfers between fair value levels.

**4. Marketable Securities**

The Company's investment policy defines allowable investments and establishes guidelines relating to credit quality, diversification, and maturities of its marketable securities to preserve principal and maintain liquidity. In accordance with the Company's investment policy, it has invested funds in marketable securities as of December 31, 2022. The Company's marketable securities are classified as available-for-sale investments.

The cost, gross unrealized holding gains, gross unrealized holding losses and fair value of marketable securities by types and classes of security at December 31, 2022 consisted of the following (in thousands):

| | DECEMBER 31, 2022 | | | | |
|---|---|---|---|---|---|
| | MATURITY IN YEARS | AMORTIZED COST | UNREALIZED GAIN | UNREALIZED LOSS | FAIR VALUE |
| Commercial paper | less than 1 | $ 25,187 | $ — | $ — | $ 25,187 |
| Corporate debt securities | less than 1 | 39,071 | 9 | (185) | 38,895 |
| Asset-backed securities | less than 1 | 8,555 | 2 | (10) | 8,547 |
| Government securities | less than 1 | 30,892 | 8 | (155) | 30,745 |
| **Short-term marketable securities** | | $ 103,705 | $ 19 | $ (350) | $ 103,374 |
| | | | | | |
| Corporate debt securities | 1 - 2 | 6,783 | — | (5) | 6,778 |
| Asset backed securities | 1 - 2 | 5,074 | — | (47) | 5,027 |
| Government securities | 1 - 2 | 2,015 | — | (3) | 2,012 |
| **Long-term marketable securities** | | $ 13,872 | $ — | $ (55) | $ 13,817 |

The Company reviews its marketable securities to identify and evaluate investments that have an indication of possible other-than-temporary impairment. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition and near-term prospects of the investee, and the Company's intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in market value. At December 31, 2022, the Company did not have any securities in material unrealized loss positions. The Company generally does not intend to sell any marketable securities prior to recovery of their amortized cost basis for any marketable securities in an unrealized loss position. Further, such marketable securities are invested in high grade securities. As such, the Company has classified these losses as temporary in nature.

The Company has determined that there were no material declines in fair value of its marketable securities due to credit-related factors as of December 31, 2022.

**5. Property and Equipment**

Property and equipment, net consisted of the following as of December 31, 2022 and 2021 (in thousands):

| | DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Computer equipment | $ 50 | $ 12 |
| Furniture and fixtures | 341 | — |
| Office equipment | 76 | — |
| Property and equipment | 467 | 12 |
| Less: accumulated depreciation | (51) | (1) |
| Property and equipment, net | $ 416 | $ 11 |

Depreciation expense for each of the years ended December 31, 2022 and 2021 was approximately $50,000 and $2,000, respectively. There were no impairments recorded to date.

**6. Accrued Expenses**

Accrued expenses consisted of the following as of December 31, 2022 and 2021 (in thousands):

| | DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Accrued research and development | $ 1,498 | $ 233 |
| Accrued legal | 164 | 199 |
| Accrued compensation and benefits | 3,130 | 1,353 |
| Accrued other | 273 | 313 |
| Restricted stock liability, current | 349 | 580 |
| Total accrued expenses and other current liabilities | $ 5,414 | $ 2,678 |

**7. License Agreement**

*Agreement Description*

In June 2018, the Company entered into a license agreement with ARIAD (the “ARIAD License Agreement”), for an exclusive, transferable (subject to certain restrictions), sublicensable (subject to certain conditions), worldwide license, under certain of ARIAD’s patent rights, know-how and compounds and a certain ARIAD chemical library, to develop, use, manufacture, market and commercialize certain compounds, and products that contain such compounds, that are therapeutically useful for the treatment of diseases and disorders in humans, including with respect to KIT (referred to as C-KIT, CD117 and stem cell factor receptor in the ARIAD License Agreement).

The Company is required to pay ARIAD tiered royalty payments that are low- to mid-single digits of the Company’s future net sales and those of its sublicensees of each product comprising a licensed ARIAD compound in each country. The Company is also responsible for costs relating to the prosecution and maintenance of the licensed patents. The agreement contains anti-stacking and generic competition provisions on the royalties whereby the Company may deduct a percentage of the amounts due for royalties from its payments if the Company enters into a third-party license agreement, and may reduce the rates in the

event a generic product is being marketed and sold by a third party and the average net sales as measured over a specified period of time are at least a certain percentage lower than the average net sales during a specified period of time immediately prior to the launch of the generic product.

The term of the agreement commenced in June 2018 and unless earlier terminated as provided in the agreement for breach of terms by either party or for convenience by the Company with advanced written notice, shall continue in full force and effect, on a country-by-country and product-by-product basis until the date on which the royalty term in such country with respect to such product expires. The royalty term is the period from the first commercial sale of such product in such country until the later of (a) the expiry of all patents that cover the product in such country or (b) ten years after the first commercial sale.

The ARIAD License Agreement terminates, on a product-by-product and country-by-country basis, on expiration of the royalty term for such product for the applicable country. Thereafter, the licenses from ARIAD to the Company with respect to such product for such country will convert to a fully paid, royalty-free, irrevocable and perpetual license.

**8. Leases**

On July 19, 2021, the Company entered into a lease agreement for office space in Cambridge, Massachusetts, on a month-to-month basis, which was determined to be a short-term lease as the Company was not reasonably certain to extend the lease beyond twelve months. The Company recognized lease payments as incurred over the lease term, and recognized short-term lease expense of $0.2 million for each of the years ended December 31, 2022 and 2021.

On September 16, 2021, the Company entered into an operating lease agreement for 7,351 rentable square feet of office space in Cambridge, Massachusetts. The premises required additional build-out at the time the lease agreement was entered into. The lease commenced in March 2022 when the space was made available for use. Upon lease commencement, the Company recorded a ROU asset of $4.7 million and a corresponding lease liability of $4.7 million. The lease has a term of 7 years and an expiration date of March 22, 2029, with lease payments made on a monthly basis. The initial annual base rent is approximately $0.8 million, subject to a 3% annual rent increase, plus an allocation of the Company’s proportionate share of building operating costs such as maintenance, utilities, and insurance that are treated as variable costs and excluded from the measurement of the lease. The Company is entitled to one option to extend the lease term for an additional period of five years. The option to extend the lease term is not reflected in the ROU asset and lease liability as it is not reasonably certain of being exercised. Pursuant to the terms of the lease, the Company provided a security deposit in the form of a letter of credit in the amount of approximately $0.4 million upon signing, which is recognized as restricted cash within other assets on the consolidated balance sheets.

As of December 31, 2022, the weighted-average remaining lease term was 6.3 years, and the weighted-average discount rate was 9.1%.

The following table presents future lease payments under the terms of the Company's operating leases as of December 31, 2022, including a reconciliation to the present value of operating lease liabilities recognized in the consolidated balance sheet (in thousands):

| Fiscal Year | Operating Lease |
|---|---|
| 2023 | $ 774 |
| 2024 | 797 |
| 2025 | 821 |
| 2026 | 846 |
| Thereafter | 1,996 |
| Total future minimum lease payments | 5,234 |
| Less: imputed interest | (1,255) |
| Present value of lease liabilities | $ 3,979 |

**9. Commitments and Contingencies**

*Legal Proceedings*

The Company may, from time to time, be party to litigation arising in the ordinary course of business. The Company was not subject to any material legal proceedings during the years ended December 31, 2022 and 2021, and no material legal proceedings are currently pending or, to the best of the Company's knowledge, threatened.

*Indemnification Agreements*

The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to the indemnification agreements, the Company agrees to indemnify, hold harmless, and to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners, in connection with any US patent or any copyright or other intellectual property infringement claim by any third-party with respect to the Company's products. The term of these indemnification agreements is generally perpetual any time after execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements.

*401(k) Plan*

The Company maintains a defined-contribution plan under Section 401(k) of the Internal Revenue Code of 1986 (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation. Matching contributions to the 401(k) Plan may be made at the discretion of management. The Company contributed $0.4 million to the 401(k) Plan during the year ended December 31, 2022. There were no employer contributions made to the 401(k) Plan during the year ended December 31, 2021.

**10. Stockholders' Equity**

***Preferred Stock***

The Company was authorized to issue up to 50,000,000 shares of preferred stock, $0.0001 par value per share, as of December 31, 2022 and 2021. There were no shares of preferred stock outstanding as of December 31, 2022 and 2021.

***Common Stock***

The Company was authorized to issue up to 500,000,000 shares of common stock, $0.0001 par value per share, as of December 31, 2022 and 2021. The voting, dividend and liquidation rights of the holders of the Company's common stock are subject to and qualified by the rights, powers and preference of the holders of any series of preferred stock.

*Voting Rights*

Each share of common stock entitles the holder to one vote on all matters submitted to the stockholders for a vote.

*Dividends*

Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of outstanding shares of the Company's common stock are entitled to receive dividends out of funds legally available if and when the Board, in its discretion, determines to issue dividends. As of December 31, 2022, no cash dividends have been declared or paid.

*Liquidation Rights*

Upon the Company's dissolution, liquidation, or winding-up, the assets legally available for distribution to stockholders are distributable ratably among holders of the Company's common stock, subject to prior satisfaction of all outstanding debt and liabilities, and the preferential rights and payment of liquidation preferences, if any, on any outstanding shares of preferred stock.

**11. Stock-Based Compensation**

*Equity Incentive Plans*

In September 2021, the Company adopted the Theseus Pharmaceuticals, Inc. 2021 Equity Incentive Plan (the "2021 Plan"), which replaced the 2018 Stock Incentive Plan (the "2018 Plan") and allows for the issuance of stock options, restricted stock awards, restricted stock units ("RSUs"), and other types of equity awards. No further awards were made under the 2018 Plan as of the effective date of the 2021 Plan. Any options or awards outstanding under the 2018 Plan are governed by their existing terms. On the first day of each fiscal year of the Company during the term of the Plan, commencing on January 1, 2023 and ending on (and including) January 1, 2031, the aggregate number of Common Shares that may be issued under the Plan shall automatically increase by a number equal to the lesser of (a) five percent (5%) of the total number of Common Shares actually issued and outstanding on the last day of the preceding fiscal year, or (b) a number of Common Shares determined by the Board. As of December 31, 2022 and 2021, the number of shares reserved for issuance upon the exercise of outstanding options was 9,132,930 and 9,094,083, respectively. Of those shares reserved for issuance, there were 1,843,494 and 3,930,440 shares available for future grant as of December 31, 2022 and 2021, respectively.

The 2021 Plan is administered by the Board (or its compensation committee), and the exercise prices, vesting and other restrictions for the awards are determined at the discretion of the Board, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the common stock on the date of grant. Stock options awarded under the 2021 Plan expire ten years after the grant date unless the Board sets a shorter term. Stock options granted to employees and nonemployees typically vest over four years. Shares of restricted stock awards granted to employees, officers, members of the Board, advisors, and consultants of the Company typically vest over five years. Certain executives who are option holders are able to early exercise stock option awards prior to full satisfaction of the vesting conditions. If and when this occurs, the executive receives restricted common stock upon exercise of the option, and the shares remain subject to the Company's right of repurchase until the remaining vesting terms are met. During the year ended December 31, 2021, options to purchase 345,930 shares of common stock were exercised early. As of

December 31, 2022 and December 31, 2021, the Company recognized $0.8 million and $1.4 million, respectively, as a liability related to the early exercise. The amount of remaining unvested shares related to the early exercise as of December 31, 2022 and December 31, 2021 were 201,793 and 345,930, respectively. There were no additional early exercises of options during the year ended December 31, 2022.

*Employee Stock Purchase Plan*

In September 2021, the Company's board of directors adopted, and its stockholders approved, the ESPP, which became effective on October 6, 2021. The number of shares of common stock initially reserved for issuance under the ESPP is 400,000. In addition, on the first day of each fiscal year of the Company during the term of the ESPP, commencing on January 1, 2023 and concluding on January 1, 2041, the aggregate number of shares of common stock reserved for issuance under the ESPP shall automatically increase by a number equal to the lesser of (i) one percent (1%) of the total number of shares of common stock actually issued and outstanding on the last day of the preceding fiscal year, and (ii) a number of shares of common stock determined by the Company's board of directors. Shares of common stock issued pursuant to the ESPP may be authorized but unissued shares or treasury shares. As of December 31, 2022, the number of shares of common stock that may be issued under the ESPP is 368,204.

The ESPP enables eligible employees to purchase shares of common stock of the Company at the end of each offering period at a price equal to 85% of the lower of the fair market value of the common stock at the commencement date of each offering period or the relevant date of purchase. Participation in the ESPP is voluntary. Eligible employees become participants in the ESPP by enrolling in the plan and authorizing payroll deductions. During the year ended December 31, 2022, 31,796 shares of common stock were issued under the ESPP, at an average price of $5.86 per share. Cash received from purchases under the ESPP for the year ended December 31, 2022 was $0.2 million. The Company recorded stock-based compensation expense related to the ESPP of $0.2 million for the year ended December 31, 2022.

*Stock Option Valuation*

The assumptions that the Company used in Black-Scholes option-pricing model to determine the grant-date fair value of stock options granted for the years ended December 31, 2022 and 2021 are as follows:

| | DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Risk-free interest rate | 1.60% - 4.20% | 1.07% |
| Expected term (in years) | 1.03 - 6.08 | 5.2 - 6.1 |
| Expected volatility | 78.00% - 90.51% | 75.58% - 83.56% |
| Expected dividend yield | 0.00% | 0.00% |

A summary of option activity under the Plans during the years ended December 31, 2022 and 2021 is as follows (in thousands except share, per share data and contractual terms):

| | SHARES | WEIGHTED-AVERAGE PER-SHARE EXERCISE PRICE | WEIGHTED-AVERAGE REMAINING CONTRACTUAL TERM | AGGREGATE INTRINSIC VALUE |
|---|---|---|---|---|
| Outstanding as of December 31, 2021 | 5,163,643 | $ 4.31 | 9.29 | $ 44,463 |
| Granted | 2,366,200 | 10.05 | | |
| Forfeited | (272,057) | (8.29) | | |
| Outstanding as of December 31, 2022 | 7,257,786 | $ 5.95 | 8.58 | 10,750.63 |
| Options vested and exercisable as of December 31, 2022 | 2,367,914 | $ 3.59 | 8.25 | $ 5,736.58 |

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 of options granted during the year ended December 31, 2022 was $6.93. Stock-based compensation expense for options granted of $10.8 million was recorded as of December 31, 2022. As of December 31, 2022, there was $23.8 million of unrecognized stock-based compensation expense related to unvested stock options. The unrecognized stock-based compensation expense is estimated to be recognized over a period of 2.5 years as of December 31, 2022.

The total fair value of options vested as of December 31, 2022 and 2021 was $10.5 million and $2.4 million, respectively.

*Restricted Stock Units*

The Company issues RSUs that generally vest over a four-year period with 25% of the RSUs vesting one year from the vesting commencement date, and the remainder vesting quarterly thereafter over the following 36 months. Any unvested shares underlying an RSU will be forfeited upon termination of services. The fair value of an RSU is equal to the fair market value price of the Company's common stock on the date of grant.

A summary of RSU activity during the year ended December 31, 2022 is as follows:

| | SHARES | WEIGHTED-AVERAGE PER-SHARE GRANT-DATE FAIR VALUE |
|---|---|---|
| Unvested shares at December 31, 2021 | — | $ — |
| Granted | 35,900 | 11.21 |
| Forfeited | (4,250) | 11.21 |
| Unvested shares at December 31, 2022 | 31,650 | $ 11.21 |

As of December 31, 2022, there was $0.2 million of unrecognized stock-based compensation expense related to unvested RSUs. The unrecognized stock-based compensation expense is estimated to be recognized over a period of 3.2 years as of December 31, 2022. There were no RSUs granted during the year ended December 31, 2021.

*Shares of Restricted Common Stock*

The Company issued shares of restricted common stock to its founders in May 2018, which vest monthly over five years through 2023. At issuance, these shares also contained certain performance-based vesting criteria which were associated with the milestone events applicable to the formerly outstanding shares of Series A preferred stock, two of which were achieved in 2020. In conjunction with the termination of the Series A preferred stock purchase agreement, the final performance-based vesting criteria was waived, leaving only service-based vesting criteria remaining for the founders' shares through the end of the requisite service period. As noted above, certain executives who are option holders are able to early exercise stock option awards prior to full satisfaction of the vesting conditions. If and when such exercise occurs, the executive receives shares of restricted common stock. Early exercise shares are included in the table below.

A summary of restricted stock activity under the Plan during the years ended December 31, 2022 and 2021 is as follows:

| | SHARES | WEIGHTED-AVERAGE PER-SHARE GRANT-DATE FAIR VALUE |
|---|---|---|
| Unvested shares at December 31, 2021 | 830,046 | $ 2.85 |
| Vesting of restricted common stock | (518,221) | 2.18 |
| Unvested shares at December 31, 2022 | 311,825 | $ 3.96 |

As of December 31, 2022, there was $1.2 million of unrecognized stock-based compensation expense related to unvested restricted stock. The unrecognized stock-based compensation expense is estimated to be recognized over a period of 1.7 years as of December 31, 2022.

*Stock-based Compensation Expense*

Total stock-based compensation expense recorded as research and development and general and administrative expenses, respectively, for employees, directors and non-employees during the years ended December 31, 2022 and 2021 was as follows (in thousands):

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Research and development | $ 6,612 | $ 2,250 |
| General and administrative | 4,800 | 2,111 |
| | $ 11,412 | $ 4,361 |

During the year ended December 31, 2022, the Company modified the terms of certain equity awards held by a departing employee, resulting in $1.8 million of stock-based compensation expense.

## 12. Income Taxes

The Company has not recorded a current or deferred tax provision for the years ended December 31, 2022 and 2021.

The effective income tax rate differed from the amount computed by applying the federal statutory rate to the Company's loss before income taxes as follows:

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Tax effected at statutory rate | 21.0 % | 21.0 % |
| State taxes | 5.6 | 5.3 |
| Stock compensation | (1.7) | (3.0) |
| Non-deductible expenses | (0.9) | — |
| Research and development credits | 3.6 | 3.3 |
| | 27.6 | 26.6 |
| Change in valuation allowance | (27.6) | (26.6) |
| Total | — % | — % |

Deferred tax assets and liabilities consist of the following at December 31, 2022 and 2021 (in thousands):

| | DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| **Deferred Tax Assets** | | |
| Net operating loss carryforwards | $ 12,957 | $ 9,420 |
| Research and development credits | 2,670 | 916 |
| Stock-based compensation expense | 1,506 | 116 |
| Accruals and reserves | 717 | 367 |
| Intangible assets | 647 | 702 |
| Operating lease liability | 1,087 | — |
| Capitalized research and development | 7,238 | — |
| Gross deferred tax assets | 26,822 | 11,521 |
| **Deferred Tax Liabilities** | | |
| Depreciation | $ (114) | $ (3) |
| Operating lease right-of-use asset | (1,184) | — |
| Gross deferred tax liabilities | (1,298) | (3) |
| Net deferred tax assets before valuation allowance | 25,524 | 11,518 |
| Valuation allowance | (25,524) | (11,518) |
| Net deferred tax asset | $ — | $ — |

As required by ASC 740, the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which is composed principally of net operating loss carryforwards. The Company has determined that it is more likely than not that the Company will not realize the benefits of its federal and state deferred tax assets, and, as a result, a valuation allowance of $25.5 million and $11.5 million has been established at 2022 and 2021, respectively. The change in the valuation allowance was $14.0 million and $7.3 million for the years ended December 31, 2022 and 2021.

Beginning in 2022, Tax Cuts and Jobs Act ("TCJA") amended Section 174 and now requires US-based and non-U.S-based research and experimental ("R&E") expenditures to be capitalized and amortized over a

period of five or 15 years, respectively, for amounts paid in tax years starting after December 31, 2021. Prior to the TCJA amendment, Section 174 allowed taxpayers to immediately deduct R&E expenditures in the year paid or incurred. The Company has applied this required change in accounting method beginning in 2022 and the computation may be adjusted pending future IRS guidance.

The Company has incurred NOLs from inception. At December 31, 2022, the Company had federal and state NOL carryforwards of approximately $47.0 million and $48.9 million, respectively, available to reduce future taxable income. The federal NOLs are not subject to expiration and the state NOLs begin to expire in 2037. As of December 31, 2022, the Company also had federal and state research and development tax credit carryforwards of approximately $1.8 million and $1.0 million, respectively, to offset future income taxes, which will begin to expire beginning in December 2035.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50 percentage points, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed numerous financings since its inception, which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

The Company follows the provisions of ASC 740-10, "*Accounting for Uncertainty in Income Taxes*," which specifies how tax benefits for uncertain tax positions are to be recognized, measured, and recorded in financial statements; requires certain disclosures of uncertain tax matters; specifies how reserves for uncertain tax positions should be classified on the balance sheet; and provides transition and interim period guidance, among other provisions. As of December 31, 2022 and 2021, the Company had no unrecognized tax benefits. The company has not identified any uncertain positions with respect to the credit computations. The Company's policy is to recognize interest and penalties accrued on any uncertain tax positions as a component of income tax expense, if any, in its statements of operations.

For the years ended December 31, 2022 and 2021, no estimated interest or penalties were recognized on uncertain tax positions. The Company does not expect any significant change in its uncertain tax positions in the next 12 months.

The Company files US federal and state income tax returns and is generally subject to income tax examinations by these authorities for all tax years after December 31, 2017. Currently, no federal or state income tax returns are under examination by the respective income tax authorities.

## 13. Net Loss Per Share

Basic and diluted loss per share is computed by dividing net loss attributable to common stockholders by the weighted-average common shares outstanding (in thousands, except share and per share data):

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Numerator: | | |
| Net loss | $ (50,608) | $ (27,308) |
| Net loss attributable to common stockholders - basic and diluted | $ (50,608) | $ (27,308) |
| Denominator: | | |
| Weighted-average common stock outstanding - basic and diluted | 38,490,104 | 9,631,818 |
| Net loss per share attributable to common stockholders - basic and diluted | $ (1.31) | $ (2.84) |

The Company's potentially dilutive securities, which include preferred stock, unvested restricted common stock, unvested RSUs and stock options, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following from the computation of diluted net loss per share attributable to common stockholders at December 31, 2022 and 2021 because including them would have had an anti-dilutive effect:

| | DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Preferred Stock | — | — |
| Unvested restricted stock | 311,825 | 830,046 |
| Unvested RSUs | 31,650 | — |
| Options to purchase common stock | 7,257,786 | 5,163,643 |
| | 7,601,261 | 5,993,689 |

## 14. Related Party Transactions

Iain Dukes is a founding member of the Company and has served as a member of the Board since June 2018. From June 2018 until April 2021, Dr. Dukes served as the Company's Chief Executive Officer under a consulting agreement, and from April 2021 until September 2021, Dr. Dukes served as the Executive Chairman. On September 15, 2021, Dr. Dukes transitioned into his role as Chairman of the Board. During the year ended December 31, 2021, Dr. Dukes earned compensation of $0.3 million, of which $54,000 was payable as of year-end. As of December 31, 2021, Dr. Dukes owned 388,324 shares of the Company's common stock, and held options to purchase an additional 464,637 shares of common stock.

## 15. Subsequent Events

Subsequent to December 31, 2022, the Company sold an aggregate of 4,816,301 shares of common stock pursuant to an "at-the-market" program for net proceeds of $49.1 million.

## 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*

We maintain "disclosure controls and procedures," as defined in Rule 13a-15(e) and Rule 15d-15(e) under the Exchange Act that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022. Our disclosure controls and procedures are designed to ensure that information we are required to disclose in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosures, and is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms.

Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at a reasonable assurance level as of December 31, 2022.

### *Management's Report on Internal Control over Financial Reporting*

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of the effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies and procedures included in such controls may deteriorate. Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control - Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, our management concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

### *Attestation Report of the Registered Public Accounting Firm*

This Annual Report does not include an attestation report of our registered public accounting firm due to an exemption provided by the JOBS Act for "emerging growth companies."

### *Changes in Internal Control over Financial Reporting*

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15(d)-15(f) under the Exchange Act) that occurred during the quarter ended December 31, 2022 that has materially affected, or is 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 contained in our definitive proxy statement to be filed with the SEC in connection with the 2022 Annual Meeting of Stockholders within 120 days after December 31, 2022 (the Proxy Statement), and is incorporated in this Annual Report on Form 10-K by reference.

We have adopted a Code of Conduct that applies to all officers, directors and employees in connection with their work for us. The full text of our Code of Conduct is posted on the investor relations page of our website at ir.theseusrx.com/corporate-governance.

We intend to satisfy any disclosure requirements under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Code of Conduct by posting such information on our website, at the Internet address and location specified above.

**ITEM 11. Executive Compensation**

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

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

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

**ITEM 13. Certain Relationships and Related Transactions and Director Independence**

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

**ITEM 14. Principal Accounting Fees and Services**

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

Our independent public accounting firm is Ernst & Young LLP, Boston, Massachusetts, PCAOB Auditor ID 42.

## PART IV

### ITEM 15. Exhibits and Financial Statement Schedules

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

(1) Financial Statements (included in Part II of this Annual Report on Form 10-K):

- Report of Independent Registered Public Accounting Firm (PCAOB ID: 42)
- Consolidated Balance Sheets
- Consolidated Statements of Operations and Comprehensive Loss
- Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)
- Consolidated Statements of Cash Flows
- Notes to Consolidated Financial Statements

(2) Financial Statement Schedules:

All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements

(b) The following exhibits are included herein or incorporated herein by reference:

### INDEX TO EXHIBITS

| Exhibit No. | Description | Form | File No. | Referenced Exhibit | Filing Date | Filed Herewith |
|---|---|---|---|---|---|---|
| 3.1 | Amended and Restated Certificate of Incorporation of the Registrant. | 10-Q | 001-40869 | 3.1 | August 11, 2022 | |
| 3.2 | Amended and Restated Bylaws of Registrant. | 10-Q | 001-40869 | 3.2 | August 11, 2022 | |
| 4.1 | Amended and Restated Investors' Rights Agreement, dated January 22, 2021, by and among the Registrant and the other parties thereto. | S-1 | 333-259549 | 4.2 | September 15, 2021 | |
| 4.2 | Description of Registrant's Securities registered pursuant to Section 12 of the Securities Exchange Act of 1934 | 10-K | 001-40869 | 4.2 | March 10, 2022 | |
| 10.1 | Form of Indemnification Agreement. | S-1/A | 333-259549 | 10.1 | September 30, 2021 | |

| | | | | | |
|---|---|---|---|---|---|
| 10.2 | 2018 Stock Plan. | S-1 | 333-259549 | 10.2 | September 15, 2021 |
| 10.3 | 2021 Equity Incentive Plan and forms of equity agreements thereunder. | S-1/A | 333-259549 | 10.3 | September 30, 2021 |
| 10.4 | 2021 Employee Stock Purchase Plan and form of subscription agreement. | S-1/A | 333-259549 | 10.4 | September 30, 2021 |
| 10.5 | Compensation Program for Non-Employee Directors. | S-1 | 333-259549 | 10.5 | September 15, 2021 |
| 10.6+ | License Agreement by and between ARIAD Pharmaceuticals, Inc. and the Registrant, dated as of June 13, 2018. | S-1 | 333-259549 | 10.6 | September 15, 2021 |
| 10.7 | Incentive Bonus Plan. | S-1 | 333-259549 | 10.7 | September 15, 2021 |
| 10.8 | Offer Letter, dated September 10, 2021, by and between the Registrant and Timothy P. Clackson. | S-1 | 333-259549 | 10.8 | September 15, 2021 |
| 10.9 | Offer Letter, dated September 10, 2021, by and between the Registrant and William C. Shakespeare. | S-1 | 333-259549 | 10.9 | September 15, 2021 |
| 10.10 | Offer Letter, dated September 10, 2021, by and between the Registrant and David C. Dalgarno. | S-1 | 333-259549 | 10.10 | September 15, 2021 |
| 10.11 | Offer Letter, dated September 10, 2021, by and between the Registrant and Victor M. Rivera. | S-1 | 333-259549 | 10.11 | September 15, 2021 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10.12 | Offer Letter, dated September 10, 2021, by and between the Registrant and Bradford D. Dahms. | S-1 | 333-259549 | 10.12 | September 15, 2021 | |
| 10.13 | Offer Letter, dated May 25, 2021, by and between the Registrant and Kathy Yi. | S-1 | 333-259549 | 10.13 | September 15, 2021 | |
| 10.14 | Offer Letter, dated July 1, 2021, by and between the Registrant and Iain D. Dukes. | S-1 | 333-259549 | 10.14 | September 15, 2021 | |
| 10.15 | Lease Agreement, dated September 16, 2021, by and between Theseus Pharmaceuticals, Inc. and MIT 314 Main Street Leasehold LLC. | S-1/A | 333-259549 | 10.15 | September 30, 2021 | |
| 10.16 | Controlled Equity Offering℠ Sales Agreement, dated as of November 3, 2022, between the Registrant and Cantor Fitzgerald & Co. | S-3 | 333-268125 | 1.2 | November 3, 2022 | |
| 21.1 | Subsidiaries of the Registrant. | | | | | X |
| 23.1* | Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm. | | | | | X |
| 24.1 | Power of Attorney (contained in the signature page to this Annual Report) | | | | | X |

| | | |
|---|---|---|
| 31.1* | Certification of Principal Executive Officer Pursuant to Securities Exchange Act Rules 13a-14(a) and 15(d)-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | X |
| 31.2* | Certification of Principal Financial Officer Pursuant to Securities Exchange Act Rules 13a-14(a) and 15(d)-14(a), 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 - The instance document does not appear in the interactive data file because its XBRL tags are embedded within the inline XBRL 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 as Inline XBRL and contained in Exhibit 101). | X |
| * | The certifications attached as Exhibit 32.1 and 32.2 that accompany this Annual Report on Form 10-K are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Theseus Pharmaceuticals, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing. | |

| | |
|---|---|
| + | Certain portions of this agreement have been omitted because the omitted portions are both not material and consists of the type of information that the Registrant both customarily and actually treats as private and confidential. |

**ITEM 16. Form 10-K Summary**

Not Applicable.

## SIGNATURES

Pursuant to the requirements 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.

THESEUS PHARMACEUTICALS, INC.

Date: March 9, 2023

By: /s/ Timothy Clackson, Ph.D.
Timothy Clackson, Ph.D.
President and Chief Executive Officer

## POWER OF ATTORNEY

*KNOW ALL PERSONS BY THESE PRESENTS*, that each person whose signature appears below hereby constitutes and appoints Timothy Clackson, Ph.D. and Bradford D. Dahms, and each of them, as his or her true and lawful attorneys-in-fact, proxies, and agents, each with full power of substitution, for him in any and all capacities, to sign any and all amendments to this registration statement (including post-effective amendments or any abbreviated registration statement and any amendments thereto filed pursuant to Rule 462(b) increasing the number of securities for which registration is sought), and to file the same, with all exhibits thereto and other documents in connection therewith, with the SEC, granting unto said 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 connection therewith, as fully for 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 substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this Annual Report has been signed by the following persons in the capacities and on the dates indicated.

| Signature | Title | Date |
|---|---|---|
| /s/ Timothy Clackson, Ph.D.<br>Timothy Clackson, Ph.D. | President, Chief Executive Officer and Director (Principal Executive Officer) | March 9, 2023 |
| /s/ Bradford Dahms<br>Bradford Dahms | Chief Financial Officer (Principal Financial and Accounting Officer) | March 9, 2023 |
| /s/ Iain D. Dukes, D.Phil.<br>Iain D. Dukes, D.Phil. | Chairman and Director | March 9, 2023 |
| /s/ Carl L. Gordon, Ph.D, CFA<br>Carl L. Gordon, Ph.D, CFA | Director | March 9, 2023 |
| /s/ Donald J. Hayden<br>Donald J. Hayden | Director | March 9, 2023 |
| /s/ Michael E. Rome, Ph.D.<br>Michael E. Rome, Ph.D. | Director | March 9, 2023 |
| /s/ Steven Stein, M.D.<br>Steven Stein, M.D. | Director | March 9, 2023 |
| /s/ Kathy Y. Yi<br>Kathy Y. Yi | Director | March 9, 2023 |

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**BOARD OF DIRECTORS**

**Timothy P. Clackson, Ph.D.**
President, Chief Executive Officer and Director

**Iain D. Dukes, MA, D.Phil.**
Venture Partner at OrbiMed Advisors LLC

**Carl L. Gordon, CFA, Ph.D.**
Founding Member and Managing Partner and Co-Head of Global Private Equity at OrbiMed Advisors LLC

**Donald J. Hayden, MBA**
Director at Otsuka America Pharmaceutical, Inc.

**Michael E. Rome, Ph.D.**
Managing Director at Foresite Capital Management

**Steven H. Stein, M.D.**
Executive Vice President and Chief Medical Officer of Incyte Corporation

**Kathy Y. Yi, MBA**
Chief Operating Officer at Affini-T Therapeutics

**EXECUTIVE OFFICERS**

**Timothy P. Clackson, Ph.D.**
President, Chief Executive Officer and Director

**Bradford D. Dahms**
Chief Financial Officer

**William C. Shakespeare, Ph.D.**
President of Research and Development

**Victor M. Rivera, Ph.D.**
Chief Scientific Officer

**David P. Kerstein, M.D.**
Chief Medical Officer

**CORPORATE HEADQUARTERS**
314 Main Street
Cambridge, Massachusetts 02142

**INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**
Ernst & Young LLP
Boston, Massachusetts

**TRANSFER AGENT**
Computershare Trust Company, N.A.
150 Royall Street
Canton, Massachusetts 02021