UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2022

OR

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

For the transition period from _____to _____

Commission file number: 001-39592

Kronos Bio, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**82-1895605**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

1300 So. El Camino Real, Suite 400
San Mateo, California 94402
(650) 781-5200
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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, $0.001 par value per share	KRON	The Nasdaq Stock Market LLC

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 or ☐ 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 or ☐ No.

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

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

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

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). ☐ Yes or ☒ No

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2022 (the last business day of the registrant's most recently completed second fiscal quarter) was approximately $204.6 million based on the closing price of the registrant's common stock on June 30, 2022 of $3.64 per share, as reported by The Nasdaq Global Select Market.

As of March 10, 2023, the registrant had 57,630,109 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement to be filed with the Securities and Exchange Commission (SEC) subsequent to the date hereof pursuant to Regulation 14A in connection with the registrant's 2023 Annual Meeting of Stockholders, are incorporated by reference into Part III of this Annual Report on Form 10-K. Such proxy statement will be filed with the SEC not later than May 1, 2023.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical fact contained in this report, including statements regarding our strategy, future financial condition, future operations, research and development, planned clinical trials and preclinical studies, expected progress and milestones related to our clinical and preclinical programs, the timing and likelihood of regulatory filings and approvals for our product candidates, our ability to commercialize our product candidates, the potential benefits of collaborations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “design,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “positioned,” “potential,” “predict,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions described in the sections of this report titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this report. Other sections of this report may include additional factors that could harm our business and financial performance. 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 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 you are cautioned not to unduly rely upon these statements.

Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors 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, or implied by, any forward-looking statements.

In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this report, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. You should refer to the section of this report titled “Risk Factors” for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

You should read this report and the documents that we reference in this report and have filed as exhibits to this report completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in this report by these cautionary statements.

RISK FACTOR SUMMARY

Below is a summary of material factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading "Risk Factors" in Item 1A of Part I of this Annual Report on Form 10-K, and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the SEC before making investment decisions regarding our common stock.

- We have incurred significant net losses since inception and we expect to incur significant losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future.
- We will need substantial additional funding. If we are unable to raise capital when needed, we would be compelled to delay, reduce, or eliminate our product development programs or commercialization efforts.
- We have a limited operating history and face significant challenges and will incur substantial expenses as we build our capabilities.
- Our discovery and development activities are focused on novel cancer therapeutics for patients with genetically-defined cancers and it is difficult to predict the time and cost of product candidate development and the likelihood of obtaining regulatory approval.
- We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- If we experience delays or difficulties in enrolling patients in our ongoing or planned clinical trials, regulatory approval could be delayed or we could fail to obtain regulatory approval.
- Our approach to the discovery and development of product candidates is unproven, and we may not be successful in our efforts to use and further develop our product engine to expand our pipeline of product candidates with commercial value.
- COVID-19 has adversely impacted, and any future health epidemic or pandemic may adversely impact, our business, including our ongoing or planned clinical trials.
- If the market opportunities for our product candidates are smaller than we estimate or if any regulatory approval that we obtain is based on a narrower definition of the patient population, it will adversely affect our revenue potential and ability to achieve profitability.
- Our success depends in part on our ability to protect our intellectual property and our proprietary technologies.
- We rely on third parties, including independent clinical investigators, developers of companion diagnostics, and CROs, to conduct certain aspects of our preclinical studies and ongoing and planned clinical trials. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements or meet expected deadlines, we may not be able to obtain approval for or commercialize our product candidates and our business could be substantially harmed.
- Our success is highly dependent on our ability to attract and retain highly-skilled executive officers and employees.
- We may attempt to use accelerated approval pathways, and if we are unable to obtain such 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 approval. Even if we receive accelerated approval from the U.S. Food and Drug Administration (FDA), if our trials required as a condition to such accelerated approval do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may withdraw approval.

TRADEMARKS AND SERVICE MARKS

“Kronos Bio,” “Kronos,” the Kronos logo and other trademarks, trade names or service marks of Kronos Bio, Inc. appearing in this report are the property of Kronos Bio, Inc. All other trademarks, trade names and service marks appearing in this report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this report may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert their rights thereto.

PART I.

ITEM 1. BUSINESS

Overview

We are an integrated discovery through clinical development biopharmaceutical company, with a focus on developing therapeutics that target the dysregulated transcription that causes cancer and other serious diseases. We are enrolling patients in clinical trials for two compounds. Our product engine, which includes our proprietary small molecule microarray (SMM) screening platform, provides us with the capability to map and target transcription regulatory networks (TRNs) in a differentiated manner to enable discovery of novel compounds and improve our ability to discover and optimize clinical development candidates. In addition to our own internal preclinical programs, we have entered into a collaboration agreement with Genentech, Inc., a member of the Roche Group (Genentech).

We are developing KB-0742, our internally discovered, oral cyclin dependent kinase 9 (CDK9) inhibitor, for the treatment of MYC-amplified and other transcriptionally addicted solid tumors. We have initiated the Phase 2 portion of our Phase 1/2 clinical trial. KB-0742 was generated from our optimization of a compound that was identified using our SMM platform.

We are also developing lanraplenib, our next generation orally-administered SYK inhibitor, and are in the dose escalation stage of our Phase 1b/2 clinical trial. This clinical trial will evaluate lanraplenib in combination with gilteritinib in patients with relapsed or refractory FLT3- mutated AML. Lanraplenib has multiple advantages over our first-generation SYK inhibitor, entospletinib. In November 2022, we announced the decision to close enrollment of our Phase 3 clinical trial of entospletinib in combination with intensive chemotherapy in patients with newly diagnosed NPM-1 mutated AML for strategic reasons, and study closure is anticipated in mid-2023.

In our research efforts, we are leveraging our product engine to drive multiple oncology discovery programs targeting dysregulated transcription factors and their associated TRNs. Some of the most powerful oncogenes in all of human cancer encode transcription factors: proteins that bind to specific DNA sequences on the genome and control how sets of genes are turned on and off. Transcription factors historically have been difficult to target in drug development because they generally lack hydrophobic pockets amenable to ligand binding to disrupt function and are typically intrinsically disordered, adopting a functional structure only when assembled with a complex of cofactors in the nucleus on the genome. Transcription factors with aberrant expression or activity result in dysregulated TRNs, which are frequently responsible for reprogramming healthy cells into cancerous tumor cells. Therapeutically modulating dysregulated transcription factors requires a sophisticated and holistic approach due to their complexity and their regulation of complex TRNs in a context-dependent manner. Based on this work, in November 2021, we announced the advancement of two programs, one focused on the MYC TRN and one focused on the androgen receptor (AR) TRN, which we are continuing to advance.

In addition, in January 2023, we entered into a research collaboration with Genentech, focused on discovering and developing small-molecule drugs that modulate transcription factor targets selected by Genentech. Under the collaboration, we will leverage our proprietary drug discovery platform, including the small molecule microarray, for hit finding, to build upon research conducted by Genentech.

We take a systems biology approach to unlocking therapeutic mechanisms within dysregulated TRNs using our differentiated product engine. Our product engine includes three interconnected components, each of which is informed by our translational expertise, and which we believe enables efficient discovery and development of new product candidates:

- ***Map TRNs*** – Leverage our computational biology expertise, engineered cell systems and high throughput transcriptomic profiling to map the structure of TRNs defined by specific dysregulated transcription factors and identify the gene expression signature of selective TRN modulation that can be carried forward into discovery and clinical translation.
- ***Define Dependencies*** – Apply causal and mechanistic insights to analyze TRNs and to identify critical nodes that may represent tractable targets for drug discovery. We do this by identifying which genetic

sequences transcription factors bind to, which proteins they interact with, and which genes they regulate in specific cellular contexts.

- ***Identify Modulators*** – Conduct high throughput screens using our proprietary SMM screening platform against dysregulated transcription factors in tumor cell lysates to identify selective TRN modulators and determine mechanism of action. Such modulators are then further optimized to refine their pharmacological properties.

KB-0742

KB-0742, generated from our product engine's SMM platform, is a highly selective, oral CDK9 inhibitor being developed to treat MYC-amplified solid tumors and other transcriptionally addicted tumors. In February 2021, we initiated the Phase 1 portion of our Phase 1/2 clinical trial of KB-0742 to evaluate its safety, PK and PD. In December 2022, we announced the selection of the recommended Phase 2 dose of 60 mg. While continuing to dose escalate in the Phase 1 portion of the trial, we also began enrollment of expansion cohorts at the recommended Phase 2 dose and schedule in patients with MYC-amplified solid tumors and other transcriptionally addicted cancers. We plan to present results of the trial, including the Phase 1 stage and initial data from the Phase 2 expansion stage, at a medical conference in the second half of 2023.

Lanraplenib

We are developing a next-generation SYK inhibitor, lanraplenib. In August 2022, we dosed the first patient in our Phase 1b/2 clinical trial, which includes a dose-escalation and an expansion cohort study design. In the Phase 1b stage of this trial, we are evaluating initial safety, PK and anti-leukemic activity of escalating once-daily doses of lanraplenib in combination with the standard approved dose of gilteritinib in relapsed or refractory FLT3-mutated AML patients. Once a recommended dose is established and pending the data from the Phase 1b stage, we plan to initiate the Phase 2 stage of the trial, with an expansion cohort of approximately 30 patients to further evaluate the safety of lanraplenib and assess its anti-leukemic activity as measured by composite CR rate and duration of response. We anticipate sharing initial data, along with the recommended Phase 2 dose, in the fourth quarter of 2023 or first quarter of 2024.

Our Team and History

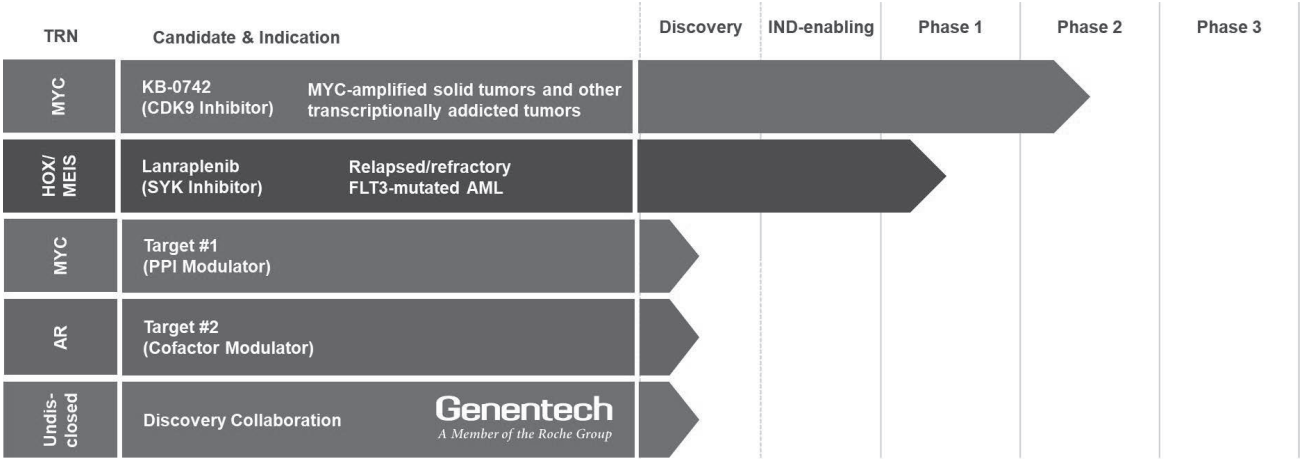
We are led by an experienced executive leadership team with an established track record and decades of scientific and business experience. Collectively, our management team has obtained regulatory approval and has successfully commercialized more than 25 therapeutic products across a broad range of disease areas, including but not limited to hematology, oncology, and virology. Norbert Bischofberger, Ph.D., our President and Chief Executive Officer, was previously Chief Scientific Officer and Executive Vice President of Research & Development at Gilead Sciences where he helped build the company over a 28-year tenure and was responsible for the regulatory approval of more than 20 products in therapeutic areas including infectious disease and oncology. Jorge DiMartino, M.D., Ph.D., our Chief Medical Officer and Executive Vice President, Clinical Development, was previously Vice President, Translational Development Oncology at Celgene Corporation, and Group Medical Director at Genentech, Inc. in the Oncology Exploratory Clinical Development group, where he led the early development to proof-of-concept of multiple agents that subsequently received FDA approval. Christopher Dinsmore, Ph.D., our Chief Scientific Officer, was previously an Entrepreneur-in-Residence at Third Rock Ventures, Vice President and Head of Chemistry at Forma Therapeutics, Inc., and a medicinal chemist at Merck & Co., Inc. for 19 years. Barbara Kosacz, J.D., our Chief Operating Officer and General Counsel, was previously head of the global life sciences practice at the international law firm Cooley LLP. She has more than 25 years of experience providing strategic and legal advice to life sciences companies and has structured and negotiated some of the most transformational life sciences transactions in the industry. Yasir Al-Wakeel, BM BCh, our Chief Financial Officer and Head of Corporate Development was previously Chief Financial Officer at Neon Therapeutics, where he played a key role in public and private financings as well as its eventual sale to BioNTech, and at Merrimack Pharmaceuticals. Prior to his industry roles, he held senior roles in both equity research and investment banking at Credit Suisse after practicing medicine in the United Kingdom.

In addition to our management team, we have built a scientific team with deep expertise in transcriptional regulation, computational and chemical biology, drug discovery platform technologies, and computational and medicinal chemistry.

Our company was initially founded by Arie Belldegrun, M.D., FACS, Joshua Kazam, David Tanen and Christopher Wilfong from Two River, LLC (Two River), a life science investment firm that partners with founders to create, finance and operate development-stage biopharmaceutical companies. Two River previously founded Kite Pharma, acquired by Gilead in 2017, and Allogene Therapeutics, Inc. Dr. Belldegrun serves as founding Chair of our board of directors. Dr. Belldegrun is a clinician scientist and biotechnology entrepreneur who also founded Agensys Corporation, acquired by Astellas Pharma, Inc. in 2007, and Cougar Biotechnology, Inc., acquired by Johnson & Johnson in 2009.

Our Pipeline

We have developed a robust clinical pipeline through a combination of internal discovery efforts and focused asset acquisition. The following chart summarizes the current stages of our development programs, including KB-0742 and lanraplenib, and our next anticipated milestones.



We are also executing on robust discovery programs across multiple TRNs, which focus on four cancer types where dysregulated transcription plays a central role: hematologic malignancies, prostate cancer, MYC-driven cancers, and small cell/neuroendocrine cancers.

KB-0742: our CDK9 Inhibitor

KB-0742 was generated from our product engine's SMM screening platform. KB-0742 is an oral CDK9 inhibitor with a differentiated biochemical selectivity and clinical PK profile. CDK9 is a serine/threonine kinase that forms the catalytic core of the positive transcription elongation factor b (P-TEFb). CDK9 is a global regulator of transcription, and has been recognized as a high-value oncology drug target due to its essential role in maintaining high levels of transcription for oncogenes and short-lived anti-apoptotic proteins.

In February 2021, the first patient was dosed in the Phase 1 stage of our Phase 1/2 clinical trial to evaluate KB-0742's safety, PK and PD properties across multiple dose levels. In November 2021, we reported initial results from the first three dose levels of our ongoing dose escalation stage of our Phase 1/2 trial of KB-0742 in patients with solid tumors. In December 2022, we announced the selection of 60mg as our recommended Phase 2 dose (RP2D). An analysis of the trial results demonstrated that treatment with a 60mg dose of KB-0742 led to a targeted reduction in PBMCs of approximately 50% in levels of phosphorylated Ser2 on RNA Polymerase II (pSer2), a direct substrate target of CDK9. This level of target engagement is consistent with demonstrating anti-tumor activity based on preclinical models. The 60mg dose appears to have an acceptable safety profile and the maximum tolerated dose has not yet been defined. This analysis further showed that KB-0742 continued to demonstrate a differentiated PK profile, with oral bioavailability and dose-proportional exposure across all four dose levels, and low to moderate variability between patients. At the time of RP2D selection, a total of 26 patients had been enrolled and treated in the dose escalation phase of the study. Among these patients, PK data were collected and analyzed for 25 patients and KB-0742 continued to demonstrate a terminal half-life of 24 hours, with approximately 2.1 to 2.5 fold accumulation between day 1 and day 10.

While continuing to dose escalate in the Phase 1 portion of the trial, we are also actively enrolling expansion cohorts of patients with MYC-amplified solid tumors and other transcriptionally addicted tumor types at the RP2D. The subsequent development path to registration will be based on the frequency, magnitude and durability of responses observed in these expansion cohorts.

Our initial development focus for KB-0742 is for potential use in advanced transcriptionally addicted solid tumors, including tumors with MYC genomic copy number gain (amplification). MYC is a well-characterized transcription factor and a long-recognized driver of cancer that is dysregulated in a significant proportion of malignancies, including lung, breast, ovarian, and various gastrointestinal cancers, as a result of genomic amplification and other mechanisms. CDK9 is a critical node in the MYC TRN, acting both as an upstream driver of MYC expression and a downstream co-factor of MYC itself that is required to drive the MYC-dependent oncogenic gene expression program. Preclinical characterization of KB-0742 has demonstrated that MYC over-expression resulting from genomic amplification and other mechanisms is associated with increased tumor sensitivity across multiple histologies, potentially enabling a tissue of origin-agnostic development strategy.

Lanraplenib: our SYK Inhibitor

Lanraplenib is a small molecule selective inhibitor targeting SYK, a critical node in a dysregulated TRN within AML defined by persistent high expression of the transcription factors HOX/MEIS. SYK is a non-receptor tyrosine kinase and is an important mediator of immunoreceptor signaling in hematopoietic cells with a clearly established role in both malignant and non-malignant hematologic disease.

SYK is a critical dependency in biomarker-defined subsets of AML patients characterized by persistent high HOX/MEIS expression. Multiple AML driver mutations, including NPM1, MLL (KMT2A) gene rearrangements (MLL-r) and DNMT3A, have been associated with elevation of HOX/MEIS, which increases quantity and activity of SYK as part of an oncogenic TRN. SYK contributes to the leukemia cell state through multiple mechanisms, including direct modulation of downstream growth-promoting transcriptional programs, phosphorylation of FLT3, a known driver of leukemogenic signaling, and participation in a positive feedback loop to MEIS1 that maintains

high MEIS1 expression. We believe these multiple oncogenic functions make SYK a compelling therapeutic target and a critical node in the HOX/MEIS TRN.

Our expertise in TRN biology allowed us to recognize SYK as a critical node in the HOX/MEIS TRN, and in July 2020, we acquired a portfolio of selective, orally bioavailable small molecule SYK inhibitors from Gilead. The acquisition included two clinical-stage product candidates:

- *Lanraplenib* – A next generation SYK inhibitor with improved PK and pharmacologic properties compared with entospletinib, including once daily (QD) dosing, no food restrictions and compatibility with proton pump inhibitors. Lanraplenib was previously studied in clinical trials that included more than 250 healthy volunteers and patients with autoimmune diseases, establishing an acceptable safety profile. Our preclinical evaluation of lanraplenib showed equivalent anti-leukemic activity in head-to-head comparisons with entospletinib. We dosed the first patient in a Phase 1b/2 clinical trial in August 2022. This clinical trial includes a dose-escalation and an expansion cohort study design. In this trial, the Phase 1b stage will evaluate initial safety, PK and anti-leukemic activity of escalating once-daily doses of lanraplenib in combination with the standard approved dose of gilteritinib in relapsed or refractory FLT3-mutated AML patients. Once a recommended dose is established and pending the data from the Phase 1 stage, we plan to initiate the Phase 2 stage of the trial, with an expansion cohort of approximately 30 patients to further evaluate the safety of lanraplenib and assess its anti-leukemic activity as measured by composite CR rate and duration of response. We anticipate sharing initial data, along with the recommended Phase 2 dose, in the fourth quarter of 2023 or first quarter of 2024.

- *Entospletinib* – An orally administered SYK inhibitor with high selectivity, dosed twice-daily (BID). In December 2021 we initiated a registrational Phase 3 clinical trial of entospletinib using MRD-negative CR as the primary endpoint in support of potential accelerated approval. In November 2022, we announced the decision to close enrollment of the Phase 3 clinical trial for strategic reasons. The trial was not discontinued due to adverse events or lack of efficacy signals. Final study closure is anticipated in mid-2023.

Discovery Programs

We continually invest in early discovery efforts utilizing our proprietary product engine, with the goal of expanding our pipeline of future product candidates, either alone or with third party collaborators. Our current efforts are focused on four cancer types where dysregulated transcription plays a central role: hematologic malignancies, prostate cancer, MYC-driven cancers, and small cell/neuroendocrine cancers (SCNC). We are developing a deep understanding of the underlying disease biology within these cancer types, engineering robust systems to characterize transcription factor perturbation signatures, and are evaluating multiple potential opportunities for therapeutic intervention through modulation of key TRN components. We select our discovery targets based on scientific, translational and competitive considerations, prioritizing those where dependency has been demonstrated in a defined patient population with high unmet medical need, and where we believe we can design an efficient early clinical translation strategy based upon our understanding of the disease biology.

We have a discovery collaboration with Genentech, a member of the Roche Group, focused on discovering and developing small-molecule drugs that modulate transcription-factor targets selected by Genentech.

Our Strategy

Our goal is to become a leading biopharmaceutical company by discovering transformational small molecule modulators of historically challenging targets in cancer and other serious diseases, and then developing those product candidates through regulatory approval, and ultimately commercializing those agents, using a precision medicine approach for patient populations with high unmet medical need. We intend to do this by continuing to employ our proprietary product engine to discover and develop product candidates. The key near-term elements of our strategy include:

- ***Establish clinical proof of concept for KB-0742 (CDK9 program)***. In February 2021, the first patient was dosed in the first stage of our Phase 1/2 clinical trial, designed to initially assess the safety, PK and PD profile of KB-0742 in patients with advanced solid tumors. We have announced a recommended Phase 2 dose and begun enrolling subsequent signal-seeking expansion cohorts in cancer patients with MYC-amplified solid tumors and other transcriptionally addicted cancers while continuing to dose escalate in the Phase 1 portion of the trial. We reported initial data from the dose escalation stage of the clinical trial in the fourth quarter of 2021, and reported the recommended Phase 2 dose and data from the Phase 1 portion of this trial in December 2022.

- ***Determine RP2D for lanraplenib and pursue rational combinations in AML (SYK program).*** In August 2022, we dosed the first patient in our Phase 1b/2 clinical trial which includes a dose-escalation and an expansion cohort study design. In the Phase 1b stage of this trial, we are evaluating initial safety, PK and anti-leukemic activity of escalating once-daily doses of lanraplenib in combination with the standard approved dose of gilteritinib in relapsed or refractory FLT3-mutated AML patients. Once a recommended Phase 2 dose is established and pending the data from the Phase 1 stage, we plan to initiate the Phase 2 stage of the trial, with an expansion cohort of approximately 30 patients to further evaluate the safety of lanraplenib and assess its anti-leukemic activity as measured by composite CR rate and duration of response. We anticipate sharing initial data, along with the recommended Phase 2 dose, in the fourth quarter of 2023 or first quarter of 2024.

- ***Leverage our product engine to grow our pipeline of internally-generated product candidates***. Our research efforts are directed to establishing a robust pipeline of additional highly differentiated product candidates targeting dysregulated transcription factors and their associated TRNs, leveraging our SMM platform, and our chemical biology, and computational and experimental biology capabilities.

- ***Selectively enter into strategic collaborations to maximize the potential of and to expand our pipeline***. We plan to pursue, selectively evaluate, and, if appropriate, enter into strategic collaborations that leverage complementary capabilities of current or future collaboration partners to advance and accelerate the clinical development of our product candidates, as well as maximize our commercial reach for product candidates that receive regulatory approval. In addition, our product engine has the potential to identify differentiated product candidates addressing a wide variety of diseases with high unmet medical need and we believe that, building on our strategic collaboration with Genentech, we may have the opportunity to enter into research collaborations with potential partners to expand upon their research to date or to explore together new areas of dysregulated transcription. We also continue to evaluate potential assets and technologies from third parties and believe we have built a team well suited for the continued identification, evaluation and acquisition of additional product candidates or technologies that complement our scientific focus, core efforts and capabilities.

- ***Leverage our experienced management team to build a fully-integrated, science-driven biopharmaceutical company addressing high unmet medical needs.*** Our management team possesses significant expertise across all stages of discovery, translation, late-stage clinical development

and commercialization. Collectively, our management team has obtained regulatory approval and has successfully commercialized over 25 therapeutic products, including several that have fundamentally transformed patient outcomes. We plan to progress our product candidates expeditiously through regulatory approval, with the vision of ultimately building a fully-integrated, science-driven biopharmaceutical company.

KB-0742: Our Investigational CDK9 Inhibitor

KB-0742 is an oral CDK9 inhibitor with a differentiated selectivity profile. CDK9 is a global regulator of transcription and a critical node in the oncogenic TRN resulting from MYC overexpression. While CDK9 is a required component of transcriptional machinery for many genes across the genome, certain tumors are "transcriptionally addicted," meaning that they require a higher level of transcription than normal cells in order to survive.

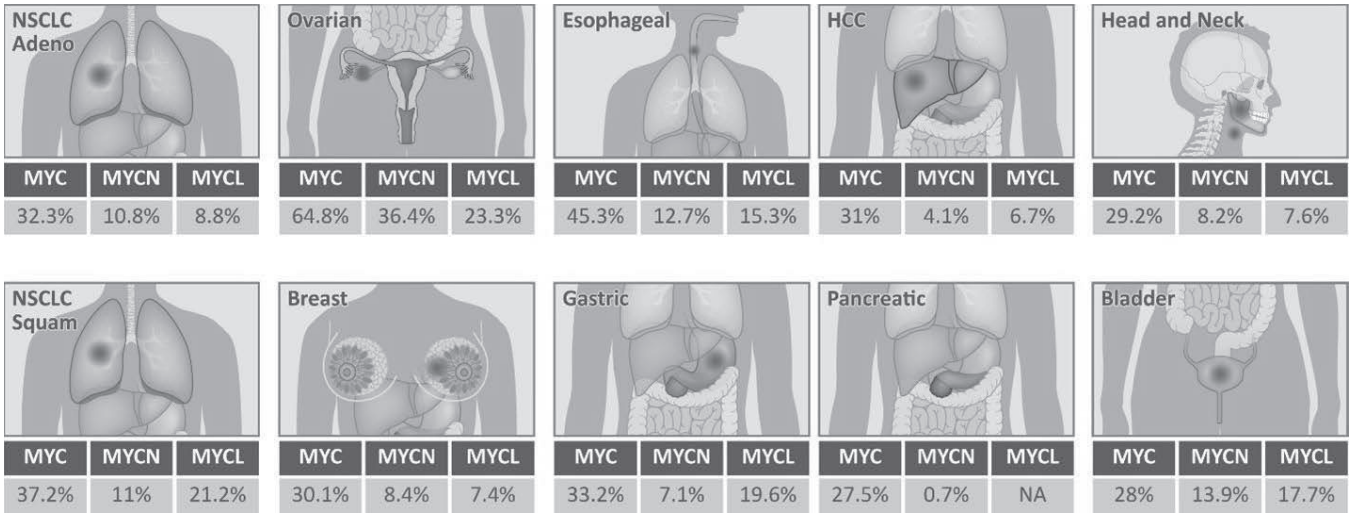
KB-0742 was internally optimized from an SMM hit and we believe it possesses differentiated selectivity for CDK9 among other attractive pharmacologic properties. While several other compounds targeting CDK9 are being clinically investigated by third parties for the treatment of cancer, their published biochemical selectivity profiles indicate the potential for cross-reactivity to cell cycle CDKs at clinical exposures. We believe this may contribute to the toxicity and limited therapeutic index observed with these agents and explain why in general they have not advanced to later-stage clinical trials. In addition, our pre-clinical models suggest that sustained partial inhibition of CDK9 is essential for anti-tumor activity while avoiding on-target toxicity. Because of its oral bioavailability and long plasma half-life, KB-0742 lends itself to achieving this target coverage profile in patients.

The FDA cleared our IND submission of KB-0742 in December 2020. In February 2021, we initiated the dose-escalation stage of our Phase 1/2 clinical trial of KB-0742 to evaluate its safety, PK and PD. While continuing to dose escalate, we are enrolling the expansion cohorts at the recommended Phase 2 clinical trial dose and schedule in patients with MYC-amplified solid tumors and pother transcriptionally addicted cancers. We reported initial data from the dose escalation stage of the clinical trial in the fourth quarter of 2021 and reported the recommended Phase 2 dose and initial data from the Phase 1 portion of this trial in December 2022.

Therapeutic Rationale in MYC-amplified tumors

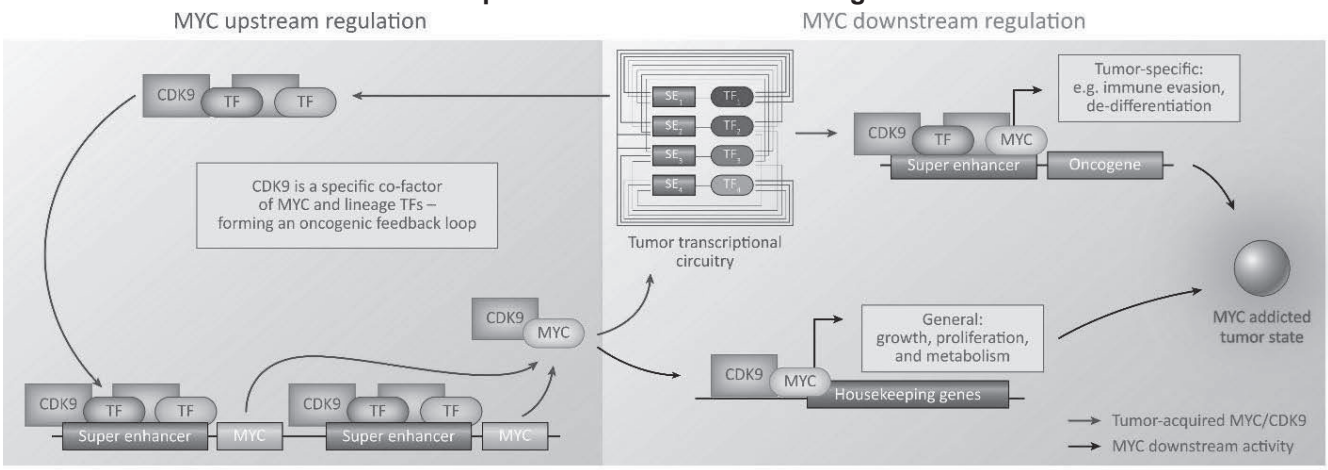
MYC family transcription factors (CMYC, MYCN and MYCL) are master regulators of cell growth, proliferation, differentiation and metabolism, and are among the most frequently dysregulated targets in malignancies. While MYC can be up-regulated through various mechanisms and participates in many oncogenic TRNs, we believe that MYC gene copy number amplification is one of the clearest markers of transcriptional addiction. MYC amplification appears frequently in many common tumor types and is associated with aggressive disease.

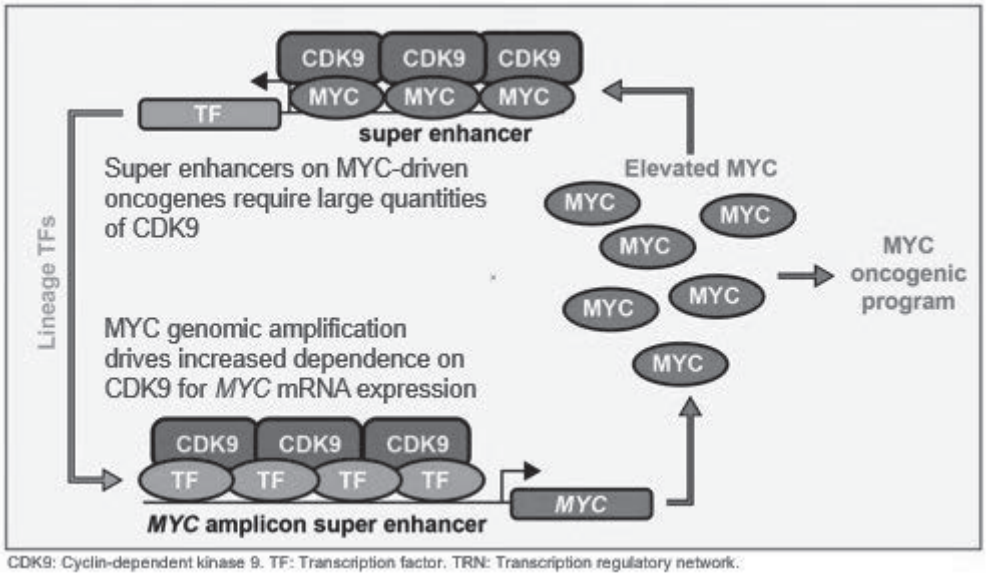
Percentage of Tumors in the National Cancer Institute's the Cancer Genome Atlas (TCGA) Dataset (2018) With Copy Number Gains of MYC, MYCN or MYCL



We believe that CDK9 is an attractive therapeutic target in transcriptionally addicted cancers, and specifically MYC-amplified solid tumors, due to its essential role in transcriptional elongation. MYC is critically dependent on CDK9 in order to drive transcription of downstream target genes and effect the oncogenic program. Additionally, a high rate of transcription is required to maintain elevated MYC protein levels, which creates an additional upstream dependency on large quantities of CDK9. These upstream and downstream dependencies are particularly acute in tumors with MYC genomic amplification, as these cells are addicted to high levels of MYC.

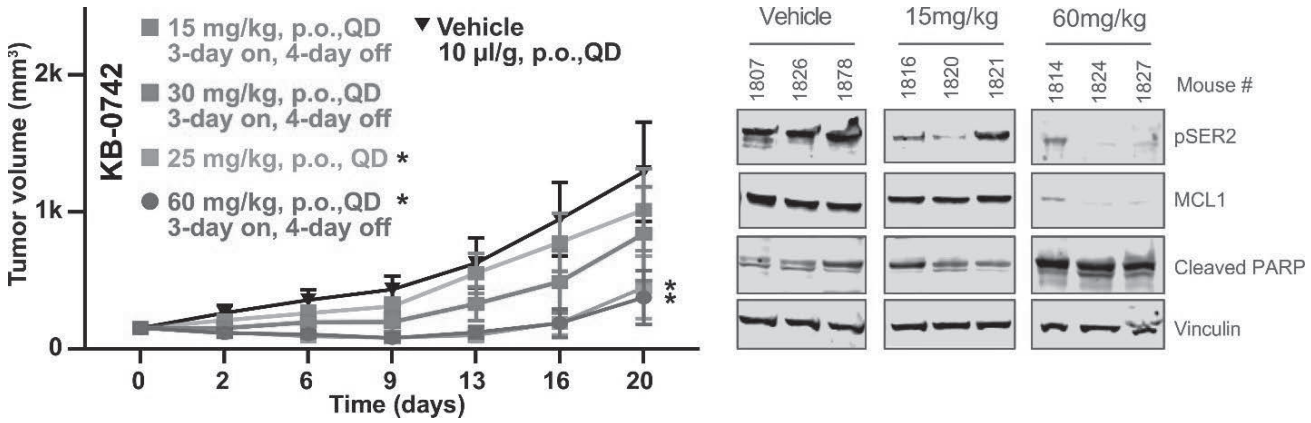
MYC Upstream and Downstream Regulation





CDK9: Cyclin-dependent kinase 9. TF: Transcription factor. TRN: Transcription regulatory network.

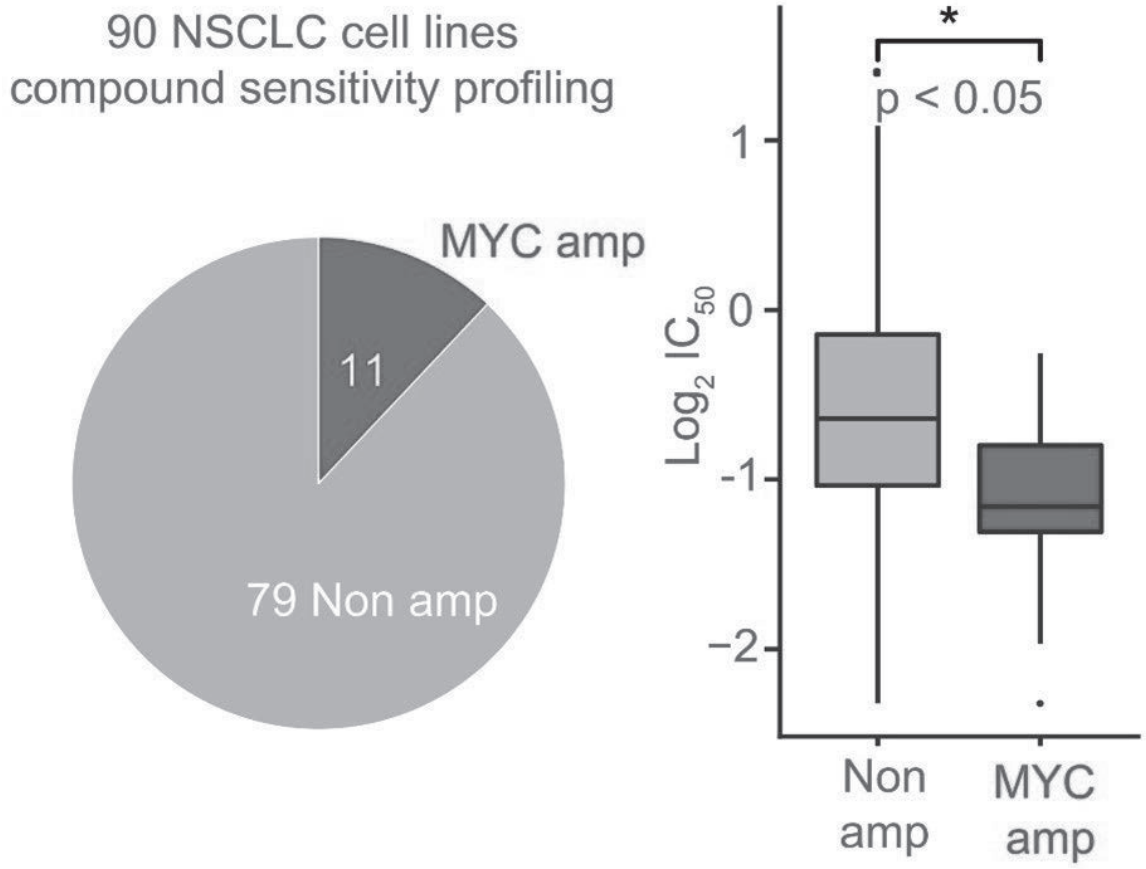
In *vivo* efficacy modeling with KB-0742 was initially conducted in a MYC-dependent AML mouse xenograft model, MV4-11, and demonstrated dose dependent tumor growth inhibition at well-tolerated doses as measured by body weight. Assessment of PD markers in tumor also showed dose-dependent effects, including levels of pSer2 (a direct phosphorylation target of CDK9), MCL1 (an anti-apoptotic oncoprotein known to depend on CDK9) and cleaved PARP (a marker of apoptotic cell death). Importantly, we demonstrated that an intermittent dosing strategy of 60 mg/kg on a three days on / four days off schedule showed equivalent activity compared to the same amount of drug delivered with continuous daily dosing (25 mg/kg QD). We believe that intermittent dosing may be better tolerated clinically and has the potential to improve the therapeutic index for CDK9 inhibition.



MYC-Driven Xenograft Model

While the initial xenograft data in the AML cell line are encouraging, we believe that a greater therapeutic opportunity lies in treating MYC-amplified solid tumors. Based on large scale in vitro viability profiling of KB-0742, we observed that MYC genomic amplification is correlated with increased sensitivity to compound treatment in non-small cell lung cancer tumors.

Differential Sensitivity in MYC-Amplified NSCLC Cell Lines



Additional in vivo experiments are ongoing to inform selection of appropriate patient populations for clinical development of KB-0742

Differentiated Opportunity

We believe that KB-0742 represents a differentiated opportunity for targeting CDK9 based on its selectivity profile, oral bioavailability and extended plasma half-life.

Multiple CDK9 inhibitors are currently being investigated clinically; however, clinical results published to date have shown limited therapeutic index and, to our knowledge, none has advanced into late-stage clinical trials. We believe that three primary factors differentiate KB-0742 and our translational strategy, and may enable an enhanced potential therapeutic index relative to other programs:

CDK Selectivity. CDK9 bears a high degree of structural similarity to other CDK family members, and many of the previously reported CDK9 inhibitors possess significant inhibitory activity on other CDKs, including cell cycle CDKs. Even many purportedly selective CDK9 inhibitors have shown a relatively narrow fold-selectivity in biochemical assays, which may not be sufficient to avoid off-target activity at the physiologically relevant concentrations achieved in a clinical setting. This off-target activity may meaningfully contribute to the clinical profile of these molecules, and in particular we believe that a lack of selectivity against cell-cycle CDKs may introduce safety liabilities unrelated to the transcriptional mechanism of CDK9. In contrast, KB-0742 was highly selective for CDK9 over other CDK family members, potentially enabling a superior opportunity to achieve therapeutically-relevant target coverage in vivo without meaningful inhibition of off-target CDKs.

Biochemical Assay Panel Showed High Selectivity of KB-0742 for CDK9 over Other CDK Family Members

Compound		KB-0742
Potency (biochemical IC_{50})	**CDK9**	**6 nM**
Fold Selectivity CDK9 vs. other CDK family members	CDK8	>1000x
	CDK7	252x
	CDK6	658x
	CDK5	303x
	CDK4	522x
	CDK3	237x
	CDK2	66x
	CDK1	497x
Route of administration		**Oral**

Transcriptional CDK

Cell cycle CDK

PK Profile and Dosing Schedule. Because of the essential role of CDK9 in all normal tissues, it is critical to optimize dosing schedule and duration of target coverage in order to achieve anti-tumor activity without eliciting undue toxicity in normal tissues. Based on our team's prior experience developing anti-cancer agents targeting epigenetic targets, we are pursuing an intermittent dosing strategy, with the goal of maintaining a consistent level of target coverage for several days followed by a drug holiday to allow for recovery in normal tissue. Many other CDK9 inhibitors possess short half-life or are administered intravenously, resulting either in pulsatile target coverage or short overall duration of target coverage. By contrast, KB-0742 has demonstrated oral bioavailability and a twenty-four hour plasma half-life in humans. We believe that this is an attractive profile and affords the flexibility to establish a therapeutic index by varying dose and schedule to achieve optimal target coverage in tumor.

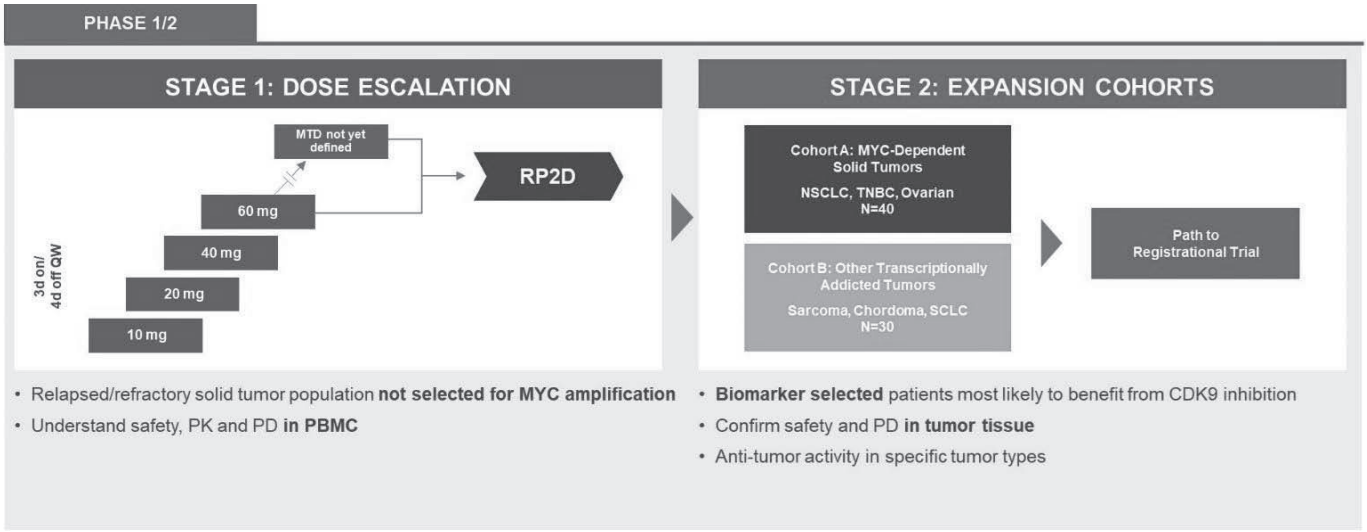
Patient Selection. We believe that the underlying biology of a tumor and degree of transcriptional addiction is critical in determining its sensitivity to CDK9 inhibition, and by extension, therapeutic index. Rather than selecting

patients solely based on a tumor's tissue of origin, we intend to take a differentiated approach to clinical translation by focusing on development in patient populations with clear genomic markers of transcriptional addiction including MYC amplification.

Development Strategy

The FDA cleared our IND for KB-0742 in December 2020. In February 2021, we initiated the dose escalation stage of our Phase 1/2 clinical trial of KB-0742 in cancer patients to evaluate its safety, PK and PD across multiple dose levels to identify a recommended dose and schedule. After having identified the recommended dose level and dosing schedule, we have begun enrolling expansion cohorts of patients with MYC-amplified solid tumors and other transcriptionally addicted tumor types, with the goal of assessing safety and PD response in these patient populations. We are continuing to dose escalate in the Phase 1 portion of the trial.

Two-Stage Phase 1/2 Dose Escalation Clinical Trial



NSCLC: Non-small cell lung cancer. PD: Pharmacodynamics. PK: Pharmacokinetics. QW: Weekly. SCLC: Small cell lung cancer. TNBC: Triple-negative breast cancer. PBMC: Peripheral Blood Mononuclear Cells. RP2D: recommended Phase 2 dose

Following identification of a recommended Phase 2 clinical trial dose and schedule, we are actively enrolling expansion cohorts in biomarker-defined patient populations with transcriptionally addicted cancers, including MYC-amplified solid tumors. Additionally, we are actively enrolling patients with transcription factor fusions and patients with chordoma, an incurable solid tumor addicted to the brachyury transcription factor. Although patients with these tumor types are relatively rare, we believe it is feasible to enroll such patients at major academic centers, which may provide a unique opportunity to demonstrate proof of concept for KB-0742. Clinical results from these expansion cohorts will inform the future development and registration strategy for KB-0742.

Our Next Generation SYK Inhibitor Product Candidate: Lanraplenib

Lanraplenib is a selective inhibitor of SYK, an important mediator of immunoreceptor signaling in hematopoietic cells with a clearly established role in both malignant and non-malignant hematologic disease. Lanraplenib was previously developed by Gilead for autoimmune indications and has been evaluated in multiple Phase 2 clinical trials in more than 250 patients including healthy volunteers and patients with autoimmune disease. Lanraplenib has exhibited improved PK properties compared with entospletinib, including an improved half-life, which is compatible with QD dosing among other benefits.

Preclinical modeling suggests that dose levels selected for Phase 2 clinical trials of lanraplenib in autoimmune disease resulted in lower SYK target engagement compared to the dose of entospletinib used in hematologic malignancies. We believe that a higher dose of lanraplenib resulting in equivalent SYK target engagement

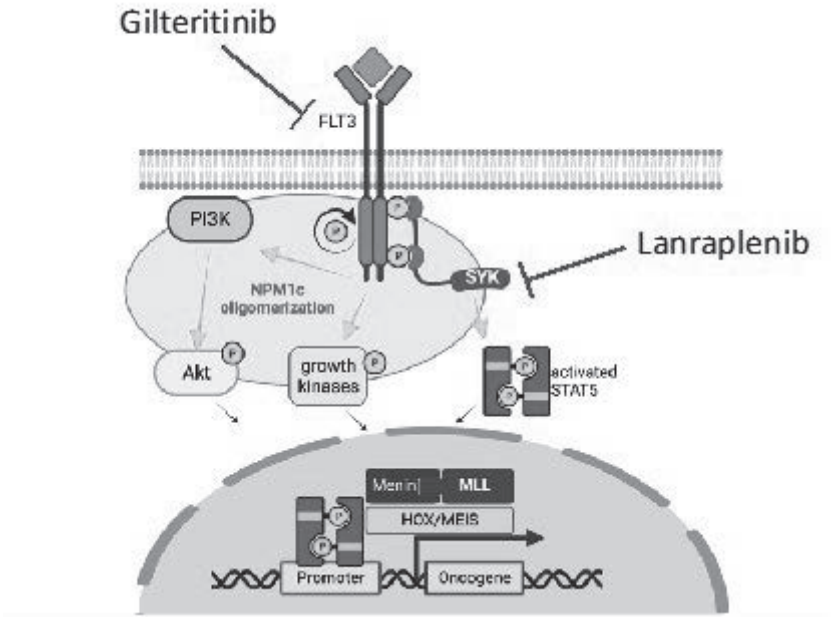
achieved with entospletinib may create an opportunity to develop lanraplenib in oncology and other indications. Based on our detailed preclinical evaluation of lanraplenib, which showed equivalent anti-leukemic activity in head-to-head comparisons with entospletinib in various AML models, we are conducting a Phase 1b/2 trial in which we enrolled the first patient in August 2022, and which will evaluate lanraplenib in combination with gilteritinib in patients with relapsed or refractory FLT3-mutated AML.

Therapeutic Rationale for Targeting SYK in Genetically Defined Subsets of AML

AML is one of the most common forms of acute leukemia in adults. Despite multiple recent drug approvals, the disease still bears a poor prognosis with less than 30% of patients surviving five years from diagnosis. Although the median age at diagnosis is 67, only younger, typically less than 65 years old, and fitter patients are eligible for intensive chemotherapy, involving seven days treatment with cytarabine and three days treatment with an anthracycline drug such as daunorubicin or idarubicin (7+ 3). Approximately 60% to 70% of these patients achieve CR, but most will experience disease relapse in less than 18 months. Among patients who achieve CR but remain positive for minimal residual disease (MRD), remissions are often particularly short-lived. For older and less fit patients, prognosis is even worse. Therapeutic options for these patients have historically been limited to palliative treatment with HMAs with CR rates of approximately 30% followed by relapse within a matter of months in a majority of responding patients.

SYK is a non-receptor tyrosine kinase that normally functions to mediate signaling between various cell surface receptors on myeloid cells and the transcriptional machinery. SYK activity becomes dysregulated because of certain recurring mutations in AML and is critical for the leukemogenic potential of these mutations. Specifically, mutated FLT3, a well-known driver of high-risk AML, needs to be phosphorylated by SYK for full leukemogenic potential. Mutations, predominantly internal tandem duplications, of FLT3 are found in approximately 30% of AML patients and are associated with a high risk of relapse and poor overall survival. A number of FLT3 inhibitors have recently been approved or are in development, including midostaurin, a first-generation inhibitor, which is approved in combination with 7 + 3 in newly diagnosed AML with FLT3 mutations. Quizartinib, a more selective second-generation inhibitor of FLT3, has also shown a survival benefit in newly diagnosed FLT3-mutated AML patients when combined with 7 + 3, but has not yet received FDA approval. Despite improved outcomes with the addition of FLT3 inhibitors to front line therapy, patients continue to relapse with FLT3-driven AML.

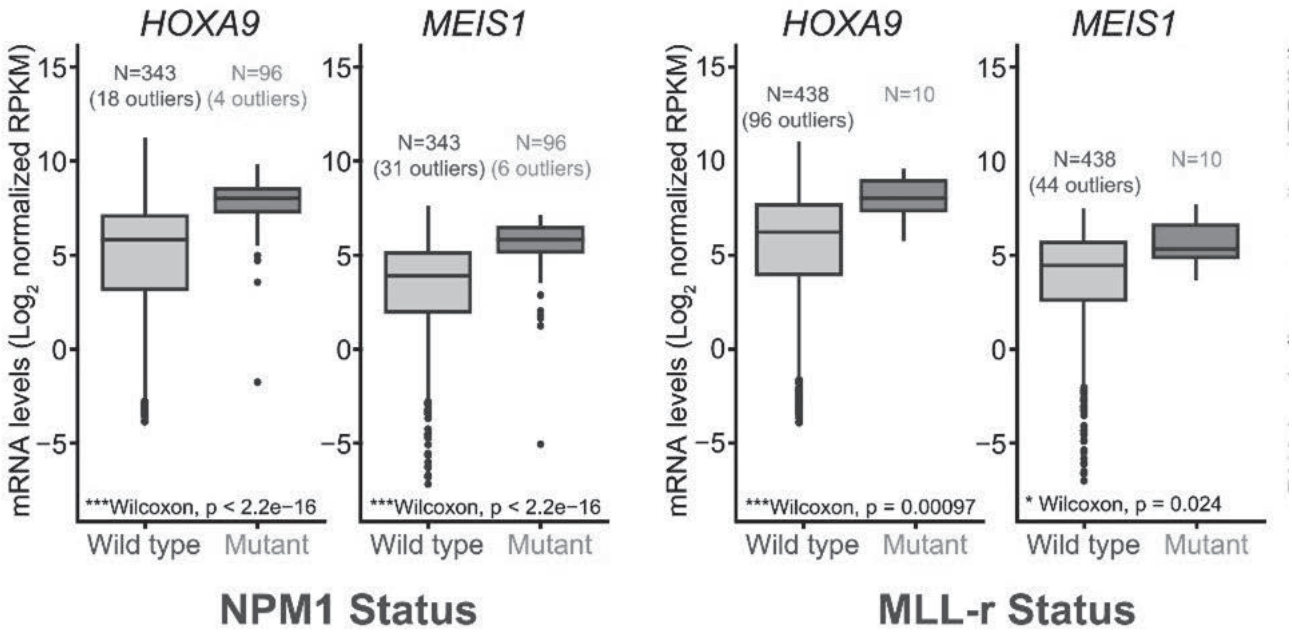
Gilteritinib is an oral, second generation FLT3 inhibitor that is approved as monotherapy for relapsed or refractory FLT3-mutated AML. In the ADMIRAL trial, patients treated with gilteritinib experienced a 21% CR rate and a median overall survival (OS) of 9.3 months as compared to 10.5% CR and 5.6 months OS with conventional salvage chemotherapy. While this was a significant improvement over the existing standard of care, fewer than 20% of relapsed or refractory FLT3-mutated AML patients treated with gilteritinib survived at two years of follow-up. Moreover, the CR rate in patients who were treated with midostaurin in the front line, which has become more common since the approval of gilteritinib, may be as low as 16%. Thus, there continues to be a significant unmet need for patients with relapsed or refractory FLT3-mutated AML. We hypothesize that concurrent inhibition of FLT3 and SYK will lead to superior anti-leukemic activity compared to inhibition of either kinase alone.



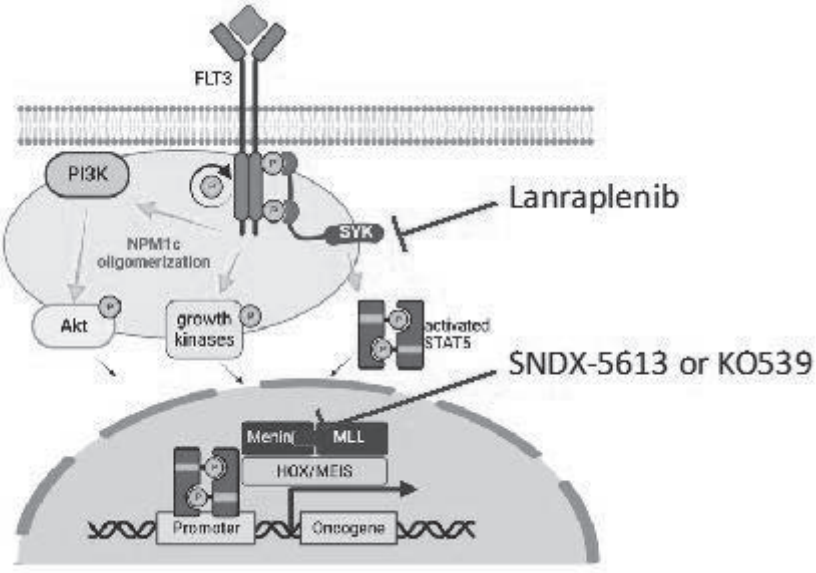
In patient-derived preclinical models of FLT3-mutation driven AML we have observed greater than additive anti-leukemic activity with the combination of lanraplenib and gilteritinib. Combination anti-leukemic activity was also seen in vivo in preclinical models of FLT3-mutation driven AML. Leukemic cell burden in mice was decreased and survival was increased when lanraplenib was administered with gilteritinib compared to lanraplenib or gilteritinib given alone.

In addition to its role as a key mediator of FLT3 leukemogenic signaling, SYK has been implicated as a critical node in AML driven by the dysregulated HOXA9/MEIS1 TRN. HOXA9 and MEIS1 are transcription factors that work together to drive a gene expression program in primitive myeloid cells. As these cells normally mature, expression of these transcription factors is down-regulated. Mutations of NPM1, found in approximately 30% of AML patients (often in association with FLT3 mutations) and rearrangements of the KMT2A (MLL) gene (MLLr) which occur in 5 – 10% of AML patients, prevent the physiologic down-regulation of HOXA9 and MEIS1. SYK expression and activity are upregulated as a consequence of high HOXA9 and MEIS1 expression and this elevated SYK activity is critical for the leukemogenic potential of NPM1 mutations and MLL rearrangements.

The figure below is based on our internal analysis of genomic and transcriptomic data from over 400 AML patient samples obtained through the Leukemia and Lymphoma Society's "Beat AML" program. The figure below depicts mRNA levels for either the HOXA9 or MEIS1 genes across the common AML driver mutations NPM1 (left) and MLL-r (right). For each AML driver mutation, HOXA9 and MEIS1 mRNA levels are shown for either patients that are wildtype for that mutation (grey boxes) or mutated (blue boxes). For each cohort (wild type or mutant), outliers are defined as those patients with mRNA levels exceeding 1.5x the interquartile range (IQR). In all cases, AML driver mutations are associated with increased mRNA levels of HOXA9 and MEIS1 that are consistent with a failure to down-regulate HOX/MEIS expression and are considered statistically significant by a two-sided Mann-Whitney-Wilcoxon test.

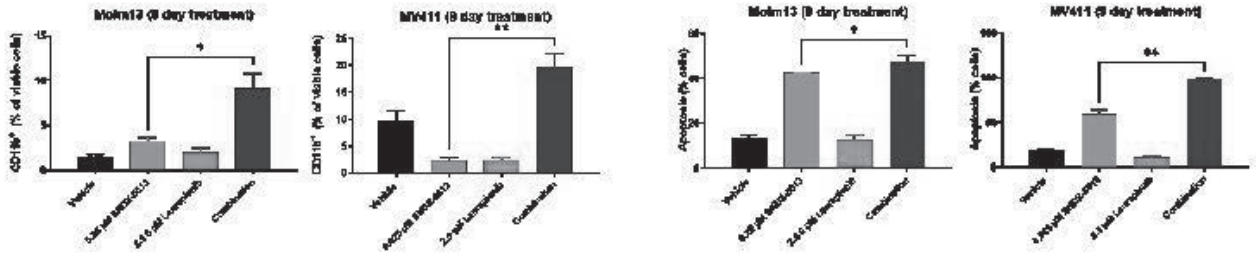


Entospletinib has shown clinical activity in these mutationally defined AML subsets including 3 CRs among 23 MLLr patients treated with entospletinib monotherapy, consistent the hypothesis that inhibiting SYK is a promising therapeutic approach for these subsets of AML. Although for strategic reasons we recently discontinued the AGILITY Phase 3 trial which was testing this hypothesis in newly diagnosed NPM1 mutated AML patients in combination with 7 + 3, we believe that this remains a compelling opportunity for lanraplenib in combination with MLL-MENIN inhibitors such as Sydax's SNDX-5613 or Kura's KO539.



Inhibitors of the interaction between MLL and its cofactor MENIN have shown promising activity in NPM1 mutated and MLLr relapsed or refractory AML. Based on published data, SNDX-5613 has been tested in 48 patients with NPM1 mutation or MLLr and has shown a composite CR rate (CR + CRh) of 27% in both subsets. Fewer patients (N = 20) have been dosed with KO539 for a composite CR rate of 5.6% in MLLr and 30% in NPM1 mutated patients.

We hypothesize that concurrent inhibition of the MLL-MENIN interaction, upstream of dysregulated HOXA9/MEIS1, and SYK, downstream of HOXA9/MEIS1, can lead to improvement in both the rate and depth of CR, leading to longer survival. Preliminary data that is consistent with this hypothesis and generated by our research team is summarized below. The MLLr AML cell lines MV411 and MOLM13 were treated in vitro with lanraplenib or SNDX-5613 individually or in combination and the effects on differentiation (CD11b expression) and apoptosis (annexin V) were measured after 9 days. The combination treatment resulted in synergistic increases in both differentiation and apoptosis.



We believe that lanraplenib and MLL-MENIN inhibitors could be a promising combination to explore in a future clinical trial.

Background on our Research and Development Strategy: Targeting the Activity of Oncogenic Transcription Factors through their Transcription Regulatory Networks (TRNs)

Transcription factors are proteins that bind to specific DNA sequences on the genome and control how sets of genes are turned on and off. This ability to exert systematic control on gene expression underlies the functional importance of transcription factors and consequently, transcription factor activity is recurrently deregulated in many human cancers. This is exemplified by two transcription factors: MYC, the most commonly amplified oncogene, and p53, the most commonly inactivated tumor suppressor gene. Together, these two genes account for two thirds of all human cancers. The human genome encodes more than 500 transcription factors, of which more than 30% have been functionally implicated in cancer, including in recent pan-cancer genetic screens that identify highly selective tumor dependencies.

While there are examples of approved therapies that directly target transcription factor activity (such as those targeting the nuclear hormone family of transcription factors which contain ligand binding domains, or those which act as molecular glues that degrade zinc finger transcription factors), transcription factors as a class remain challenging drug targets. Traditional drug discovery approaches have struggled to target transcription factors for two main reasons. First, most are considered intrinsically disordered proteins, which means that when recombinantly purified they fail to adopt a defined structure, rendering most biochemical and biophysical drug screening approaches unusable. Second, most transcription factors lack active sites or “ligandable” pockets within their protein structure that can be used to modulate their activity. The core biological activity of transcription factors is their ability to recruit cofactors and form large multi-subunit protein complexes on the genome; however, it is only in a cellular context that transcription factors bind to such cofactors and form a unique and defined protein structure. To overcome these two challenges, we believe transcription factors must be drugged in their appropriate physiological context.

Our approach to drug discovery addresses this by mapping and understanding transcription factor activity within the context of its TRN. Within a tumor, a dysregulated network of hundreds of regulatory proteins, including cell-signaling proteins, transcription factors, epigenetic regulators and core transcriptional machinery, coordinate to drive the oncogenic gene expression program. These interactions are dynamic, interdependent and frequently contain redundant pathways, compensatory mechanisms or feedback loops that may drive resistance to targeted therapies. Collectively these hundreds of interactions make up an oncogenic TRN.

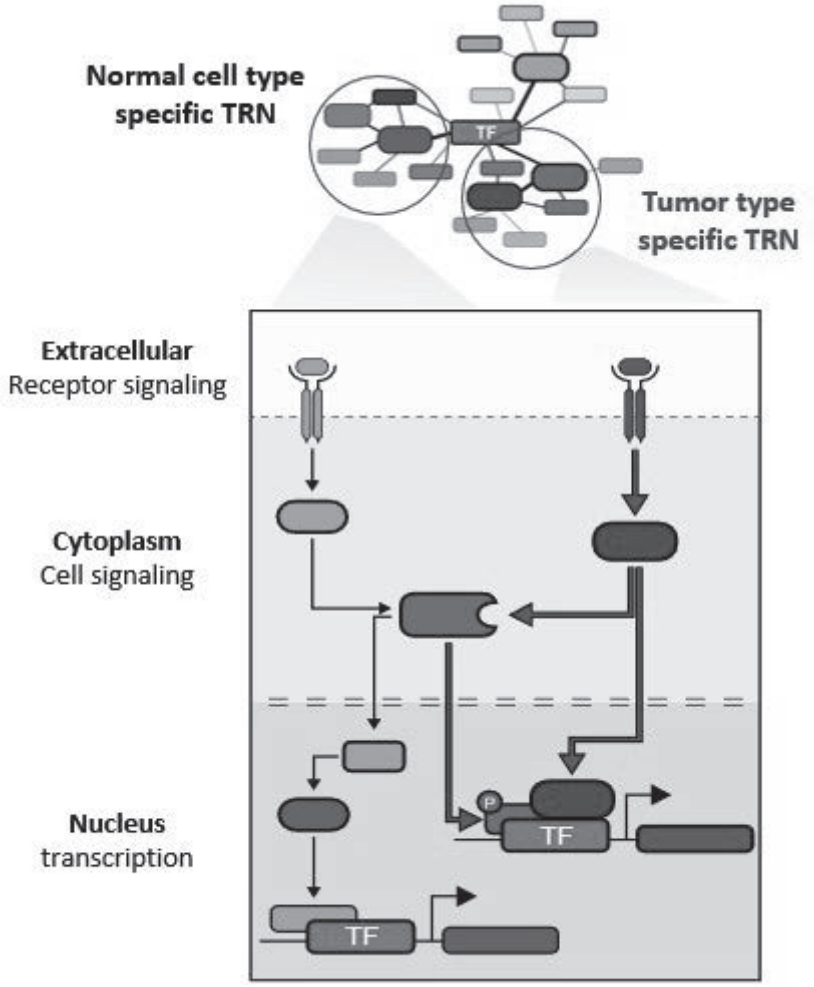
By mapping a specific oncogenic TRN, we believe we are better able to understand the context of transcription factor dependency, which can inform both model selection at the discovery stage and patient biomarker strategy in the clinic. Additionally, TRN maps enumerate the specific inputs and outputs of gene

expression, which can provide insights into how TRNs can be perturbed as well as direct readouts of TRN perturbation. Such direct readouts are crucial in enabling the development of assays to identify on-target TRN perturbation and to distinguish selective inhibition of transcription factor activity from less desirable global inhibition of transcription.

Understanding the structure of a TRN also helps inform our target selection. In an oncogenic TRN, many parallel signals and feedback loops converge to define and drive cancer. Dysregulated transcription factors are the proteins that directly control aberrant transcription of the genome and are critical nodes in oncogenic TRNs. These TRNs may also contain additional critical nodes of signaling or epigenetic regulation that play an essential role in perpetuating the oncogenic TRN. Our core hypothesis is that TRNs are most easily targeted by drugging their critical nodes. We believe these critical nodes present attractive therapeutic targets that expand the opportunity to target transcription factor activity in cancer. By potentially collapsing the oncogenic TRN, therapies directed to these targets hold the promise of limiting potential mechanisms for resistance.

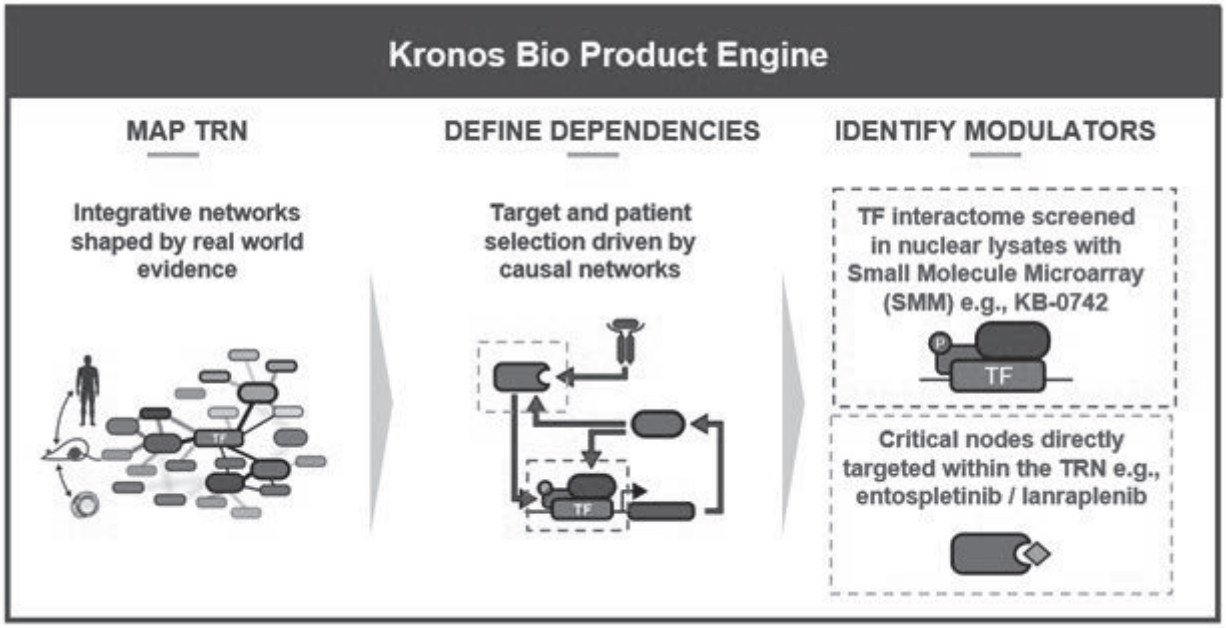
The figure below illustrates an example TRN and shows how the structure of a TRN can be altered in a tumor specific context. In this diagram, nodes represent distinct proteins and edges represent functional, regulatory, or genetic interactions. Upregulation of oncogenic signaling can alter the activity of nodes and edges (shown in red) leading to oncogenic activation of gene expression at tumor specific loci across the genome. These subnetworks within the TRN are associated with tumor specific activity and are likely to contain critical nodes, proteins that play an outsized role in maintaining a tumor specific TRN and are relied upon for the survival of the tumor. Critical nodes may be points of convergence for multiple signaling pathways, components of positive feedback loops, or effector proteins that regulate many other processes. Since transcription factors themselves can regulate many hundreds or more genes, transcription factors are often critical nodes within TRNs.

Example Output of Mapping TRN in Oncogenic versus Normal Context



Our Product Engine

Our differentiated product engine comprises three interconnected components. First, we integrate diverse multiomic data from cancer model systems with clinical real-world evidence to map the TRN of interest. Next, we apply our expertise in systems biology and drug discovery to define the mechanistic basis of TRN tumor dependency. Third, we use this tumor dependency information to identify small molecule modulators in one of two ways: either through use of our proprietary SMM screening platform in an "unbiased" manner, or through a more "biased" approach where we direct our screening efforts against identified TRN critical nodes. These elements of our product engine are shown in the figure below.



Mapping TRNs by Integrating multiomic data and real-world evidence

TRN maps represent the summation of multiple regulatory layers (genetic, signaling, chromatin, epigenomic, protein-protein interaction) that converge in the nucleus to establish and maintain the cell's gene expression program. In mapping TRNs, we address two major challenges that enable, which enables us to better generate actionable drug discovery insights that drive our drug discovery efforts.

First, we seek to identify TRN maps in the appropriate context that capture their tumor-specific deregulation. As an example, to map the MYC TRN, we analyze how MYC amplification rewires the tumor cell TRN to create positive feedback loops that stabilize and upregulate MYC activity in a manner not seen in normal cells. To ensure that the TRN maps faithfully recapitulate true patient tumor biology, we integrate pan-cancer multiomic data, which helps us understand a broader and more defined TRN map, with clinical real-world evidence drawn from thousands of cancer patients. This also lays the foundation for later patient selection and biomarker development.

Defining the mechanistic basis of TRN tumor dependencies

Our initial TRN maps, like many big-data networks, contain many thousands of nodes and edges and are too complex to be immediately actionable. To address this, we have developed computational biology capabilities that we deploy to identify direct transcription factor regulatory modules that we validate using high throughput functional perturbations. These modules allow us to transform our TRN maps from being associative and correlative to causal and predictive. This enables us to understand the consequences of perturbing individual nodes in the TRN, which in turn can drive assay development and the nomination of critical nodes in target selection.

We believe our approach to TRN mapping may reveal actionable critical nodes throughout the TRN, including lineage-defining transcription factors, epigenetic factors and non-redundant pathway or co-factor dependencies required to execute the oncogenic program. This is especially valuable when targeting dysregulated transcription factors that act in a highly context-dependent manner and are difficult to target using conventional methods.

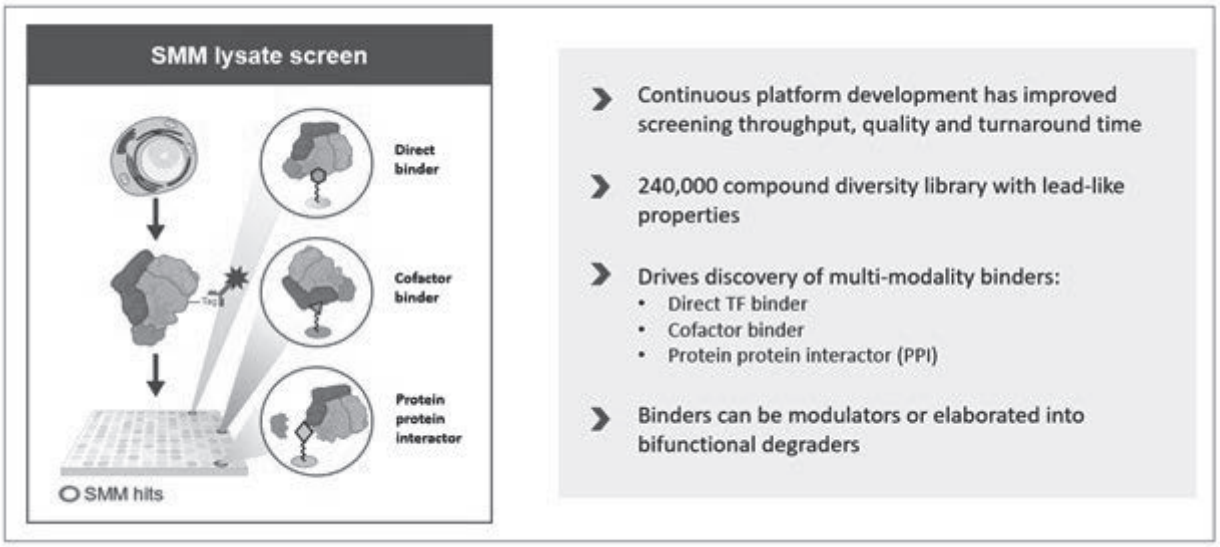
Identifying TRN modulators by using our SMM screening platform or by direct targeting of critical nodes

Our proprietary SMM screening platform addresses the historical challenges of context-dependent structures and complexes by allowing us to conduct a high throughput screen for protein complex binders directly in a tumor cell lysate.

Because SMM lysate screens probe the entire target protein interactome in a single assay, SMM hits have the potential to engage the target protein and its complexes through at least three distinct binding modes:

- *Direct binder*. These molecules may directly engage the target protein either at an active domain or an allosteric site.
- *PPI Modulator*. These molecules may bind a pocket or groove that is created by a protein-protein interface in complexes containing the target protein.
- *Co-factor binder*. These molecules may bind an essential co-factor of the target protein.

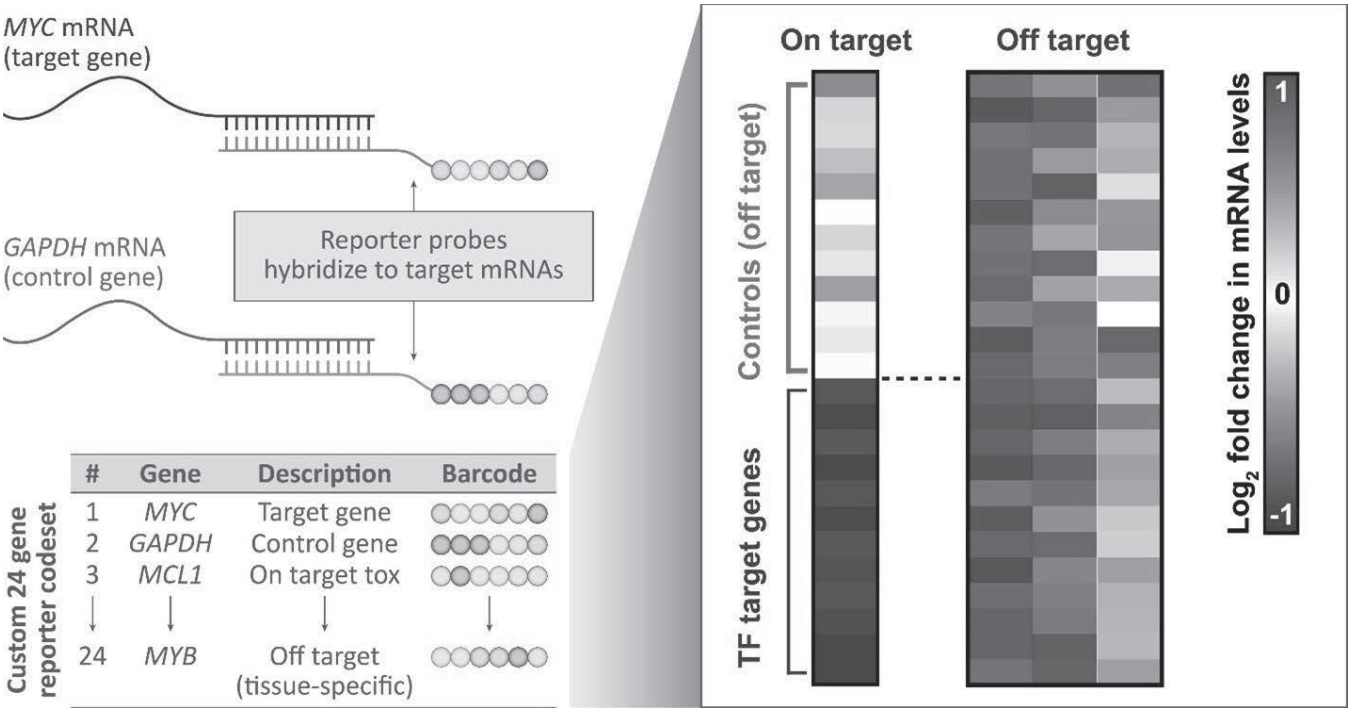
Small Molecule Microarray Identifies Binders to TRN Constituents



Hits derived from an SMM screen have the potential to bind different members of the target protein complex and act through a variety of mechanisms. Our approach is to identify selective modulators of TRNs rather than modulators that globally alter transcription. We hypothesize that selective on-target TRN modulators should have a better therapeutic index in that they will selectively inhibit TRN-driven oncogenic gene expression programs while sparing normal transcription. Our ability to properly characterize the transcriptional selectivity of small molecule perturbations will be crucial in developing and optimizing TRN modulators and is akin to assessing the substrate selectivity and off targets of more traditional drugs like enzymatic inhibitors. In contrast to traditional drug discovery triages, which focus on identifying compounds with a particular activity or profile, SMM hit triage must account for multiple distinct hit profiles.

From our context dependent TRN maps, one way that we characterize SMM hits is by generating and experimentally validating signatures of gene expression response that can delineate various forms of TRN perturbation ranging from degradation of a key transcription factor to inhibition of cofactors in upstream signaling pathways. As shown in the figure below, we generate signatures of approximately 24-48 genes whose change in expression we know to be associated with known perturbations of the TRN, such as genetic knockdown of a key transcription factor or chemical inhibition of a cofactor. Signatures include TRN responsive genes as well as control genes, such as GAPDH, which we know to be invariant to TRN perturbation. We use NanoString gene expression to profile how SMM hits impact these TRN signatures in a high throughput manner. For each gene in a signature, NanoString generates a hybridization reporter with a unique fluorescent barcode, as seen on the left. These reporters enable a multiplexed readout of mRNA abundance of these signature genes which allow us to profile the gene expression changes caused by SMM hits. This robust transcriptomic profiling enables us to rapidly advance hits that selectively perturb the oncogenic TRN and exclude compounds with dominant off-target/ off-pathway activity, as depicted in the figure below.

Hit Prioritization for On-target TRN Activity



The second way we characterize SMM hits is by investigating specific mechanisms of action that emerged as critical nodes from our TRN maps, including for example assaying SMM hits for their ability to disrupt a protein-protein interaction or their ability to inhibit a druggable cofactor. In any given SMM TRN screen we may have multiple of these critical node mechanisms that we can bias our hit triage towards. Having two methods of hit characterization allows us to characterize both hits that have on-target gene expression activity in an unbiased manner as well as to find hits that modulate predefined mechanisms of interest.

In addition to identifying functional binders using gene expression signatures, we mine our SMM hits for non-functional binders to known critical node proteins. Because they bind to the target protein while also being covalently attached to the array slide via a chemical linker, SMM hits are well positioned to be transformed into heterobifunctional molecules. The attachment site of this chemical linker is used as a starting point to rapidly functionalize these SMM hits, including converting these hits into heterobifunctional proteolysis targeting chimera (PROTAC) degraders, in order to achieve TRN modulatory activity.

Independent of our SMM screen, we have used other aspects of our product engine to identify critical nodes for which there are existing drugs or chemical matter. For example, we acquired the SYK inhibitor portfolio from Gilead because we perceived an opportunity to target a dysregulated AML TRN driven by high levels of the HOX/MEIS transcription factor family. From our mapping of this TRN, we identified mutations to NPM1 (NPM1c) as directly driving high HOX/MEIS levels and SYK as participating in a key positive feedback loop with HOX/MEIS. This provided a mechanistic basis for SYK dependency in the NPM1c mutant AML patient subset. We used detection of NPM1c mutations as a clinical biomarker for patient selection and from our HOX/MEIS TRN map we developed a more refined signature of on-target SYK inhibition and its downstream consequences for use in our pharmacodynamics measurements. Our product engine enables us to take different approaches to modulating TRNs and identify context-specific critical nodes that can be more easily acted upon either by traditional drug discovery approaches or through existing external programs.

Optimizing Lead TRN Modulator Molecules

Once we have identified a lead molecule, we investigate the connection between molecular characteristics and target engagement to refine or optimize the pharmacological properties of the molecule to match the desired clinical product profile. We employ our robust medicinal chemistry, computational chemistry and assay development capabilities to support such lead optimization.

We tailor our lead optimization strategy to the specific program that gave rise to the lead molecule. We design structure-activity relationship studies to guide optimization toward a specific transcriptional signature in relevant cancer cell lines. For hits with a known binding site and ordered structure, we also leverage computational modeling, structure-based drug design and a suite of biochemical or biophysical assays to rapidly advance lead optimization programs. For hits against historically challenging targets not amenable to biochemical or biophysical screening assays, we have the capability to advance chemistry programs using structure-blind medicinal chemistry approaches that are informed by transcriptional readouts in cell-based assays.

Our Approach to Clinical Trial Design

We leverage our extensive computational biology capabilities to identify predictive biomarkers for drug response and key pharmacodynamic markers of activity within the oncogenic TRN. We then seek to establish in preclinical models the required extent and duration of target coverage required to achieve clinical efficacy without eliciting undue toxicity in normal tissue. For example, while continuous dosing strategies may be appropriate for certain targets, such as SYK, intermittent dosing strategies may be essential for establishing a therapeutic index for other targets, such as CDK9.

We apply this understanding of predictive markers and the pharmacodynamic/efficacy relationship to design early clinical studies that can efficiently identify an optimal dose and dosing schedule for a given product candidate, and potentially achieve clinical proof of concept in a biomarker-defined patient population. This targeted approach may also enable a more efficient late-stage clinical development and registration strategy by focusing on the patients most likely to benefit from treatment and potentially to pursue more efficient regulatory approval pathways.

Discovery Programs

We continually invest in early discovery efforts utilizing our proprietary product engine, with the goal of expanding our pipeline of future product candidates. Our current efforts are focused on four cancer types where dysregulated TRNs play a central role. We believe that we can develop a deep understanding of the underlying cancer dependency, engineer robust systems to characterize perturbation signatures, and identify multiple potential opportunities for therapeutic intervention through modulation of key TRN components. We select our discovery targets based on multiple scientific, translational and competitive considerations, prioritizing those where dependency has been demonstrated in a defined patient population with high unmet medical need, and where we believe we can design an efficient early clinical translation strategy based upon our understanding of the disease biology.

- ***HOX/MEIS, MYB, IRF4 and Hematologic Malignancies***. Despite significant advances in medical management of patients with hematologic malignancies, the majority of patients eventually progress through standard of care therapy and long-term outcomes remain poor. There is a demonstrated need for novel and more durable treatments for hematologic malignancies, including AML and multiple myeloma. In addition to our clinical SYK inhibitor program in HOX/MEIS-high AML, we are actively conducting discovery efforts targeting MYB, a key lineage transcription factor in early hematopoiesis that is dysregulated in leukemia and interacts with many known leukemia driver genes. We are also actively conducting discovery efforts on IRF4, which is a major driver of multiple myeloma and which is downstream of the primary resistance pathway for thalidomide analogs.

- ***AR and Prostate Cancer***. Dysregulation of the androgen receptor (AR) TRN is a primary driver of prostate cancer. Multiple approved products target the AR TRN by directly inhibiting AR, such as enzalutamide or apalutamide, or by inhibiting androgen biosynthesis, such as abiraterone acetate. Although androgen deprivation therapy is effective in controlling disease, a large number of patients ultimately develop therapy resistance and succumb to castration-resistant prostate cancers. Castration resistance is commonly induced by certain AR variants, such as ARv7, that lack the ligand binding domain and consequently are no longer considered conventionally druggable. Critically, these AR variant tumors still are driven by and depend on increased activity of the AR TRN. Our discovery efforts seek to identify novel modulators of AR TRN activity that are effective in tumor lines expressing AR variants.

- ***MYC and MYC-Driven Cancers***. The MYC family of dysregulated transcription factors is among the small number of proto-oncogenes capable of driving tumor formation and growth in a wide variety of contexts. In normal cells, MYC acts at the nexus of multiple signaling pathways to coordinate gene expression

programs associated with cell growth, metabolism and proliferation. In tumors, MYC dysregulation is defined by increased levels and activity of the full length MYC transcription factor. MYC is dysregulated in a significant proportion of malignancies and its dysregulation is associated with aggressive disease and poor clinical outcomes. As such, targeting MYC has long been considered one of the great challenges in developing cancer therapeutics. In many MYC dysregulated tumors, oncogenic driver events rewire the MYC TRN to introduce positive feedback loops that lead to runaway MYC activation. In addition to our CDK9 program, which focuses on the treatment of patients with MYC-amplified solid tumors, we are focusing discovery efforts to find additional modulators of the MYC TRN.

- ***ASCL1 and SCNC***. Tumor cells can transition between cell states, or subtypes, in response to therapy as a means of acquiring resistance and becoming more aggressive. In particular, many solid tumors adapt to and eventually overcome standard of care therapy as a result of transitions into a SCNC subtype. SCNC state transitions are common in small cell lung cancer, and are also observed in neuroblastoma, prostate cancer, and pancreatic cancer, and patients with these cancers face a very poor prognosis. The transcription factor ASCL1 has emerged as a critical node in the SCNC TRN. It is both a biomarker of the SCNC subtype and a demonstrated dependency in these cancers. Our discovery efforts currently focus on identifying modulators of ASCL1 transcription factor activity within the SCNC TRN.

Future Opportunities

While many opportunities remain within oncology, dysregulated TRNs also play a central role in many other disease states. Future applications of our differentiated product engine in the immunology field may hold particular promise, especially with respect to targeting TRNs that influence the tumor microenvironment and anti-tumor immune response or tolerance. As our discovery organization continues to grow, we intend to regularly re-evaluate our discovery pipeline and seek to identify additional opportunities to fully exploit our differentiated product engine.

Strategic Agreements

Genentech Collaboration Agreement

On January 6, 2023, we entered into a Collaboration and License Agreement with Genentech, a member of the Roche Group. Pursuant to the agreement, the parties have agreed to initially collaborate on two discovery research programs in oncology, each focused on a designated transcription factor, to discover small-molecule GLP-Tox-ready candidates that modulate transcription factor targets selected by Genentech. Each discovery research program will primarily consist of (i) a mapping phase with the goal of identifying the transcription regulatory network for such designated transcription factor, and (ii) a screening phase having the goal of identifying and characterizing multiple screening hits suitable for nomination as a preclinical development program.

We will lead discovery and research activities under the discovery research programs and will use our proprietary drug discovery platform, including our SMM, for hit finding. Following the completion of initial discovery and research activities, Genentech will have the exclusive right to pursue further preclinical and clinical development and commercialization of compounds identified in the discovery research programs and designated by Genentech (each, a Hit Program).

In connection with the agreement, we received an upfront payment of $20.0 million from Genentech. In addition, we are eligible for additional milestone payments upon achievement of certain preclinical, clinical and regulatory (including first-sale) milestones, totaling up to $177.0 million for the first development candidate per hit program, and are eligible to receive net sales milestones of up to $100.0 million for the first licensed product per hit program. We are also eligible to receive tiered royalties in the low- to high-single digits on any products that are commercialized by Genentech as a result of the collaboration.

The term of the discovery research programs will be up to 24 months, which may be extended by six months at our option subject to satisfying certain conditions.

Unless earlier terminated, the agreement will remain in effect for each product licensed under the agreement until the expiration of the royalty term for such licensed product. Genentech has the right to terminate the agreement in its entirety, or with respect to a particular discovery research program or Hit Program, in its sole

discretion, at any time by providing 60 days' advance written notice to us. Each party may also terminate the agreement upon the other party's material breach that remains uncured for 90 days (or 45 days in the event of nonpayment), or in the event of certain insolvency events involving the other party.

Tempus R&D Services Agreement

In October 2021, we entered into an agreement for research and development services (Tempus Agreement) with Tempus Labs, Inc. (Tempus), pursuant to which Tempus agreed to provide us with research and development services for a period of three years. The three primary services are analytical services, data licensing, and organoid services. We intend to utilize the services contemplated under the Tempus Agreement to advance the development of KB-0742 and lanraplenib.

In consideration for the access to the services throughout the term of the Tempus Agreement, we have agreed to pay an annual minimum commitment of $1.5 million in year one, $2.0 million in year two, and $2.5 million in year three. Payments are made in quarterly installments. As of December 31, 2022, we have paid $1.1 million under the Tempus Agreement.

In addition, we are required to make milestone payments upon successful achievement of certain regulatory milestones for KB-0742, lanraplenib, and other discovery pipeline compounds up to a combined maximum of $22.4 million. For each milestone payment that becomes due, we have the right to pay up to 50% of such milestone payment amount in shares of our common stock as long as certain regulatory requirements are met.

Gilead Asset Purchase Agreement

In July 2020, we entered into the Gilead Asset Purchase Agreement, pursuant to which we acquired certain assets from and assumed certain liabilities of Gilead related to entospletinib and lanraplenib, and patents and other intellectual property covering or related to the development, manufacture and commercialization of entospletinib and lanraplenib.

In consideration for such assets, on the date of the Gilead Asset Purchase Agreement, we made a $3.0 million upfront cash payment and issued a $3.0 million principal amount convertible promissory note, which was settled in exchange for 188,567 shares of common stock in connection with the closing of our IPO at a settlement price of $16.15 per share. We also made a $0.7 million payment to reimburse Gilead for certain liabilities we assumed pursuant to the Gilead Asset Purchase Agreement. In addition, we are required to make milestone payments upon successful achievement of certain regulatory and sales milestones for lanraplenib, entospletinib and other SYK inhibitor compounds covered by the patent rights acquired pursuant to the Gilead Asset Purchase Agreement and developed by us as a back-up to entospletinib or lanraplenib (Other Compounds). Upon successful completion of certain regulatory milestones in the United States, European Union and United Kingdom for lanraplenib, entospletinib and any Other Compounds, across up to two distinct indications, we will be required to pay to Gilead an aggregate total of $51.3 million. Upon achieving certain thresholds for the aggregate annual net sales of lanraplenib, entospletinib, and any Other Compounds combined, we would owe to Gilead potential milestone payments totaling $115.0 million.

Gilead is also eligible to receive (i) tiered marginal royalties ranging from high-single digits to the mid-teens on annual worldwide net sales of lanraplenib, (ii) tiered marginal royalties ranging from the very low-teens to high-teens on annual worldwide net sales of entospletinib, and (iii) tiered marginal royalties ranging from the low single digits to mid-single digits on annual worldwide net sales of any Other Compounds. The royalties in the foregoing clauses are subject to reduction, on a country-by-country basis, for products not covered by certain claims within the assigned patents, for generic entry and, in the case of lanraplenib and entospletinib, for any royalties paid for future licenses of third-party intellectual property required to develop or commercialize lanraplenib or entospletinib. Our royalty obligation with respect to a given product in a given country begins upon the first commercial sale of such product in such country and ends on the latest of (i) expiration of the last claim of a defined set of the assigned patent rights covering such product in such country, (ii) loss of exclusive data or marketing rights to such product in such country or (iii) 10 years from the first commercial sale of such product in such country.

Under the Gilead Asset Purchase Agreement, we are required to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize either entospletinib or lanraplenib.

Gilead is required, subject to certain limitations, to indemnify us against damages arising out of any breach in the representations or warranties made by Gilead, any breach of a covenant by Gilead, any use or exploitation of the acquired assets by or on behalf of Gilead prior to the closing of the Gilead Asset Purchase Agreement, or any liability not specifically assumed by us under the Gilead Asset Purchase Agreement, subject to certain caps. Likewise, we are required, subject to certain limitations, to indemnify Gilead against damages arising out of any breach of our representations and warranties, any breach of a covenant made in the agreement, any use or exploitation of the acquired assets by us or on our behalf on or after the closing of the Gilead Asset Purchase Agreement, or any assumed liability, subject to certain caps.

Harvard License Agreement

In January 2018, we entered into a license agreement with President and Fellows of Harvard College (Harvard), pursuant to which Harvard granted us a non-exclusive, worldwide, royalty-free license to certain patent rights covering aspects of our SMM platform. We paid a one-time license fee in the amount of $10,000 on the date of the agreement and an annual license maintenance fee of $20,000 on each of the first two anniversaries. We are required to pay $25,000 on each subsequent anniversary until the last to expire of any valid claim included in the licensed patents.

Unless earlier terminated in accordance with the agreement, the agreement will continue until the last to expire of any valid claim of the licensed patents. In addition, the agreement can be terminated (i) by either party for the other party's material breach that remains uncured for 30 days after written notice, (ii) by Harvard if we fail to meet certain insurance obligations immediately without notice, and for certain insolvency-related events upon notice, and (iii) by us, for any reason, upon 60 days' written notice.

Sales and Marketing

We intend to build a commercial infrastructure to support sales of any of our product candidates that receives regulatory approval. We expect to manage sales, marketing and distribution through internal resources and third-party relationships. While we may commit significant financial and management resources to commercial activities, we will also consider collaborating with one or more pharmaceutical companies to enhance our commercial capabilities.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely for the foreseeable future, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture of any products that we may commercialize. In this regard, while we have purchased initial inventory of active pharmaceutical ingredients (APIs) and clinical drug supply for lanraplenib from Gilead under the Gilead Asset Purchase Agreement, we will need to obtain further supplies of APIs and clinical drug supply for lanraplenib and KB-0742 from third-party manufacturers. We are initially obtaining our supplies from manufacturers on a purchase order basis without long-term supply arrangements in place. We do not currently have arrangements in place for redundant supply for APIs and drug product. For all of our product candidates, we intend to identify and qualify manufacturers to provide the APIs and drug product prior to submission of an NDA to the FDA or other marketing authorization applications to other regulatory authorities.

All our product candidates are compounds of low molecular weight, generally called small molecules. They can be manufactured from readily available starting materials in reliable and reproducible synthetic processes that are amenable to scale-up and do not require specialized equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. We operate in the segments of the pharmaceutical, biotechnology and other related markets that address inhibition of kinases and targeting transcriptional regulation in cancer. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages we hope to exploit, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies,

academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and ultimately commercialize will compete with existing products and new products that may become available in the future.

In the case of lanraplenib, there are currently no approved products on the market that combine with gilteritinib in relapsed or refractory AML with FLT3 mutation. However, there are product candidates that are currently in clinical development which, if approved, could compete or potentially be complementary with lanraplenib including: (i) HMPL-523, a SYK inhibitor being developed by Hutchison Medipharma Ltd. that is in Phase 1 evaluation in hematologic malignancies; (ii) product candidates in early clinical development that target the interaction between MLL and MENIN in MLL-r and AML patients with NPM1 mutations, including (a) DS-1594, being developed by Daiichi Sankyo Company in a Phase 1 clinical trial with or without azacitidine/venetoclax in relapsed/refractory AML; (b) JNJ-75276617, being developed by Janssen Research & Development, LLC in a Phase 1 clinical trial in acute leukemias; (c) KO-539, being developed by Kura Oncology, Inc. in a Phase 1 clinical trial as monotherapy in relapsed or refractory AML; and (d) SNDX-5613, being developed by Syndax Pharmaceuticals, Inc. in a Phase 1 clinical trial as monotherapy in relapsed or refractory AML in patients with MLL-r/KMT2A gene rearrangement or NPM1 mutations; and (iii) product candidates that address the subset of AML patients with FLT3 mutations and are currently in development in combination with FLT3 inhibitors, including (a) venetoclax, a BCL-2 inhibitor being developed by Abbvie; (b) CC-90009, a A Cereblon E3 ligase modulating drug that promotes selective degradation of GSPT1, in Phase 1b, being developed by Bristol-Myers Squibb; (c) CPX-351, a liposomal formulation of daunorubicin and cytarabine being developed by Jazz Pharmaceuticals; and (d) ladademstat, an LSD1 inhibitorm in Phase 1 dose escalation being developed by Oryzon.

If we are successful in developing and receiving approval for KB-0742, we expect it would compete against various multi-CDK inhibitors that are currently in early-stage clinical development if they are ultimately approved, including: (a) AZD4573, being developed by AstraZeneca; (b) fadraciclib (CYC-065), being developed by Cyclacel Pharmaceuticals; (c) voruciclib, being developed by MEI Pharma; (d) dinaciclib, being developed by Merck & Co.; (e) zotiraciclib, being developed by the National Cancer Institute; and (f) TP-1287 (alvocidib), being developed by Tolero Pharmaceuticals. We also expect it to compete against (a) GFH009, a CDK9 inhibitor in Phase 1 dose escalation, being developed by Genfleet Therapeutics; (b) PRT2527, a CDK9 inhibitor in Phase 1 dose escalation by Prelude Therapeutics; and (c) VIP152, a PTEFb/CDK9 inhibitor in early-stage clinical development by Vincerx Pharma, Inc.

Many of the companies against which we may ultimately compete have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our potential competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient enrollment in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We could see a reduction or elimination in our commercial opportunity if other companies develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or with a more favorable label than any of our product candidates. These companies also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in their establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our most advanced product candidates, lanraplenib and KB-0742, our future product candidates, as well as novel discoveries, product development technologies, and know-how. Our commercial success also depends in part on our ability to operate without infringing the proprietary rights of others and to prevent others from infringing our

proprietary rights. Our policy is to develop and maintain protection of our proprietary position and freedom to operate by, among other means, filing and prosecuting, or in-licensing or acquiring U.S. and foreign patents and patent applications covering those products, technologies, inventions, and improvements that are important to our business.

We also rely on trademarks, trade secrets, know-how, continuing technological innovation, confidentiality agreements, and invention assignment agreements to develop and maintain our proprietary position. The confidentiality agreements are designed to protect our proprietary information and the invention assignment agreements are designed to grant us ownership of technologies that are developed by our employees, consultants, or other third parties. We seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in our agreements and security measures, either may be breached, and we may not have adequate remedies. In addition, our trade secrets may otherwise become known or independently discovered by competitors.

With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of using and manufacturing the same.

We are actively building our intellectual property portfolio around our product candidates and our discovery programs, based on our own intellectual property as well as licensed intellectual property. Following the execution of the Gilead Asset Purchase Agreement, we are the owners of multiple patents and patent applications in the United States and worldwide directed to the composition of matter and methods of use of lanraplenib and entospletinib and other related SYK inhibitor compounds.

Our patent portfolio in general includes patents and patent applications directed to our lead product candidates, lanraplenib and KB-0742 and our other research-stage candidates, all of which are solely owned by us. We also have patents and patent applications directed to entospletinib.

With respect to lanraplenib as of February 1, 2023, our patent portfolio included seven issued U.S. patents, 106 issued or granted foreign patents, and 28 pending U.S. and foreign patent applications claiming lanraplenib as a composition-of-matter, methods of using lanraplenib, and its polymorphic forms and their use, all with nominal terms extending to between 2034 and 2043. Nominal patent terms are determined as 20 years from the earliest non-provisional filing date to which priority is claimed, and do not take into account extensions that are or may be available.

With respect to KB-0742, as of February 1, 2023, we have one issued U.S. patent, two issued or granted foreign patents, and 42 pending U.S. and foreign patent applications directed to the KB-0742 compound, compositions, methods of treating CDK9-mediated diseases with KB-0742, analogs and polymorphic forms of KB-0742, and other research-stage candidate compounds that modulate CDK9 activity, all with nominal terms extending to between 2039 and 2042. Nominal patent terms are determined as 20 years from the earliest non-provisional filing date to which priority is claimed, and do not take into account extensions that are or may be available.

As of February 1, 2023, our patent portfolio related to entospletinib included over 17 issued U.S. patents, 149 issued or granted foreign patents, and 28 pending U.S. and foreign patent applications, claiming entospletinib as a composition of matter, formulations, polymorphic forms or their methods of use or manufacture, all with nominal terms extending to between 2029 and 2043. Nominal patent terms are determined as 20 years from the earliest non-provisional filing date to which priority is claimed, and do not take into account extensions that are or may be available.

Our SMM platform component of our product engine is protected both by certain patents that we have licensed under the Harvard License, as well as proprietary know-how we have generated, including with respect to its use in drug discovery screening against transcription factors in tumor cell lysate. We continue to assess the extent to which we may seek additional patent protection for aspects of our product engine or instead maintain such intellectual property as trade secrets.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing of the first non-provisional application to which priority is claimed. In the United States, patent term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office in granting a patent or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. In the United States, the term of a patent that covers an FDA-approved drug may also be eligible for a patent term extension of up to five years under the Hatch-Waxman Act, which is designed to compensate for the patent term lost during the FDA regulatory review process. The length of the patent term extension is calculated based on the length of time it takes for regulatory review. A patent term extension under the Hatch-Waxman Act cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be restored. Moreover, a patent can only be restored once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the NDA process before it may be legally marketed in the United States.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act (FDCA), and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with FDA's good laboratory practice requirements and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent IRB ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with GCP requirements to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA after completion of all pivotal trials;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, PK, pharmacology, and PD characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

Post-approval trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, 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.

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

U.S. Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act (PDUFA), guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after it the application is submitted. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

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, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase 3 trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA or, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a REMS to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may also require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

In addition, the Pediatric Research Equity Act (PREA), requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Expedited Development and Review Programs

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. With regard to a fast track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, 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. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials and report to FDA regularly on the progress of such trials. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval, which could adversely impact the timing of the commercial launch of the product.

The Food and Drug Administration Safety and Innovation Act established a category of drugs referred to as “breakthrough therapies” that may be eligible to receive breakthrough therapy designation. A sponsor may seek FDA designation of a product candidate as a “breakthrough therapy” if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.

Fast track designation, breakthrough therapy designation, priority review, and accelerated approval do not change the standards for approval, but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for our product candidates as appropriate.

Post-approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, or untitled letters;
- clinical holds on clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

Marketing Exclusivity

Market exclusivity provisions authorized under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain 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 approve or even accept for review an abbreviated new drug application (ANDA), or an NDA submitted under Section 505(b)(2) (505(b)(2) NDA), submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to any preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials. In addition, orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

Other Healthcare Laws

Pharmaceutical and medical device manufacturers are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws may constrain the business or financial arrangements and relationships through which we research, as well as, sell, market and distribute any products for which we obtain marketing approval and include, without limitation:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;

- the federal false claims laws, including the civil False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalties laws prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose obligations on covered entities, including certain healthcare providers, health plans, and healthcare clearinghouses, and their respective business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity as well as their covered subcontractors, with respect to safeguarding the privacy, security and transmission of individually identifiable health information; and

- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to the Centers for Medicare and Medicaid Services (CMS) information regarding payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. The information reported is publicly available on a searchable website, with disclosure required annually.

State and local healthcare laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may be broader in scope than their federal counterparts and apply to business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information; state and local laws which require tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities or that require the registration of pharmaceutical sales representatives; and state and local laws that require the registration of pharmaceutical sales representatives; and state and local laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, imprisonment, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment.

Privacy Laws

We may be subject to diverse laws and regulations relating to data privacy and security as a result of our employee data or other personal information that we may collect. In addition, when we collect personal data as part of any clinical trials or other testing, we may be subject to regulatory obligations. This includes, (i) in the U.S., the California Consumer Privacy Act of 2018, or CCPA, (ii) in the European Union, or EU, and the European Economic Area, or EEA, the EU General Data Protection Regulation, or EU GDPR, (iii) in the United Kingdom, or UK, the UK GDPR, and (iv) the national rules of the individual EU Member States. New privacy rules are being enacted in the U.S. and globally, and existing ones are being expanded, updated and strengthened.

For example, California enacted the CCPA, which became effective in January 2020. The CCPA establishes a privacy framework for covered businesses, including an expansive definition of personal information and data privacy rights for California residents. The CCPA includes a framework with potentially severe statutory damages and private rights of action. The CCPA requires covered companies to provide new disclosures to California consumers (as that word is broadly defined in the CCPA), provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. the California Privacy Rights Act (CPRA) significantly modifies the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. Both the CCPA and CPRA could impact our business activities depending on how they are interpreted and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

Additionally, the GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing activities and implement policies as part of its mandated privacy governance framework. It also requires data controllers to be transparent and disclose to data subjects (in a concise, intelligible and easily accessible form) how their personal data is to be used, imposes limitations on retention of personal data; defines pseudonymized (i.e., key-coded) data; introduces mandatory data breach notification requirements; and sets higher standards for data controllers to demonstrate that they have obtained valid consent for certain data processing activities. We are also subject to EU rules with respect to cross-border transfers of personal data out of the EU and EEA. Although there are currently various mechanisms that may be used to transfer personal data from the EEA to the United States in compliance with law, such as the EU's standard contractual clauses, these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. Fines for certain breaches of the GDPR are significant: up to the greater of €20 million or 4% of total global annual turnover. In addition to the foregoing, a breach of the GDPR or other applicable privacy and data protection laws and regulations could result in regulatory investigations, reputational damage, orders to cease/change our use of data, enforcement notices, or potential civil claims including class action type litigation.

Coverage and Reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufactures to provide scientific and clinical support for the use of a product to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. 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.

In addition, third-party payors are increasingly reducing reimbursements for pharmaceutical products and services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are more and more challenging the prices charged, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical products, in addition to questioning their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Coverage policies and third-party payor reimbursement rates may change at any time. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products and may also compete with imported foreign products. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payors' reimbursement policies will not adversely affect the ability for manufacturers to sell products profitably.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, (collectively, the ACA) was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States. By way of example, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; required collection of rebates for drugs paid by Medicaid managed care organizations; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded eligibility criteria for Medicaid programs; creates a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for

such research; and established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. \On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is unclear how any additional challenges and healthcare reform measures of the Biden administration will impact the ACA and our business.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers, which will remain in effect until 2031 absent additional congressional action. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. Additionally, 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.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries, presidential executive orders, and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. At the federal level, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the U.S. Department of Health and Human Services (HHS) released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" for such drugs and biologics under the law, and (ii) imposes rebates with respect to certain drugs and biologics covered under Medicare Part B or Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but it is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future. In addition, individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

FDA Approval and Regulation of Companion Diagnostics

If safe and effective use of a therapeutic depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, if FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. The review of *in vitro* companion diagnostics in conjunction with the review of our therapeutic treatments for cancer will, therefore, likely involve coordination of review by the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health Office of In Vitro Diagnostics and Radiological Health.

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, 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 applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval (PMA approval).

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation (QSR), which imposes elaborate testing, control, documentation and other quality assurance requirements.

PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards are not maintained or problems are identified following initial marketing.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's

manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

Human Capital Resources

As of January 1, 2023, we had 97 employees, all of whom were full-time. Substantially all of our employees work out of our offices in either San Mateo, California, or Cambridge, Massachusetts. We have three dedicated, full-time employee equivalents responsible for executing our human capital management strategy and overseeing all aspects of our human resources processes in place to support our employees. Our employees are not represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good. Since our founding, we have had relatively low turnover of employees, which we attribute to our shared mission of transforming the lives of those affected by cancer.

Our employees are essential to our success. We have been purposeful, within our resource constraints, in our efforts to hire, develop and retain diverse talent as well as create an inclusive culture. We are investing in building and maintaining a work environment that prioritizes the health, safety and wellness of our team, and where our employees are inspired to deliver their best every day. All employees are responsible for upholding the Kronos Bio Code of Conduct, which forms the foundation of our policies and practices. We are continuing to expand our systems to track key human capital metrics such as demographics, diversity, compensation and benefits, and engagement.

Diversity, Equity and Inclusion

We are committed to creating and maintaining a diverse, inclusive and safe work environment. Our employees bring diversity to our workplace across many critical categories, and we believe our company is stronger as a result of their variety of experiences and backgrounds. For example, just under half our employees self-identify as women, and over half of our employees in medical or scientific roles self-identify as members of underrepresented communities and nearly half self-identify as women. As we grow and mature, we look forward to establishing programs that bring in speakers on specific topics, assemble resources for employees on diversity and inclusion, provide support for our female and underrepresented employees to help advance their careers, all while continuing to focus on hiring, developing and promoting diverse talent at all levels of the company.

Compensation and Benefits

Our commitment to our employees starts with benefit and compensation programs that value employees' contributions and offer financial and health programs for employees and their families. We strive to provide competitive compensation, benefits and services that serve to attract and retain employees. Our compensation package includes market-competitive salary, bonuses and broad-based stock awards, healthcare and retirement benefits, and unlimited paid time off. We also offer an Employee Stock Purchase Program through which employees can purchase company stock at a discounted price, and offer stipends to cover expenses associated with working from home and the use of personal devices for work purposes. Additionally, we continue to advance transparency in our pay and representation data by complying with all applicable statutory filing requirements.

Communication and Engagement

We strongly believe that Kronos Bio's success depends on our employees understanding how their work contributes to the company's overall mission and strategy. We strive to foster open and direct communication and seek to empower our employees to be our greatest ambassadors. We use a variety of channels to facilitate this, including quarterly business updates from the senior management team; regular town hall meetings, open forums and online platforms, and company-wide written communications; and employee engagement surveys.

Health, Wellness and Safety

Employee safety and well-being is of paramount importance to us. We provide productivity and collaboration tools and resources, allow flexible schedules and support employees' information technology needs. We also regularly promote employee assistance programs to support our employees' physical, financial and mental well-being.

Corporate Information

We were incorporated under the laws of the State of Delaware on June 2, 2017. Our principal executive offices are located at 1300 So. El Camino Real, Suite 400, San Mateo, California 94402, and our telephone number is (650) 781-5200. Our corporate website address is www.kronosbio.com. We make available, free of charge on our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and any amendments to those reports, as soon as reasonably practicable after filing such reports with the Securities and Exchange Commission (SEC). Alternatively, you may access these reports at the SEC's website at www.sec.gov. Information contained on, or accessible through, our website shall not be deemed incorporated into and is not a part of this report. We have included our website in this report solely as an inactive textual reference.

ITEM 1A. RISK FACTORS

RISK FACTORS

We have identified the following material factors that make an investment in our common stock speculative or risky. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10-K, including our financial statements and the related notes included elsewhere in this Annual Report on Form 10-K and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before making investment decisions regarding our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. The risks described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Our Financial Condition and Capital Requirements

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

Investment in biopharmaceutical product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we will continue to incur significant research and development and other expenses related to our ongoing operations. We have financed our operations primarily through our IPO and, before that, private placements of our convertible preferred stock and convertible notes.

We have incurred significant net losses in each period since we commenced operations in June 2017. For the years ended December 31, 2022 and 2021, we reported net losses of $133.2 million and $151.1 million, respectively. As of December 31, 2022, we had an accumulated deficit of $396.2 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if and as we:

- conduct preclinical studies and clinical trials for our current and future product candidates;
- continue our research and development efforts, submit INDs and clinically develop our product candidates;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, negative or mixed clinical trial results, safety issues or other regulatory challenges, the risk of which in each case may be exacerbated by COVID-19 or another health epidemic or pandemic;
- establish a sales, marketing and distribution infrastructure and establish manufacturing capabilities, whether alone or with third parties, to commercialize product candidates for which we may obtain regulatory approval, if any;
- obtain, expand, maintain, enforce and protect our intellectual property portfolio; and
- hire additional clinical, regulatory and scientific personnel.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop, seek regulatory approval for and potentially market our product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability, if ever, to generate revenue from our product candidates. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity (deficit) and working capital.

We have not generated any revenue from our product candidates and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from any of our product candidates. We do not expect to generate significant revenue unless or until we successfully complete clinical development and obtain regulatory approval of, and then successfully commercialize, our product candidates. Lanraplenib and KB-0742 are our only product candidates in the clinical stage of development. In addition, all of our product candidates will require additional clinical development, regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. Our ability to generate revenue from our product candidates depends on a number of factors, including, but not limited to:

- timely completion of our preclinical studies and ongoing and planned clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- our ability to complete IND-enabling studies and successfully submit and receive authorizations to proceed under INDs or comparable applications;
- whether we are required by the FDA or similar foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the potential approval and commercialization of our product candidates or of any future product candidates;
- our ability to demonstrate to the satisfaction of the FDA and similar foreign regulatory authorities the safety, potency, purity, efficacy and acceptable risk-benefit profile of our product candidates or any future product candidates and such regulatory authorities' acceptance of our biomarker-driven development strategy (i.e., our pursuit of approval based on a biomarker rather than a specific cancer indication);
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates or future product candidates, if any;
- the timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;
- the willingness of physicians, operators of clinics and patients to utilize or adopt any of our product candidates or future product candidates over or to use in combination with alternative or more established therapies, such as intensive chemotherapy and HMAs, to treat AML and MYC-amplified solid tumors and other transcriptionally addicted cancers;
- the actual and perceived availability, cost, risk profile and side effects and efficacy of our product candidates, if approved, relative to existing and future alternative cancer therapies and competitive product candidates and technologies;
- our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our product candidates or any future product candidates, remain in good standing with regulatory authorities and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices (cGMP);

- our ability to successfully develop a commercial strategy and thereafter commercialize our product candidates or any future product candidates in the United States and internationally, if approved for marketing, reimbursement, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- patient demand for our product candidates and any future product candidates, if approved; and
- our ability to establish and enforce intellectual property rights in and to our product candidates or any future product candidates.

Many of the factors listed above are beyond our control and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercializing any of our product candidates. Even if we are able to commercialize our product candidates, we may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient revenue through the sale of our product candidates or any future product candidates, we may be unable to continue operations without continued funding.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be compelled to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we progress our ongoing clinical trials and commence our planned clinical trials and any other future clinical trials, and continue our discovery and preclinical development activities to identify new product candidates, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations, and we may need to raise additional funding sooner than expected if we choose to expand more rapidly than we presently anticipate. We cannot be certain that additional funding will be available on acceptable terms, or at all. Further, geopolitical events such as the military action initiated by Russia against Ukraine (and responses by the United States and certain other countries, including significant sanctions and trade actions against Russia), inflation, high interest rates, bank failures, a resurgence of COVID-19 or another health epidemic or pandemic, could adversely affect the economy and financial markets in general and our ability to raise additional capital. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of public or private equity offerings, debt financings, collaborations, strategic partnerships and alliances or marketing, distribution or licensing arrangements with third parties. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate our discovery, preclinical and clinical development programs or any future commercialization efforts.

We had cash, cash equivalents, and investments of $247.9 million as of December 31, 2022. We believe that, based upon our current operating plan, our existing capital resources will enable us to fund our planned operating expenses and capital expenditure requirements into the second half of 2025. However, we have based this estimate on our current development plans and assumptions that may prove to be wrong. Additionally, changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control, including as a result of global supply chain issues, inflation, high interest rates, a resurgence of COVID-19 or another health epidemic or pandemic. In any event, our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of our ongoing Phase 1/2 clinical trial of KB-0742;
- the scope, progress, results and costs of our ongoing Phase 1b/2 clinical trial of lanraplenib;
- the costs associated with the wind down of the discontinued Phase 3 AGILITY trial of entospletinib;
- the scope, progress, results and costs of discovery, preclinical development and clinical trials for our other product candidates;
- the costs, timing and outcome of regulatory review of our product candidates and any required companion diagnostic;
- the extent to which we develop, in-license or acquire other pipeline product candidates or technologies;

- the costs of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the costs associated with completing any post-marketing studies or trials required by the FDA or other regulatory authorities;
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, obtaining, maintaining, enforcing and protecting our intellectual property rights and defending intellectual property-related claims; and
- to the extent we pursue strategic collaborations, including collaborations to commercialize any of our product candidates or any companion diagnostic collaborations, our ability to establish and maintain collaborations on favorable terms, if at all.

We will require additional capital to complete our clinical development programs for our current product candidates to obtain regulatory approval. Any additional capital-raising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our current and future product candidates, if approved.

Risks Related to the Discovery and Development of our Product Candidates

We have a limited operating history and face significant challenges and will incur substantial expenses as we build our capabilities.

We were incorporated in June 2017 and acquired certain rights to lanraplenib and other orally bioavailable small molecule SYK inhibitors from Gilead in July 2020. We have a limited operating history and are subject to the risks inherent in a growing company, including, among other things, risks that we may not be able to hire sufficient qualified personnel and establish operating controls and procedures. We currently do not have complete in-house resources to enable our operations. As we continue to build our capabilities, we expect to encounter risks and uncertainties frequently experienced by growing companies in new and rapidly evolving fields. If we are unable to continue to build our capabilities, our operating and financial results could differ materially from our expectations, and our business could suffer.

We cannot be certain that the clinical trials of our product candidates, including our ongoing Phase 1/2 clinical trial of KB-0742, our only internally generated product candidate, and our Phase 1b/2 clinical trial of lanraplenib will be completed when we currently expect, or at all.

We may not realize the benefits of our asset acquisition from Gilead or any future acquisitions or strategic transactions.

In the third quarter of 2020, we completed the transfer from Gilead of a portfolio of selective, orally bioavailable small molecule SYK inhibitors, including entospletinib and lanraplenib. After a review of enrollment, we made the decision to close our Phase 3 trial of entospletinib to further enrollment in the fourth quarter of 2022. In this assessment, we projected significant delays due to several factors, including the operational challenges we faced enrolling a genetically defined subset of patients in the frontline setting, the impacts of COVID-19 on clinical trial site staffing and the loss of access to planned clinical trial sites in Ukraine and Russia. Patients who had already enrolled in the Phase 3 study are able to complete their course of treatment. Final study closure is anticipated in mid-2023. We do not currently anticipate any further Kronos Bio-led clinical development of entospletinib after final study closure. With respect to lanraplenib, it is possible that we will encounter challenges with integrating the data and technology, along with the related regulatory materials, related to this acquired product candidate into our business. In such event, our clinical development plans related to this acquired SYK product candidate, including our ongoing Phase 1b/2 clinical trial of lanraplenib in a genetically-defined subset of AML patients, or the associated or subsequent regulatory filings, could be delayed or otherwise adversely affected.

In addition, we may acquire other businesses, products or technologies as well as pursue joint ventures or investments in complementary businesses. The success of our SYK portfolio acquisition from Gilead, and any

future acquisitions or strategic transactions depends on the risks and uncertainties involved including, but not limited to, the following:

- unanticipated liabilities related to acquired assets, companies or joint ventures;
- difficulties integrating acquired personnel, technologies and operations into our existing business;
- retention of key employees;
- diversion of management time and focus from operating our business to management of strategic alliances or joint ventures or acquisition integration challenges;
- increases in our expenses and reductions in our cash available for operations and other uses;
- disruption in our relationships with collaborators or suppliers as a result of such a transaction; and
- possible write-offs or impairment charges relating to acquired assets, businesses or joint ventures.

If any of these risks or uncertainties occur, we may not realize the anticipated benefit of any acquisition or strategic transaction. Additionally, foreign acquisitions and joint ventures are subject to additional risks, including those related to integration of operations across different cultures and languages, currency risks, potentially adverse tax consequences of overseas operations and the particular economic, political and regulatory risks associated with specific countries.

Future acquisitions or dispositions could also result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities or amortization expenses or write-offs of goodwill, any of which could harm our financial condition.

Our discovery and development activities are focused on novel cancer therapeutics for patients with genetically-defined cancers and it is difficult to predict the time and cost of product candidate development and the likelihood of obtaining regulatory approval.

The discovery and development of novel cancer therapeutics by targeting dysregulated transcription using a biomarker-driven precision medicine strategy is an emerging field, and the scientific discoveries that form the basis for our efforts to discover and develop product candidates are relatively new. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. Although we believe, based on our preclinical work, and the data for entospletinib and lanraplenib generated in clinical trials conducted by Gilead, the TRNs targeted by our programs drive oncogenic activity, future clinical results may not confirm this hypothesis or may only confirm it for certain mutations or certain tumor types. The patient populations for our product candidates are limited to those with cancers that exhibit specific target mutations that we believe serve as a genomic biomarker of transcription factor dysregulation, and may not be completely defined but are substantially smaller than the general treated cancer population. We will need to screen and identify those patients who have the targeted mutations. Successful identification of patients is dependent on several factors, including achieving certainty as to how specific genetic alterations respond to our product candidates and developing or otherwise obtaining access to satisfactory companion diagnostics to identify such genetic alterations. Furthermore, even if we are successful in identifying patients, we cannot be certain that the resulting patient populations for each mutation will be large enough to allow us to successfully obtain approval for each mutation type and commercialize our products and achieve profitability. In any event, we do not know if our approach of treating patients with genetically defined cancers will be successful, and if our approach is unsuccessful, our business will suffer and you may lose all or part of your investment.

In addition, we are pursuing a biomarker-driven development strategy (i.e., pursuing regulatory approval based on efficacy of our product candidates in a biomarker-defined subset of patients with a specific cancer indication, rather than all such patients who suffer from a specific cancer indication). There is currently a limited number of approved biomarker-specific therapies. We may not receive approval for a biomarker-specific indication or may be delayed in receiving biomarker-specific approval.

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

We are unable to predict when or if our products candidates will prove effective or safe in humans or will obtain marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim or preliminary results of a clinical trial do not necessarily predict final results. It is not uncommon to observe results in clinical trials that are unexpected based on preclinical studies and early clinical trials, and many product candidates fail in clinical trials despite very promising early results. Moreover, preclinical and clinical data may be susceptible to varying interpretations and analyses. A number of companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to obtain marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards (IRBs)/ethics committees (ECs) may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts with prospective trial sites;
- clinical trials for our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials, delay clinical trials or abandon product development programs;
- the number of patients required for clinical trials for our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate or the duration of these clinical trials may be longer than we anticipate;
- competition for clinical trial participants from investigational and approved therapies may make it more difficult to enroll patients in our clinical trials;
- third-party collaborators may undergo a change of control, thus delaying progression of a clinical trial;
- we or potential future third-party collaborators may fail to obtain the clearance or approval of any required companion diagnostic on a timely basis, or at all;
- our third-party contractors, including those developing companion diagnostic tests, may fail to meet their contractual obligations to us in a timely manner, or at all, or may fail to comply with regulatory requirements;
- we may have to suspend or terminate clinical trials for our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- our product candidates may have undesirable or unexpected side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs/ECs to suspend or terminate the trials;
- the cost of clinical trials for our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials for our product candidates may be insufficient or inadequate and result in delays or suspension of our clinical trials; and
- we or potential future third-party collaborators may fail to receive regulatory approval of a companion diagnostic for one or more of our product candidates, or for use with a marketed product.

Our product development costs will increase if we experience delays in preclinical studies or clinical trials or in obtaining marketing approvals. We do not know whether any of our planned preclinical studies or clinical trials will begin on a timely basis or at all, will need to be restructured or will be completed on schedule, or at all.

Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Any delays in the commencement or completion, or termination or suspension, of our planned or future clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Before we can initiate clinical trials of a product candidate in any indication, we must submit the results of preclinical studies to the FDA along with other information, including information about the product candidate's chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND or similar regulatory submission under which we must receive authorization to proceed with clinical development.

Before obtaining marketing approval from the FDA of any product candidate in any indication, we must conduct extensive clinical studies to demonstrate safety and efficacy. Clinical testing is expensive, time consuming and uncertain as to outcome. In addition, we expect to rely in part on preclinical, clinical and quality data generated by our CROs and other third parties for regulatory submissions for our product candidates. While we have or will have agreements governing these third parties' services, we have limited influence over their actual performance. If these third parties do not make data available to us, or, if applicable, make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may be significantly delayed and we may need to conduct additional studies or collect additional data independently. In either case, our development costs would increase. We are required to submit an IND to the FDA, which must be cleared prior to initiating any clinical trials in the United States, for our preclinical product candidates.

The FDA may require us to conduct additional preclinical studies for any product candidate before it allows us to initiate clinical trials under any IND, which may lead to additional delays and increase the costs of our preclinical development programs.

Any delays in the commencement or completion of our planned or future clinical trials could significantly affect our product development costs. We do not know whether our planned trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- obtaining FDA or foreign regulatory authority authorization to commence a clinical trial or reaching a consensus with the FDA or a foreign regulatory authority on clinical trial design;
- failing to obtain regulatory clearance or approval of companion diagnostics we may use to identify patients for enrollment in or test the possible effects of our product candidates in patients enrolled in our clinical trials;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval from one or more IRBs/ECs;
- IRBs/ECs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- changes to clinical trial protocol;
- clinical sites deviating from trial protocol or dropping out of a trial;
- failing to manufacture or obtain sufficient quantities of product candidate or, if applicable, combination therapies for use in clinical trials;

- patients failing to enroll or remain in our trial at the rate we expect, or failing to return for post-treatment follow-up, including patients failing to remain in our trials due to movement restrictions, health reasons or contraction of or concerns associated with an infectious disease, such as COVID-19;
- patients choosing an alternative treatment, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- patients experiencing severe or unexpected drug-related adverse effects;
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies;
- selecting or being required to use clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- a facility manufacturing our product candidates or companion diagnostics or any of their components being ordered by the FDA or applicable foreign regulatory authorities to temporarily or permanently shut down due to violations of cGMP regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- interruptions to operations of clinical sites, manufacturers, suppliers, or other vendors from geopolitical events, such as the military action initiated by Russia against Ukraine, or from COVID-19 or another health epidemic or pandemic;
- any changes to our manufacturing process that may be necessary or desired;
- third-party 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 (GCP) or other regulatory requirements;
- us, or our third-party contractors not performing data collection or analysis in a timely or accurate manner or improperly disclosing data prematurely or otherwise in violation of a clinical trial protocol;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of 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; or
- disruptions caused by COVID-19 or another health epidemic or pandemic, which may increase the likelihood that we encounter difficulties or delays in initiating, enrolling, conducting or completing our ongoing or planned clinical trials.

In addition, our proposal for new or emerging biomarker surrogate endpoints may result in data that is not accepted by certain regulatory bodies or industry professionals, or if such endpoints are later found to be insufficient to establish clinical efficacy, may require us to change the design of our clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs/ECs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a pharmaceutical, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs/ECs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

We may also experience delays if our current or planned clinical trials are impacted by geopolitical, economic or military instability. For example, we had anticipated utilizing clinical trial sites in Ukraine and Russia for our

Phase 3 clinical trial of entospletinib in combination with intensive chemotherapy in AML patients with NPM1 mutations. However, due to the military conflict in the region, we revised our plans to open clinical trial sites in the region and were planning to utilize clinical trial sites in other countries. The failure to identify and operationalize alternative clinical sites contributed to delays in enrollment for this trial.

Certain of our current or future scientific advisors or consultants who receive compensation from us may become investigators for our future clinical trials. Under certain circumstances, we may be required to report some of these relationships to the FDA. Although we expect any such relationships to be within the FDA's guidelines, the FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected the interpretation of the study. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of our product candidates. If we experience delays in the completion of, or termination of, any clinical trial, the commercial prospects of such product candidate will be harmed, and our ability to generate product revenues will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our development and approval process and jeopardize our ability to commence product sales and generate revenues which may harm our business, financial condition, results of operations and prospects significantly.

If we experience delays or difficulties in enrolling patients in our ongoing or planned clinical trials, regulatory approval could be delayed or we could fail to obtain regulatory approval.

We may not be able to initiate or continue our ongoing or planned clinical trials for our product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA. In addition, some of our competitors may have ongoing clinical trials for product candidates that would treat the same or a similar patient population as we plan to treat with our product candidates in clinical trials, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

We are conducting a Phase 1/2 clinical trial of KB-0742 in patients with cancer to evaluate the safety, PK and PD of the compound across multiple dose levels. We are currently enrolling expansion cohorts of biomarker-defined patient populations with transcriptionally addicted cancers. While we believe it is feasible to enroll such patients at major academic centers, patients with these tumor types are relatively rare, and we may be unable to enroll or maintain a sufficient number of these patients in any such cohort, which could adversely affect our development and registration strategy for KB-0742.

Our Phase 3 trial of entospletinib in NPM1-mutated AML patients was discontinued in part due to the difficulties in identifying the small number of patients with this mutation, including the time required for screening diagnostics when physicians and patients have an urgency to begin treatment for their AML. We may encounter similar risks in future trials of our product candidates, which may result in delays and potentially the discontinuation of such trials.

Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- our ability to recruit clinical trial investigators of appropriate competencies and experience;
- the incidence and prevalence of our target indications;
- clinicians' and patients' awareness of, and perceptions as to the potential advantages and risks of our product candidates in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- invasive procedures required to enroll patients and to obtain evidence of the product candidate's performance during the clinical trial;
- availability and efficacy of approved medications for the disease under investigation;
- eligibility criteria defined in the protocol for the trial in question;

- the size of the patient population required for analysis of the trial's primary endpoints;
- efforts to facilitate timely enrollment in clinical trials;
- whether we are subject to a partial or full clinical hold on any of our clinical trials;
- reluctance of physicians to encourage patient participation in clinical trials;
- the ability to monitor patients adequately during and after treatment;
- our ability to obtain and maintain patient consents;
- proximity and availability of clinical trial sites for prospective patients; and
- our ability to timely activate clinical trial sites and other delays and complications resulting from COVID-19 or another health epidemic or pandemic.

Enrollment in our trials has been adversely impacted by COVID-19 on a rolling basis as healthcare facilities and patients experienced periodic delays in visits, scheduling and staffing that adversely impacted enrollment. As a result of ongoing global challenges in clinical trial enrollment for our Phase 3 AGILITY clinical trial of entospletinib in combination with intensive chemotherapy in patients with newly diagnosed NPM1-mutated AML, we closed enrollment in the fourth quarter of 2022 and are discontinuing Kronos Bio-led clinical development of entospletinib. Our inability to enroll the required number of patients for our other ongoing and planned clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If adverse side effects or unexpected characteristics are identified during the development of our product candidates, we may need to abandon or limit the development of a product candidate.

Results of our ongoing or planned clinical trials, including those for lanraplenib and KB-0742, could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could result in the delay, suspension or termination of clinical trials by us or the FDA or foreign regulatory authorities for a number of reasons. Additionally, due to the high mortality rates of the cancers for which we are initially pursuing development of lanraplenib and KB-0742, a significant percentage of patients in these clinical trials may die during a trial, which could impact development of these product candidates. If we elect or are required to delay, suspend or terminate any clinical trial, the commercial prospects of our product candidates will be harmed and our ability to generate product revenues from this product candidate will be delayed or eliminated. Serious adverse events observed in clinical trials could hinder or prevent market acceptance of our product candidates. Any of these occurrences may harm our business, prospects, financial condition and results of operations significantly.

Moreover, if our product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon or limit their 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, which may limit the commercial expectations for our product candidates, if approved. We may also be required to modify our study plans based on findings in our clinical trials. Many drugs that initially showed promise in early stage testing have later been found to cause side effects that prevented further development. In addition, regulatory authorities may draw different conclusions or require additional testing to confirm these determinations.

It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, including with different dosing regimens, or as the use of our product candidates becomes more widespread following any regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition, results of operations and prospects significantly.

In addition, if any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by treatment with such drug, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of the product;
- we may be required to recall a product or we may voluntarily remove it from the marketplace;
- we may be required to change the way the product is administered to patients or conduct additional clinical trials;
- regulatory authorities may require additional warnings on the label, such as a “black box” warning or a contraindication, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to implement a Risk Evaluation and Mitigation Strategy (REMS) or create a medication guide outlining the risks of such side effects for distribution to patients;
- additional restrictions may be imposed on the marketing or promotion of the particular product or the manufacturing processes for the product or any component thereof;
- we could be sued and held liable for harm caused to patients;
- the drug could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates, if approved, and could significantly harm our business, financial condition, results of operations and prospects.

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

From time to time in the future, we may publicly disclose preliminary, interim or topline data from our ongoing or planned clinical trials. These updates are typically based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial or following the completion of such clinical trial or stage of such clinical trial. 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. As a result, the interim, topline or preliminary results that we may report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Interim, topline and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, such data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim, topline, or preliminary data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse changes between interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim, topline or preliminary data by us or by our competitors in the future could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a

particular drug, product candidate or our business. If the interim, topline or preliminary 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, our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

If we are unable to successfully develop companion diagnostic tests for our product candidates that require such tests, experience significant delays in doing so, or are unable to obtain any necessary FDA approvals of such tests, we may not be able to obtain approval for our product candidates, may be delayed in doing so, or may not realize the full commercial potential of these product candidates.

In developing a product candidate for certain indications, we may decide to use a biomarker-based test to identify patients for enrollment or monitor patients in clinical trials. For example, we used a biomarker-based test to identify patients for enrollment in our discontinued registrational Phase 3 clinical trial of entospletinib in combination with intensive chemotherapy for the treatment of AML patients with NPM1 mutations, and would plan to use a biomarker-based test to identify patients for enrollment if lanraplenib moves into a registrational Phase 3 trial. 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 for that indication. The FDA generally requires contemporaneous approvals of a new companion diagnostic with the proposed therapeutic. To date, the FDA has required premarket approval of all companion diagnostics for cancer therapies. As such, if a satisfactory companion diagnostic is not commercially available, we may be required to create or obtain one that would be subject to regulatory approval or clearance requirements.

We plan to develop, either by ourselves or with collaborators, companion diagnostic tests for our product candidates for certain indications, which will include lanraplenib for the treatment of AML patients with FLT3 mutations. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. Companion diagnostics are regulated as medical devices, and we have no prior experience with medical device or diagnostic test development. If we choose to or are required to develop and seek FDA approval for companion diagnostic tests on our own, we will require additional personnel. We may rely on third parties for the design, development and manufacture of companion diagnostic tests for our product candidates that require such tests. If these parties are unable to successfully develop companion diagnostics for these product candidates, or experience delays in doing so, we may be unable to enroll enough patients for our current and planned clinical trials, the development of these product candidates may be adversely affected, these product candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these products that obtain marketing approval. As a result, our business, results of operations and financial condition could be materially harmed.

COVID-19 has adversely impacted, and any future health epidemic or pandemic may adversely impact, our business, including our ongoing or planned clinical trials.

COVID-19 has caused, and a resurgence of COVID-19 or another health epidemic or pandemic may cause, significant disruptions that could severely impact our business, including:

- delays or difficulties in screening and enrolling patients in our ongoing and planned clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff, such as the challenges we experienced with clinical site staffing for our Phase 3 AGILITY trial of entospletinib;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- inability or unwillingness of subjects to travel to the clinical trial sites;
- delays or difficulties in data collection and analysis and other related activities;
- decreased implementation of protocol-required clinical trial activities and quality of source data verification at clinical trial sites;

- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials and our other research and development activities, including because of sickness of employees or their families or mitigation measures such as lock-downs and social distancing;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials;
- interruption in global shipping that may affect the transport of clinical trial materials, such as investigational drug product used in our clinical trials;
- changes in local regulations as part of a response to a resurgence of COVID-19 or another health epidemic or pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, delays, or to discontinue the clinical trials altogether;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- refusal of the FDA or foreign regulatory authorities to accept data from clinical trials in affected geographies; and
- adverse impacts on global economic conditions which could have an adverse effect on our business and financial condition, including impairing our ability to raise additional capital when needed.

Such disruptions could impede, delay, limit or prevent completion of our preclinical studies or commencement or the continuation of ongoing, planned or future clinical trials and ultimately lead to the delay or denial of regulatory approval of our product candidates, which would seriously harm our operations and financial condition and increase our costs and expenses. In addition, we also experienced delays in our discovery and development activities as a result of the COVID-19 pandemic, primarily due to temporary and partial shutdowns at certain of our CROs that have since resumed normal operations, and due to the previous California and Massachusetts stay-at-home orders where our operations are located. Future stay-at-home orders could result in additional delays or otherwise negatively impact our discovery and development activities. A resurgence of COVID-19 or another health epidemic or pandemic could also affect the business of the FDA or other health authorities which could result in delays in meetings related to our ongoing and planned clinical trials and ultimately of reviews and approvals of our product candidates.

The extent to which a resurgence of COVID-19 or another health epidemic or pandemic may impact our business, preclinical development activities and ongoing and planned clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate duration and severity of the public health crisis, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

We 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 and managerial resources, we focus on research programs and product candidates that we identify for specific 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 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.

Our approach to the discovery and development of product candidates is unproven, and we may not be successful in our efforts to use and further develop our product engine to expand our pipeline of product candidates with commercial value.

A key element of our strategy is to use our product engine to further develop our pipeline of product candidates and progress these product candidates through clinical development and ultimately achieve approval for the treatment of various cancers by focusing on dysregulated transcription factors and the TRNs through which they drive oncogenic activity. The discovery and development activities that we are conducting may not be successful in developing product candidates that are useful in treating cancer or other diseases.

With respect to internally developed product candidates, our research and development efforts to date have resulted in our discovery and preclinical development of KB-0742 as well as several early-stage discovery programs. KB-0742 may not be safe or effective as a cancer treatment and, with respect to our early-stage discovery programs, we may not identify suitable product candidates for preclinical or clinical development. Our product engine may not be successful in generating additional contributions to our pipeline of product candidates. For example, we may not be successful in identifying novel product candidates that can selectively modulate oncogenic TRNs. Even if we are successful in building our pipeline of product candidates, the potential product candidates that we identify may not be suitable for clinical development or generate acceptable clinical data, including as a result of being shown to have unacceptable toxicity or other characteristics that indicate that they are unlikely to be products that will receive marketing approval from the FDA or other regulatory authorities or achieve market acceptance. If we do not successfully develop and commercialize product candidates, we will not be able to generate product revenue in the future, which likely would result in significant harm to our financial position and adversely affect our stock price.

As a company, we have not completed any clinical trials to date.

We have not as a company completed any clinical trials to date. We therefore cannot be certain that our ongoing Phase 1/2 clinical trial of KB-0742 or our ongoing Phase 1b/2 trial of lanraplenib will be completed on time, if at all. In addition, COVID-19 may continue to create additional challenges in initiating, enrolling or conducting such clinical trials.

In addition, large-scale clinical trials require significant financial and management resources and reliance on third-party clinical investigators, CROs, CMOs and consultants. Relying on third-party clinical investigators, CROs, CMOs 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, CMOs and consultants on a timely basis, or at all.

Because of the relatively small number of patients that are being or are planned to be dosed in our Phase 1/2 trials of KB-0742 and lanraplenib, the results from such clinical trials, if completed, may be less reliable than results achieved in larger clinical trials, which may hinder our efforts to further develop and obtain regulatory approval for these product candidates.

In our Phase 1/2 clinical trial of KB-0742 we are evaluating the safety, PK and PD profile of KB-0742 in patients with advanced solid tumors, and are currently enrolling expansion cohorts while continuing to dose escalate. In our Phase 1b/2 clinical trial of lanraplenib, we are evaluating the safety, PK and PD profile of lanraplenib in combination with gilteritinib in patients with FLT3-positive relapsed/refractory AML, and we plan to define an optimal dose and schedule. Though enrollment is still ongoing in both trials, the total number of patients we expect to enroll in these clinical trials will be significantly smaller than the number of patients that would need to be enrolled in a registrational or other late-stage clinical trial. The results of clinical trials with smaller sample sizes, such as our ongoing Phase 1/2 clinical trial of KB-0742 and our ongoing Phase 1b/2 trial of lanraplenib, can be disproportionately influenced by various biases associated with the conduct of small clinical trials, such as the potential failure of the smaller sample size to accurately depict the features of the broader patient population, which limits the ability to generalize the results across a broader community, thus making the clinical trial results less reliable than clinical trials with a larger number of patients. As a result, there may be less certainty that such product candidates would achieve a statistically significant effect in any future clinical trials. If we conduct any future clinical trials of KB-0742 or lanraplenib, we may not achieve a statistically significant result or the same level of statistical significance, if any, that we might have anticipated based on the results observed in our initial Phase 1/2 clinical trial.

Risks Related to the Commercialization of Our Product Candidates

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

The total addressable market opportunity for our product candidates will ultimately depend upon, among other things, the final label for each product candidate, acceptance by the medical community and patient access, drug and any related companion diagnostic pricing and reimbursement. The number of patients in our targeted commercial markets and elsewhere may turn out to be lower than expected, patients may not be amenable to treatment with our products, or new patients may become increasingly difficult to identify, all of which would adversely affect our results of operations and our business.

The market opportunities for certain of our product candidates may be relatively small as they may be limited to those patients who are ineligible for or have failed prior treatments and our estimates of the prevalence of our target patient populations may be inaccurate.

Cancer therapies are sometimes characterized as first line, second line, or third line, and the FDA often approves new therapies initially only for a particular line of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy, surgery, or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more or different chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies. In some instances we may initially seek approval of our product candidates as a second- or third-line therapy. Subsequently, for those product candidates that prove to be sufficiently safe and beneficial, if any, we would expect to seek approval as a second line therapy and potentially as a first line therapy, but there is no guarantee that our product candidates, even if approved as a second or third or subsequent line 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.

Our projections of both the number of people who have the cancers we are targeting, who may have their tumors genetically sequenced, 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 our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new therapies may change the estimated incidence or prevalence of the cancers that we are targeting. Consequently, even if our product candidates are approved for a second or third line of therapy, the number of patients that may be eligible for treatment with our product candidates may turn out to be much lower than expected. In addition, we have not yet 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.

Even if any of our product candidates are approved, they may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments, as well as other perceived advantages and disadvantages;
- the approval, availability, market acceptance, and reimbursement of any companion diagnostic;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which the product candidate is approved;

- restrictions on the use of our product candidates, such as boxed warnings or contraindications in labeling, or a REMS, if any, which may not be required of alternative treatments and competitor products;
- the ability to offer the product candidate for sale at competitive prices;
- the availability of coverage and adequate reimbursement by third-party payors, including government authorities;
- acceptance by hospital pharmacy and therapeutics committees in the U.S., E.U., and other geographies;
- the availability of the approved product candidate for use as a combination therapy, where applicable;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- unfavorable publicity relating to our products or product candidates or similar approved products or product candidates in development by third parties; and
- the approval of other new therapies for the same indications.

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

We currently have no marketing and sales organization and have no experience as a company in marketing products. If we are unable to establish and maintain marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may not be able to generate product revenue.

We currently have no sales, marketing, or distribution capabilities and have no experience as a company in marketing products. We currently intend to build a commercial infrastructure to support sales of our product candidates. We expect to manage sales, marketing, market access and distribution through internal resources and third-party relationships. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing, market access and sales personnel. While we may commit significant financial and management resources to commercial activities, we will also consider collaborating with one or more pharmaceutical companies to enhance our commercial capabilities.

If we are unable or decide not to establish internal sales, marketing and distribution capabilities in the United States, or any other geographic regions, we will pursue arrangements with third-party sales, marketing, and distribution collaborators regarding the sales and marketing of our products, if approved. However, there can be no assurance that we will be able to establish or maintain such arrangements on favorable terms or if at all, or if we are able to do so, that these third-party arrangements will provide effective sales forces or marketing and distribution capabilities. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates.

There can be no assurance that we will be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas.

Product liability lawsuits could cause us to incur substantial liabilities and could limit the commercialization of any product candidates that we develop.

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 FDA, EMA or other regulatory authority investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs. FDA, EMA or 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 marketing any of our 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.

Any product candidates we develop may become subject to unfavorable third-party coverage and reimbursement policies, third-party reimbursement practices, or health care reform initiatives, which could harm our business.

The availability and extent of coverage and adequate reimbursement by third-party payors, including government health administration authorities, private health coverage insurers, managed care organizations and other third-party payors is essential for most patients to be able to afford expensive treatments. Sales of any of our product candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of our product candidates will be covered and reimbursed by third-party payors. If coverage is not available, or is available only to limited indications or strict coverage criteria, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize an adequate return on our investment. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval. 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.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs will be covered and reimbursed. The Centers for Medicare & Medicaid Services (CMS), an agency within the U.S. Department of Health and Human Services (HHS) responsible for administering the Medicare program, determines whether and to what extent a new product will be covered and reimbursed under Medicare. One third-party payor's determination to provide coverage for a drug product, however, does not assure that other payors will also provide coverage for the product. 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 applied consistently or obtained in the first instance.

For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be 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 pharmacoeconomic studies to demonstrate the medical necessity and cost effectiveness of our products. Nonetheless, our 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.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the European Union, medical product prices are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after a product receives marketing approval. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, product prices under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

If we are unable to establish or sustain coverage and adequate reimbursement for any future 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. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

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

The development and commercialization of pharmaceutical products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. We operate in the segments of the pharmaceutical, biotechnology and other related markets that address inhibition of kinases and targeting transcriptional regulation in cancer. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages we hope to exploit, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and ultimately commercialize will compete with existing products and new products that may become available in the future.

In the case of lanraplenib, there are product candidates that are currently in clinical development which, if approved, could compete with lanraplenib including: (i) HMPL-523, a SYK inhibitor being developed by Hutchison Medipharma Ltd. that is in Phase 1 evaluation in hematologic malignancies; (ii) product candidates in early clinical development that target the interaction between MLL and MENIN in MLL-r and AML patients with NPM1 mutations, including (a) DS-1594, being developed by Daiichi Sankyo Company in a Phase 1 clinical trial with or without azacitidine/venetoclax in relapsed/refractory AML; (b) JNJ-75276617, being developed by Janssen Research & Development, LLC in a Phase 1 clinical trial in acute leukemias; (c) KO-539, being developed by Kura Oncology, Inc. in a Phase 1 clinical trial as monotherapy in relapsed or refractory AML; and (d) SNDX-5613, being developed by Syndax Pharmaceuticals, Inc. in a Phase 1 clinical trial as monotherapy in relapsed or refractory AML in patients with MLL-r/KMT2A gene rearrangement or NPM1 mutations; and (iii) product candidates that address the subset of AML patients with FLT3 mutations and are currently in development in combination with FLT3 inhibitors, including (a) venetoclax, a BCL-2 inhibitor being developed by Abbvie; (b) CC-90009, a A Cereblon E3 ligase modulating drug that promotes selective degradation of GSPT1, in Phase 1b, being developed by Bristol-Myers Squibb; (c) CPX-351, a liposomal formulation of daunorubicin and cytarabine being developed by Jazz Pharmaceuticals; and (d) ladademstat, an LSD1 inhibitorm in Phase 1 dose escalation being developed by Oryzon.

If we are successful in developing and receiving approval for KB-0742, we expect it would compete against various multi-CDK inhibitors that are currently in early-stage clinical development if they are ultimately approved, including: (a) AZD4573, being developed by AstraZeneca; (b) fadraciclib (CYC-065), being developed by Cyclacel Pharmaceuticals; (c) voruciclib, being developed by MEI Pharma; (d) dinaciclib, being developed by Merck & Co.; (e) zotiraciclib, being developed by the National Cancer Institute; and (f) TP-1287 (alvocidib), being developed by Tolero Pharmaceuticals. We also expect it to compete against (a) GFH009, a CDK9 inhibitor in Phase 1 dose escalation, being developed by Genfleet Therapeutics; (b) PRT2527, a CDK9 inhibitor in Phase 1 dose escalation by Prelude Therapeutics; and (c) VIP152, a PTEFb/CDK9 inhibitor in early-stage clinical development by Vincerx Pharma, Inc.

We also expect that our product candidates, if approved, will compete against more established therapies, such as intensive chemotherapy and HMAs to treat AML and other agents to treat MYC-amplified solid tumors and other transcriptionally addicted cancers.

Many of the companies against which we may ultimately compete have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our potential competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient enrollment in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We could see a reduction or elimination in our commercial opportunity if other companies develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or with a more favorable label than any of our product candidates. These companies also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in their establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. Generic products are currently on the market for some of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

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

We may seek marketing approvals of our product candidates outside of the United States and, accordingly, we may be subject to additional risks related to operating in foreign countries if we obtain the necessary foreign marketing approvals, including:

- differing regulatory requirements in foreign countries, for example, no country other than the United States has a pathway for accelerated drug approval and so obtaining regulatory approvals outside of the United States will take longer and be more costly than obtaining approval in the United States;
- differing intellectual property and regulatory laws in foreign countries, including the availability of obtaining patent term extensions, orphan disease status, or data exclusivity in those countries with respect to the patents covering our products;
- 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 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;
- differing pricing, payment and reimbursement regimes;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the U.S. Foreign Corrupt Practices Act (FCPA) 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 United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with international operations may materially adversely affect our ability to attain or maintain profitable operations.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

We may be unable to obtain U.S. or foreign regulatory approvals and, as a result, may be unable to commercialize our product candidates.

Rigorous preclinical testing and clinical trials and an extensive regulatory approval process must be successfully completed in the United States and in many foreign jurisdictions before a new drug can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. 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.

As a company, we have not completed any clinical trials of any product candidates, nor have we managed the regulatory approval process with the FDA or any other regulatory authority. The time required to obtain approvals from the FDA and other regulatory authorities is unpredictable, and requires successful completion of extensive clinical trials which typically takes many years, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its foreign counterparts use when evaluating clinical trial data can and often changes 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 FDA policy during the period of drug development, clinical trials and FDA regulatory review.

Any delay or failure in seeking or obtaining required approvals would have a material and adverse effect on our ability to generate revenue from the particular product candidate for which we are developing and seeking approval. Furthermore, any regulatory approval to market a drug may be subject to significant limitations on the approved uses or indications for which we may market the drug or the labeling or other restrictions. In addition, the FDA has the authority to require a REMS as part of approving a 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.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries, and 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 are conducting, and may in the future conduct, clinical trials for our product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We are currently conducting, and may in the future choose to conduct, clinical trials outside the United States, or include study sites outside the United States, including in Europe or Asia. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the sole basis of foreign data unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence; and (iii) the data are considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Otherwise, for studies that are conducted at sites outside of the United States and not subject to an IND and which are intended to support a marketing application, the FDA requires the clinical trial to have been conducted in accordance with good clinical practice (GCP) requirements and the FDA must be able to validate the data from the clinical trial through an onsite inspection if it deems such inspection necessary. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

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

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

Even if our product candidates receive regulatory approval, they will be subject to significant post-marketing regulatory requirements and oversight. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions on marketing or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems.

Following any regulatory approvals, our products will 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, marketing and distribution of drugs. Any regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and 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. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or foreign regulatory authorities approve our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as on-going compliance with cGMPs and GCP for any clinical trials that we conduct post-approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other 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. In addition, failure to comply with FDA and comparable foreign regulatory requirements may subject our company to administrative or judicially imposed sanctions, including:

- delays in or the rejection of product approvals;
- 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; and
- imposition of restrictions on operations, including costly new manufacturing requirements.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the current U.S. administration may impact our business and industry.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we might become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription pharmaceutical products, such as our product candidates. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label based on the physician's independent medical judgment. However, if we are found to have promoted such off-label uses, we may become subject to significant liability. The U.S. 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 FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our 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 to obtain approval of a companion diagnostic test in connection with approval of any of our product candidates, and we do not obtain or face delays in obtaining FDA approval of a diagnostic device, we will not be able to commercialize such product candidate and our ability to generate revenue will be materially impaired.

If safe and effective use of any of our product candidates depends on an *in vitro* diagnostic that is not otherwise commercially available, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves our product candidates if at all. If a

satisfactory companion diagnostic is not commercially available, we may be required to create or obtain one that would be subject to regulatory approval requirements. The process of obtaining or creating such diagnostic is time consuming and costly.

Companion diagnostics are developed in conjunction with clinical programs for the associated therapeutic product candidate and are subject to regulation as medical devices by the FDA and comparable regulatory authorities, and, to date, the FDA has required premarket approval of all companion diagnostics for cancer therapies. The approval of a companion diagnostic as part of the therapeutic product's labeling limits the use of the therapeutic product to only those patients who express the specific genetic alteration that the companion diagnostic was developed to detect.

If the FDA or a comparable foreign regulatory authority requires approval of a companion diagnostic for any of our product candidates, whether before or after it obtains marketing approval, we, and/or future collaborators, may encounter difficulties in developing and obtaining approval for such product candidate. Any delay or failure by us or third-party collaborators to develop or obtain regulatory approval of a companion diagnostic could delay or prevent approval or continued marketing of such product candidate.

We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process for the companion diagnostic or in transferring that process to commercial partners or negotiating insurance reimbursement plans, all of which may prevent us from completing our clinical trials or commercializing our product candidate, if approved, on a timely or profitable basis, if at all.

Disruptions at the FDA, the SEC or other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, 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 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, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC, and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies 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. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of foreign and domestic manufacturing facilities and products from May 2020 to July 2020, and thereafter resumed on-site inspections of manufacturing facilities subject to a risk-based prioritization system. Regulatory authorities outside the United States adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

We may attempt to use accelerated approval pathways, and if we are unable to obtain such 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, if our trials required as a condition to such accelerated approval do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may withdraw approval.

We may in the future seek an accelerated approval for one or more of our product candidates. 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, such as MRD-negative CR, or intermediate clinical endpoint that it determines 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. If granted, accelerated approval is usually contingent, or conditioned on the sponsor's agreement to conduct additional post-approval confirmatory studies or extend one or more ongoing trials to capture additional endpoints to verify and describe the drug's clinical benefit, and to report regularly to the FDA on the progress of such studies. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of ultimate FDA approval.

Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive 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 FDA feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so.

We may face difficulties from changes to current regulations and future legislation.

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

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 (collectively, the ACA), was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. There have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Further, prior to the U.S. Supreme Court ruling. on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (the Inflation Reduction Act) into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The Inflation Reduction Act also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and through a newly established manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and litigation, and the healthcare reform measures of the Biden administration will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect until 2031 unless additional congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. Additionally, 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. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations.

Moreover, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several 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 programs, and reform government program reimbursement methodologies for drug products.

For example, in July 2021, the Biden administration release an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to President Biden's executive order, on September 9, 2021, HHS release a Comprehensive Plain for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. Further, the Inflation Reduction Act, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the Inflation reduction Act will be implemented but it is likely to have a significant effect on the pharmaceutical industry. The Biden Administration released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. In addition, Congress is considering other health reform measures. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control 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 the ACA, the IRA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to attain profitability or commercialize our product candidates.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be.

Our relationships with healthcare professionals, clinical investigators, 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, and government price reporting, which could expose us to, among other things, criminal sanctions, administrative and 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 conduct our research as well as market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation.

- the federal false claims laws, including the civil False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalties laws, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to CMS information regarding payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. The information reported is publicly available on a searchable website, with disclosure required annually;

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and
- some state laws that require biotechnology companies to comply with the biotechnology industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; some state laws that require biotechnology companies to report information on the pricing of certain drug products; and certain state and local laws that require the registration of pharmaceutical sales representatives.

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare laws and regulations will involve on-going substantial costs. It is possible that governmental authorities will conclude that our business practices, including, without limitation, our consulting agreements with certain physicians, who may be in a position to order and/or influence the purchase of our product candidates, if approved, and are compensated in the form of stock or stock options for services provided to us, may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant 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. 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 criminal, civil or administrative sanctions, including exclusion from government funded healthcare programs.

We are subject to stringent and changing U.S. and foreign laws, regulations, rules, contractual obligations, policies, and other obligations related to data privacy and information security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; a disruption of our business operations; reputational hard; and other adverse business impacts.

In the ordinary course of business, we and the third parties upon whom we rely collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) a large quantity of personal data and sensitive data, including proprietary and confidential business data, trade secret, sensitive third-party data, and patient health data in connection with our preclinical studies, clinical trials and our employees, and are subject to data privacy and information security laws and regulations that apply to the collection, transmission, storage and use of personal data, which among other things, impose certain requirements relating to the privacy, security and transmission of personal data. We are also subject to obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, and contractual requirements, that apply to our processing of sensitive information or processing of sensitive information on our behalf. In addition, privacy advocates and industry groups have regularly proposed, and may propose in the future, self-regulatory standards that may legally or contractually apply to us.

In the United States, there are numerous federal, state and local privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal data, including federal and state health information privacy laws, federal and state security breach notification laws, and federal, state and local consumer protection laws (such as Section 5 of the Federal Trade Commission Act) and other similar laws, to which we are or may become subject. In particular, regulations promulgated pursuant to HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), establish privacy and security standards that limit the use and disclosure of certain individually identifiable health data, or protected health data, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health data and ensure the confidentiality, integrity and availability of electronic protected health data. Determining whether protected health data has been handled in compliance with applicable privacy standards and

our contractual obligations can be complex and may be subject to changing interpretation. Further, if we fail to comply or are perceived to have not fully complied with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face significant administrative, civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

In addition, the California Consumer Privacy Act of 2018 (CCPA) applies to personal information of consumers, business representatives, and employees, and requires businesses to provide specific disclosures in privacy notices and honor requests of California residents to exercise certain privacy rights. The CCPA allows for statutory fines for noncompliance up to $7500 per violation and allows private litigants affected by certain data breaches to recover significant statutory damages. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA may increase compliance costs and potential liability with respect to other personal data maintained about California residents. In addition, the California Privacy Rights Acts of 2020 (CPRA), effective January 1, 2023, expands the CCPA. The CPRA established a new California Privacy Protection Agency to implement and enforce the CCPA (as amended), and adds a new right for individuals to correct their personal information. Other states, such as Colorado, Utah and Connecticut, have enacted data privacy laws and similar laws are also being considered in several other states, as well as at the federal and local levels. While these laws, like the CCPA, also exempt some data processed in the context of clinical trials, these developments may further complicate compliance efforts and may increase legal risk and compliance costs for us, the third parties upon whom we rely.

Outside the United States, an increasing number of laws, regulations, and industry standards apply to data privacy and security. For example, the European Union's General Data Protection Regulation (EU GDPR) and the United Kingdom's GDPR (UK GDPR) impose strict requirements for the processing of personal data of individuals located, respectively, within the European Economic Area (EEA) and the United Kingdom (UK). For example, under the EU GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines of up to 20 million Euros or 4% of the annual global revenue of the company, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

Certain jurisdictions, such as the EU, Switzerland and the UK, have enacted cross-border personal data transfers laws regulating personal data flows to third countries. In particular, the EEA and UK have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it believes are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer laws. The European Commission released a set of "Standard Contractual Clauses" that are designed to be a valid mechanism by which entities can transfer personal data out of the EEA to jurisdictions that the European Commission has not found to provide an adequate level of protection. Currently, these Standard Contractual clauses are a valid mechanism to transfer personal data outside of the EEA. The Standard Contractual Clauses, however, are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. In addition, the Standard Contractual Clauses require parties that rely upon that legal mechanism to comply with additional obligations such as conducting transfer impact assessments to determine whether additional security measures are necessary to protect the at-issue personal data. In addition, laws in Switzerland and the UK similarly restrict personal data transfers outside of those jurisdictions to countries such as the United States of America that do not provide an adequate level of personal data protection. In addition to European restrictions on cross-border personal data transfers, other jurisdictions have enacted or are considering similar cross-border personal data transfer laws and local personal data residency laws, any of which could increase the cost and complexity of doing business. If we cannot implement a valid compliance mechanism for cross-border personal data transfers, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, increased exposure to regulatory actions, substantial fines, and injunctions against processing or transferring personal data from Europe or elsewhere. Inability to import personal data to the United States may significantly and negatively impact our business operations, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere; limiting our ability to collaborate with parties subject to European and other data protection laws or requiring us to increase our personal data

processing capabilities in Europe and/or elsewhere at significant expense. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the EU GDPR's cross-border data transfer limitations.

Our obligations related to data privacy and security are quickly becoming increasingly stringent and creating regulatory uncertainty. These obligations may be subject to differing applications and interpretations, which may be inconsistent among jurisdictions or in conflict. Preparing for and complying with these obligations requires us to devote significant resources (including, without limitation, financial and time-related resources).

We are also bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. For example, certain privacy laws, such as the GDPR and the CCPA require our partners to impose specific contractual restrictions on their own service providers. We publish privacy policies and notices and other statements regarding data privacy and security. If these policies, notices or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences.

These obligations may necessitate changes to our information technologies, systems, and practices and those of any third parties that process personal data on our behalf. In addition, these obligations may even require us to change our business model. We, or the third parties on which we rely, may at times fail (or be perceived to have failed) to do so. If we, or third parties on which we rely, fail, or are perceived to have failed, to address or comply with data privacy and security obligations, we could face significant consequences. These consequences may include, but are not limited to, government enforcement actions (e.g., investigations, fines, penalties, audits, inspections and similar); litigation (including class-related claims); additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials.

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

Our employees, independent contractors, consultants, commercial 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, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA requirements, provide accurate information to the FDA, comply with federal and state health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, 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. 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.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and waste. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our research and development activities could be affected or delayed as a result of possible restrictions on animal testing.

Certain laws and regulations require us to test our product candidates on animals before initiating clinical trials involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted, delayed or become more expensive.

We may be subject to U.S. and foreign anti-bribery and anti-corruption laws with respect to our operations, as well as U.S. and certain foreign export controls, trade sanctions, and import laws and regulations. Non-compliance with these laws can subject us to criminal or civil liability and harm our business.

If we further expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits companies and their employees and third party intermediaries from offering, promising, giving or authorizing the provision of anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, hospitals owned and operated by the government, and doctors and other hospital employees would be considered foreign officials under the FCPA. Recently the SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents or contractors, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers or our employees, disgorgement, and other sanctions and remedial measures, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international activities, our ability to attract and retain employees and our business, prospects, operating results and financial condition.

In addition, our products and activities may be subject to U.S. and foreign export controls, trade sanctions and import laws and regulations. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products, when applicable, could harm our international sales and adversely affect our revenue. Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, U.S. export control laws and economic sanctions prohibit the shipment of certain products and services to countries, governments, and persons targeted by U.S. sanctions. If we fail to comply with export and import regulations and such economic sanctions, penalties could be imposed, including fines and/or denial of certain export privileges. Moreover, any new export or import restrictions, new legislation or shifting approaches in the enforcement or scope of existing regulations, or in the countries, persons, or products targeted by such regulations, could result in decreased use of our products by, or in our decreased ability to export our products to existing or potential customers with international operations. Any decreased use of our products or limitation on our ability to export or sell access to our products would likely adversely affect our business.

Risks Related to Our Intellectual Property

Our success depends in part on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses, as well as our ability to operate without infringing the proprietary rights of others. If we or our licensors are unable to protect our intellectual property rights or if our intellectual property rights are inadequate for our technology or our product candidates, our competitive position could be harmed. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates, proprietary technologies and their uses that are important to our business. Our 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 read on the technology. There can be no assurance that our patent applications will result in patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents, if issued, will not be infringed, designed around, invalidated or rendered unenforceable by third parties. 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. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and such protection 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 our product candidates could have a material adverse effect on our financial condition and results of operations.

Although we have issued patents in the United States and foreign countries, we cannot be certain that the claims in our other pending U.S. patent applications, corresponding international patent applications and patent applications in certain foreign countries will be considered patentable by the United States Patent and Trademark Office (USPTO), courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued patents will not be found invalid or unenforceable if challenged.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or our licensors or any of our potential future collaborators will be successful in protecting our technologies and 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 which have substantially greater resources than we or our licensors have and many of which have made significant investments in competing technologies, may seek or may have already obtained patents that could or will limit, interfere with or block our ability to make, use and sell our product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing products.

The patent prosecution process is also expensive and time-consuming, and we or our licensors 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 also possible that we or our licensors may not identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control, or are subject to certain obligations with respect to, the preparation, filing and prosecution of patent applications, or to maintain the patents, directed to technology that we license or acquire, including those from our licensors and from third parties. We also may require the cooperation of our licensors, whether current or future, in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by our licensors have been or will be conducted in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. If they fail to do so, this could cause us to lose rights in any applicable intellectual property that we in-license, and as a result our ability to develop and commercialize products or product candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products. Furthermore, the terms of the license agreements with some of our licensors may be non-exclusive, such that we would have no rights to enforce the licensed intellectual property against a competitor.

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, licensors, 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.

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

In July 2020, we acquired a portfolio of selective, orally bioavailable small molecule SYK inhibitors from Gilead, including lanraplenib, pursuant to the Gilead Asset Purchase Agreement. We also have a non-exclusive worldwide right to certain patents under a license agreement with Harvard University that provides us with rights to use the SMM screen, which is a key component of our product engine. These agreements impose on us, and we expect that any future license or other agreements where we in-license or acquire intellectual property will impose on us, various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations.

We may need to obtain licenses or acquired intellectual property from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not exist that might be enforced against our product candidates in the absence of such a license or acquisition. We may fail to obtain any of these licenses on commercially 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 develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected

product candidates, which could materially harm our business, and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation. Licensing and acquisitions of intellectual property involve complex legal, business and scientific issues. Disputes may arise between us and our existing or future licensors and other third parties regarding intellectual property subject to a license or purchase agreement, including:

- the scope of rights granted under the license or purchase agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe intellectual property of the licensor or other third party that is not subject to the license or purchase agreement;
- our right to sublicense patents and other rights to third parties;
- our diligence obligations with respect to the use of the licensed or acquired technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- the effects of termination;
- our right to transfer or assign the license or purchase agreement; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and their affiliates and sublicensees and by us and our partners and sublicensees.

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 increase what we believe to be our financial or other obligations under the relevant agreement. And if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may not be able to successfully develop and commercialize the affected product candidates, which would have a material adverse effect on our business.

In addition, certain of our agreements may limit or delay our ability to consummate certain transactions, may impact the value of those transactions, or may limit our ability to pursue certain activities.

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

The patent position of biopharmaceutical 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 existence, issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our product candidates or that effectively prevent others from commercializing competitive product candidates.

Moreover, the scope of claims in a patent application can be significantly reduced before any claims in a patent issue, and claim scope can be reinterpreted after issuance. Even if patent applications we currently have issue as patents in the future, 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 have 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 our 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 by developing similar or alternative technologies or products in a non-infringing manner, which could materially and 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 may not cover our product candidates or may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant review (PGR) and inter partes review (IPR), or other similar proceedings in the USPTO or foreign patent offices challenging our patent rights. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity of our patents, for example, we cannot be certain that there is no invalidating prior art, of which we or third parties from whom we acquired our patents, their counsel, and the patent examiner were unaware during prosecution. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found. There is also no assurance that there is not prior art of which we or third parties from whom we acquired patents and patent applications are aware, but which we or the third parties do not believe affects the validity or enforceability of a claim in our patents and patent applications, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. 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 our product candidates and compete directly with us, without payment to us. Such loss of patent rights, loss of exclusivity or patent claims being narrowed, invalidated or held unenforceable 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 our 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 is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

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

We or our licensors may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position. It is possible that defects as to form in the preparation or filing of our owned or in-licensed patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our licensors, whether current or future, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current or future licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our owned or in-licensed patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

As a licensee of third parties, whether currently or in the future, we rely and may rely on third parties to file and prosecute patent applications and maintain patents and otherwise protect the licensed intellectual property under in-license agreements. We have not had, do not have, and may not have in the future, primary control over these activities for certain of our patents or patent applications and other intellectual property rights. We cannot be certain that such activities by third parties have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with some of our licensors, whether current or future, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents, and even if we are permitted to pursue such enforcement or defense, we will require the cooperation of our licensors. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. Even if we are not a party to these legal actions, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. If any of our licensors or any of our future licensors or future collaborators fails to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, 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. Furthermore, the terms of the license agreements with some of our licensors may be non-exclusive, such that we would have no rights to enforce the licensed intellectual property against a competitor. In such cases, the licensors to our non-exclusive licenses may offer licenses to our competitors.

In addition, even where we have the right to control patent prosecution of patents and patent applications we have acquired or 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 us assuming control over patent prosecution.

Our technology acquired or licensed from various third parties, including our licensors, whether currently or in the future, may be subject to retained rights. Our licensors, whether current or future, may often retain certain rights under their agreements with us, including the right to use the underlying technology for use in fields other than the fields licensed to us or for use in noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

If we are limited in our ability to utilize acquired or licensed technologies, or if we lose our rights to critical in-licensed technology, we may be unable to successfully develop, out-license, market and sell our products, which could prevent or delay new product introductions. Our business strategy depends on the successful development of licensed and acquired technologies into commercial products. Therefore, any limitations on our ability to utilize these technologies may impair our ability to develop, out-license or market and sell our product candidate.

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 develop products that are similar to our product candidates but that are not within the scope of the claims of the patents that we own or license;
- we, third parties from whom we acquired intellectual property, or our licensors might not have been the first to make the inventions covered by the issued patents or patent application that we own or license;
- we, third parties from whom we acquired intellectual property, or our licensors might not have been the first to file patent applications directed to 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 patent applications 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; and
- the patents of others may have an adverse effect on our business.

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 in part on avoiding infringement of the patents and proprietary rights of third parties. However, 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. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical industry, including patent infringement lawsuits, oppositions, reexaminations, inter partes review proceedings and post-grant review proceedings before the USPTO and/or foreign patent offices. Numerous third-party U.S. 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 our product candidates.

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published, we may be unaware of third-party patents that may be infringed by development or commercialization of any of our product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology. 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 our 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. As such, we may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might subject us to infringement claims or adversely affect our ability to develop and market our product candidates. We cannot guarantee that any of our or our licensors' patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending patent application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. 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 of our product candidates until the asserted patent expires or is held finally invalid or unenforceable 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 filing, others may hold proprietary rights that could prevent our product candidates from being marketed or could require us to pay significant royalties or other damages. Any patent-related legal action against us claiming damages and seeking to enjoin activities relating to our product candidates or processes could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license, if available, to manufacture or develop our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and 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 future strategic partners were able to obtain a license, the rights may be non-exclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product candidates 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 our product candidates, which could harm our business, financial condition and operating results.

Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

We may become involved in lawsuits or administrative disputes to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our patents, trademarks, copyrights, trade secrets or other intellectual property. To counter infringement, misappropriation or other violations, we may be required to file infringement, misappropriation or other violation claims, which can be expensive and time-consuming and divert the time and attention of our management and business and scientific personnel. In addition, many of our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. 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.

Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their patents or their other intellectual property, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In patent litigation in the United States, counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. Similarly, third parties may initiate legal proceedings against us seeking a declaration that certain of our intellectual property is not infringed, invalid or unenforceable. The outcome of any such proceeding is generally unpredictable.

In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering one of our product candidates, we could lose at least a part, and perhaps all, of the patent protection covering such a product candidate. Competing drugs may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit, alleging our infringement of a competitor's patents, we could be prevented from marketing our drugs in one or more foreign countries. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Furthermore, third parties may also raise invalidity or unenforceability claims before administrative bodies in the United States or foreign authorities, even outside the context of litigation. Such mechanisms include re-examination, inter partes review, post-grant review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation, cancellation or amendment to our patents in such a way that they no longer cover and protect our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, enablement or written description. Grounds for an unenforceability assertion could be an allegation that someone connected with the prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution of the patent. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, third parties from whom we acquired patents and patent applications and their patent counsel, our licensors, our patent counsel, patent counsel for licensors or third parties, and the patent examiner were unaware during prosecution. Moreover, it is possible that prior art may exist that we, our licensors, or third parties from whom we acquired patents and patent applications are aware of but do not believe is relevant to our current or future patents, but that could nevertheless be determined to render our patents invalid. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product candidates. Any such loss of patent protection could have a material adverse impact on our business, financial condition, results of operations and prospects.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

In September 2011, the Leahy-Smith America Invents Act (Leahy-Smith Act) was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States 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 the date of filing of our patents 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. 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 United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or the third parties from which we acquired our patents were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our patents or patent applications.

The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications are 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 United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or licensors' patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in U.S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States 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. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us.

For example, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our or our licensors' ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on legislation and decisions made by the U.S. Congress, the U.S. federal courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our or our licensors' ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

We, Gilead, or our licensors, may be subject to claims by third parties asserting that our, Gilead's, or our licensor's, employees or consultants or we, Gilead, or our licensors, have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

As is common in the biopharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Some of our employees and consultants, or employees or consultants of Gilead or our licensors, are currently or have been previously employed at universities or at other biotechnology or pharmaceutical companies, or may have previously provided or may be currently providing consulting services to other biopharmaceutical companies, including our competitors or potential competitors. These employees and consultants may have executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such other current or previous employment. Although we, and likely Gilead and our licensors, try to ensure that our and their employees and consultants do not use the proprietary information or know-how of others in their work for us or them, we or they may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of third parties or former employers or former or current clients, or claims that we, Gilead, or our licensors have wrongfully hired an employee from a competitor. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property or personnel or sustain damages. Such intellectual property could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our management. Any of the foregoing would have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. Likewise, Gilead and our licensors may have been or may be unsuccessful in executing such an agreement with each party who conceived or developed intellectual property that we purchased or licensed, which may result in additional such claims by or against us. In addition, such agreements may not be self-executing such that the intellectual property subject to such agreements may not be assigned to us without additional assignments being executed, and we, Gilead, or our licensors may fail or may have failed to obtain such assignments. In addition, such agreements may be breached. Accordingly, we, Gilead, or our licensors may be forced to bring claims against third parties, or defend claims that they may bring against us, Gilead, or our licensors to determine the ownership of what we regard as our owned or licensed intellectual property. If we, Gilead, or our licensors fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel, which would 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 our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the term of a patent, and the protection it affords, is limited. In addition, the term of a patent may be reduced if a terminal disclaimer is or was filed in that patent, limiting the term of the patent to that of one or more other patents referenced in the terminal disclaimer. Even if patents directed to our product candidates are obtained, once the patent term 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 product candidates, patents directed to our product candidates might expire before or shortly after such candidates are commercialized, and patent term extensions or other means of obtaining market exclusivity, such as data exclusivity, may not be available or adequately protective in countries where we market our products. As a result, our 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 our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984 (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 our product candidates, but may not be available in other countries. However, we or our licensors 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 or our licensors 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 clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

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

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

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

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

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. We have systems in place to remind us to pay these fees, and we rely on third parties to pay these fees when due. 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. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business.

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

In addition, 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, licensors 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. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary information will be effective. 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 United States 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 or our licensors 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.

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.

Our registered or unregistered 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 collaborators 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 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. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, 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 business, financial condition, results of operations and prospects.

Risks Related to Our Reliance on Third Parties

We rely on third parties, including independent clinical investigators, developers of companion diagnostics, and CROs, to conduct certain aspects of our preclinical studies and ongoing and planned clinical trials. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to rely in the future upon third parties, including independent clinical investigators, developers of companion diagnostics, and CROs, to conduct certain aspects of our preclinical studies and ongoing and planned clinical trials and to monitor and manage data for our ongoing preclinical and planned clinical programs.

We rely or will rely on these parties for execution of our preclinical studies and ongoing and planned clinical trials, and may not control, or will only control certain aspects of, their activities. Nevertheless, we are or will be responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our products candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be adversely affected 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.

Further, these investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Additionally, they may undergo a change in control, which could extend, delay or terminate our clinical trials. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed or precluded entirely.

We have CROs located in China and India. International tension or conflict with these countries could result in a material disruption in our contractual relationship with the CROs, which could delay or otherwise negatively impact progress in our preclinical programs. Our CROs have the right to terminate their agreements with us in the event of an uncured material breach, upon clinical trial subject safety concerns, or upon our insolvency.

The effects of the COVID-19 pandemic and government measures taken in response previously had a significant impact on our CROs, and they have in the past faced disruptions and in the future may face further disruption as a result of a resurgence of COVID-19 or another health epidemic or pandemic which may affect our ability to initiate and complete our preclinical studies and ongoing and planned clinical trials.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Additionally, CROs may lack the capacity to absorb higher workloads or take on additional capacity to support our needs. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

If our collaboration with Genentech does not result in the successful discovery, development, and commercialization of product candidates or if it were to be terminated, our business could be adversely affected.

In January 2023, we entered into a Collaboration and License Agreement with Genentech to collaborate on two discovery research programs in oncology. We will lead discovery and research activities under the discovery research programs and will use our proprietary drug discovery platform, including our SMM screening platform, for hit finding. Following the completion of initial discovery and research activities, Genentech will have the exclusive right to pursue further preclinical and clinical development and commercialization of compounds identified in the discovery research programs and designated by Genentech (each, a Hit Program).

Under the agreement, we are eligible for milestone payments upon achievement of certain preclinical, clinical and regulatory (including first-sale) milestones, totaling up to $177.0 million for the first development candidate per Hit Program to achieve such milestone event, and are eligible to receive net sales milestones of up to an aggregate of $100.0 million for the first licensed product per Hit Program to achieve such milestone event. We are also eligible to receive tiered royalties in the low- to high-single digits on any products arising under the collaboration that are commercialized by Genentech.

Genentech has the right to terminate the agreement in its entirety, or with respect to a particular discovery research program or Hit Program, in its sole discretion, at any time by providing 60 days' advance written notice to us.

If the discovery and research activities led by us for either discovery program do not produce any compounds that Genentech finds attractive, or if Genentech otherwise elects not to pursue further research or development of any compounds identified from such activities, we may have incurred significant research expenses for such program, depending on the point at which it was terminated, but will not be eligible to receive milestone or royalty payments related to such program. Additionally, if Genentech elects not to pursue development one or more Hit Programs, although we have certain rights in certain circumstances to progress such programs ourselves, with appropriate license grants from Genentech, we may not be able to negotiate suitable terms of such reversion, and therefore we may not be able to progress such programs ourselves. In addition, the perception of our drug discovery platform and our business could be materially and adversely affected, which in turn may make it difficult for us to attract new collaborators for such programs or additional programs based on our platform.

If Genentech elects to pursue further development of a compound in a Hit Program, we will be reliant on Genentech to successfully advance the compound into and through clinical development, and to obtain regulatory approval of and successfully commercialize the product, any of which may not occur for a multitude of reasons, and because Genentech will have exclusive rights to the compound and any related product, our ability to generate revenue from these compounds and any related products will depend in large part on Genentech. Genentech's decisions or objectives in connection with the collaboration, including any commercialization activities, may not be consistent with our best interests. It is possible that Genentech could take actions that may be adverse to us, or it could halt, slow, or deprioritize its development and commercialization efforts under the collaboration. In any such instances, our business, financial condition, results of operations and prospects could be materially harmed.

We may form or seek collaborations or strategic alliances or enter into additional strategic arrangements in the future, which involve risks, and we may not realize the benefits of such collaborations, alliances or strategic arrangements.

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

In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our 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 our product candidates as having the requisite potential to demonstrate safety, potency, purity and efficacy and obtain marketing approval. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or 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.

Further, collaborations involving our product candidates are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization of our product candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property. If we are unable to obtain exclusive licenses to any such co-owner's interest in such

intellectual property, such co-owner may be able to license their rights to third parties, including our competitors, and our competitors could market competing products and technology.

As a result, if we enter into collaboration agreements and strategic partnerships or license our product candidates, 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. Any delays in entering into new collaborations or strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

We will rely on third parties to manufacture our clinical product supplies, and we may rely on third parties to produce and process our product candidates, if approved.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely for the foreseeable future, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture of any products that we may commercialize. In this regard, while we have purchased initial inventory of active pharmaceutical ingredients (APIs) and product candidates for lanraplenib from Gilead under the Gilead Asset Purchase Agreement, we will need to obtain further supplies of APIs and clinical drug supply for lanraplenib and KB-0742 from third-party manufacturers. We do not currently have arrangements in place for redundant supply for APIs or our clinical product candidates.

We will need to negotiate and maintain contractual arrangements with outside vendors for the supply of our future product candidates and we may not be able to do so on favorable terms. In addition, these third-party manufacturing providers may not be able to provide adequate resources or capacity to meet our needs. We expect to initially obtain our supplies from manufacturers on a purchase order basis without long-term supply arrangements in place We have not yet caused any product candidates to be manufactured on a commercial scale and may not be able to do so for any of our product candidates. In the future, we may be unable to enter into agreements with third-party manufacturers for commercial supplies of any product candidate, or may be unable to do so on acceptable terms.

Reliance on third-party manufacturers entails risks, including reliance on single sources for product components and lack of qualified backup suppliers for those components purchased from a sole or single source supplier. We cannot be sure that single source suppliers for our product components will remain in business or that they will not be purchased by one of our competitors or another company that is not interested in continuing to produce these components for our intended purpose. In addition, the lead time needed to establish a relationship with a new supplier can be lengthy, and we may experience delays in meeting demand in the event we must switch to a new supplier. The time and effort to qualify a new supplier could result in additional costs, diversion of resources or reduced manufacturing yields, any of which would negatively impact our operating results.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or other foreign regulatory authorities following inspections that will be conducted after we submit an application to the FDA or other foreign regulatory authorities. We may not control the manufacturing process of, and may be completely dependent on, our contract manufacturing partners for compliance with cGMPs and any other regulatory requirements of the FDA or other regulatory authorities for the manufacture of our product candidates. Beyond periodic audits, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any approval in the future, we may need to find alternative manufacturing facilities, which would require the incurrence of significant additional costs and significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Similarly, if any third-party manufacturers on which we will rely fail to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability, our business, financial condition and prospects could be materially and adversely affected.

Manufacturing our product candidates is complex and we may encounter difficulties in production. If we encounter such difficulties, our ability to provide supply of our product candidates for preclinical studies and clinical trials or for commercial purposes could be delayed or stopped.

The process of manufacturing our product candidates is complex and highly regulated.

We expect to rely on third parties for the manufacture of our product candidates. These third-party manufacturers may incorporate their own proprietary processes into our product candidate manufacturing processes. We will have limited control and oversight of a third party's proprietary process, and a third party may elect to modify its process without our consent or knowledge. These modifications could negatively impact our manufacturing, including product loss or failure that requires additional manufacturing runs or a change in manufacturer, both of which could significantly increase the cost of and significantly delay the manufacture of our product candidates.

As our product candidates progress through preclinical studies and clinical trials towards approval and commercialization, it is expected that various aspects of the manufacturing process will be altered in an effort to optimize processes and results. Such changes may require amendments to be made to regulatory applications which may further delay the timeframes under which modified manufacturing processes can be used for any of our product candidates and additional bridging studies or trials may be required.

In addition, in order to conduct clinical trials of our product candidates, we will need to have them manufactured in potentially large quantities. Our third-party manufacturers may be unable to successfully increase the manufacturing capacity for any of our clinical drug supplies (including key starting and intermediate materials) in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities and at any other time. If the third-party manufacturers are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of that product candidate may be delayed or not obtained, which could significantly harm our business.

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

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

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

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

To succeed, we must recruit, 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. 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. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. The competition for qualified personnel in the biotechnology field is intense and as a result, we may be unable to continue to

attract and retain qualified personnel necessary for the future success of our business. We could in the future have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Many of the other 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 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 our product candidates will be limited and the potential for successfully growing our business will be harmed.

We have grown rapidly and will need to continue to grow the size of our organization and expand our capabilities, and we may experience difficulties in managing this growth.

As of January 1, 2023, we had 97 full-time employees. As of January 1, 2019, we had nine full-time employees and since then, we have expanded our executive and leadership team with the additions of our Chief Medical Officer and Executive Vice President, Clinical Development, our Chief Scientific Officer, our Chief Operating Officer and General Counsel, our Chief Financial Officer, our Senior Vice President, Pharmaceutical Development and Manufacturing, and our Senior Vice President of Clinical Development. We expect to experience continued growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, research science, clinical operations, manufacturing, and regulatory affairs. In addition, we are building a self-sufficient accounting and finance group within our company, and have relied and continue to rely on a third-party accounting consulting firm to augment our internal accounting and finance function. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel.

Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth and with building clinical development, manufacturing and internal accounting and finance infrastructure, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources.

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

If we are not able to effectively manage growth and expand our organization, we may not be able to successfully implement the tasks necessary to further develop and commercialize lanraplenib, KB-0742, our other pipeline product candidates or any future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our information technology systems, or those used by our third-party CROs or other contractors or consultants, may fail, be disrupted or suffer security breaches, which could result in a material disruption of our discovery and development programs or otherwise materially and adversely affect our business.

Despite the implementation of security measures, our internal computer systems and those of our current and future CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, and telecommunication and electrical failures. If such an event occurs and causes interruptions in our operations, it could result in a material disruption of our discovery and development

programs and our business operations. For example, the loss of data from completed or future preclinical studies and clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our product candidates and will rely on third parties to conduct our clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business.

To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

If our information technology systems or data, or those of the third parties upon which we rely, are or were compromised, we could experience adverse impacts resulting from such compromise, including, but not limited to, regulatory investigations or actions, litigation, fines and penalties, interruptions to our operations such as our clinical trials, claims that we breached our data protection obligations, harm to our reputation, and a loss of future customers or sales and other adverse consequences.

In the ordinary course of business, we, or the third parties upon which we rely, may collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) proprietary, confidential, and sensitive data (including but not limited to intellectual property, proprietary business information, clinical trial information, and personal data). We have also outsourced elements of our operations to third parties, and as a result we rely on a number of third-party contractors who have access to our proprietary, confidential, and sensitive data, including health-related data. We may share or receive sensitive data with or from third parties. Our ability to monitor these third parties' cybersecurity practices is limited, and these third parties may not have adequate information security measures in place.

Cyberattacks, malicious internet-based activity, and online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive information and information technology systems, and those of the third parties upon which we rely. Such threats are prevalent, continue to rise, increasingly difficult to detect, and come from a variety of sources. In addition to traditional computer "hackers," threat actors, "hacktivists," organized criminal threat actors, personnel misconduct or error (such as theft or misuse), sophisticated nation-state and nation-state supported actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts. During times of war and other major conflicts, we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks that could materially disrupt our systems and operations, supply chain, and ability to conduct clinical trials. We, and the third parties on which we rely, may be subject to a variety of evolving threats, including but not limited to social engineering attacks (including through phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks (such as credential stuffing), credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunction, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fire, flood, and other similar threats. Ransomware attacks, including those perpetrated by organized criminal threat actors, nation-states, and nation-state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, loss of data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting payments. Remote work has become more common and has increased risks to our information technology systems and data, as more of our employees utilize network connections, computers, and devices outside our premises or network, including working at home, while in transit, and in public locations.

Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of or access to our sensitive information or our information technology systems, or those of the third parties upon whom we rely. A security incident or other interruption could disrupt our (and third parties upon whom we rely) ability to operate our business or conduct clinical trials. Certain of our vendors have previously experienced specific instances of cyber events, including email compromise and wire fraud targeting payments to be made by us.

We may expend significant resources or modify our business activities (including our clinical trial activities) in an effort to protect against security incidents. Certain data privacy and security obligations may require us to implement and maintain specific security measures, or industry-standard or reasonable security measures to protect our information technology systems and sensitive information. While we have implemented security measures designed to protect against a security incident, there can be no assurance that these measures will be effective. We also take steps to detect and remediate vulnerabilities, but we may not be able to detect and remediate all vulnerabilities because the threats and techniques used to exploit the vulnerability change frequently and are often sophisticated in nature. Therefore, such vulnerabilities could be exploited but may not be detected until after a security incident has occurred. Despite our efforts to identify and remediate any vulnerabilities in our information technology systems, our efforts may not be successful. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities. These vulnerabilities pose material risks to our business.

Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosures or the failure to comply with such requirements, could lead to adverse impacts. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences. These consequences may include: government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing data (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may impact our ability to conduct clinical trials or bring any approved products to market, and negatively impact our ability to grow and operate our business. There can be no assurance that limitations of liability in our contracts are sufficient to protect us from claims related to our data security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our CROs, contract manufacturing organizations (CMOs) and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, epidemics and pandemics, bank failures, wars and other geopolitical conflicts (such as the Russia-initiated military action against Ukraine) and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

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

Under current law, federal net operating losses incurred in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to federal tax law. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage point change (by value) in the equity ownership of certain stockholders over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income and taxes may be limited. As a result of our private placements and other transactions that have occurred within the three years prior to and including our IPO, which we completed in October 2020, we may have experienced, an "ownership change." We may also experience ownership changes in the future as a result of subsequent issuances of our common stock or other shifts in our stock ownership. We anticipate incurring significant additional net losses for the foreseeable future, and our ability to utilize net operating loss carryforwards associated with any such losses to offset future taxable income may be limited to the extent we incur future ownership changes. In addition, at the state level, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, we may be unable to use all or a material portion of our net operating loss carryforwards and other tax attributes, which could adversely affect our future cash flows.

Risks Related to Our Common Stock

Provisions in our corporate charter documents and under Delaware law could make a merger, tender offer or proxy contest difficult, thereby depressing the trading price of our common stock.

Provisions of our amended and restated certificate of incorporation and amended and restated bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our amended and restated certificate of incorporation and amended and restated bylaws:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate (including the right to approve an acquisition or other change in our control);
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that our board of directors or any individual director may only be removed with cause and the affirmative vote of the holders of at least 66-2/3% of the voting power of all of our then-outstanding common stock;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide our board of directors into three classes;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner and also specify requirements as to the form and content of a stockholder's notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- provide that special meetings of our stockholders may be called only by the chair of our board of directors, our Chief Executive Officer or by the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors; and

- provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws; (iv) any action or proceeding to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws; (v) any action or proceeding as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and (vi) any action asserting a claim against us or any of our directors, officers or other employees governed by the internal affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants; provided these provisions of our amended and restated certificate of incorporation and amended and restated bylaws will not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended (Exchange Act), or any other claim for which the federal courts have exclusive jurisdiction; and provided that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended (Securities Act).

The amendment of any of these provisions, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, would require approval by the holders of at least 66-2/3% of our then-outstanding common stock.

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.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' 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, to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants, the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;
- any action or proceeding asserting a breach of fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders;
- any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees arising out of or pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or bylaws;
- any action or proceeding to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws;
- any action or proceeding as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and

- any action asserting a claim against us or any of our directors, officers or other employees that is governed by the internal affairs doctrine.

This provision does not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

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

Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- the degree of success of competitive products or technologies;
- the commencement, enrollment or results of clinical trials and preclinical studies of our product candidates or those of our competitors;
- adverse results from, delays in or termination of clinical trials;
- unanticipated serious safety concerns related to the use of our product candidates;
- regulatory or legal developments in the United States and other countries;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- receipt of, or failure to obtain, regulatory approvals;
- changes in the structure of healthcare payment systems;
- lower than expected market acceptance of our product candidates following approval, if any, for commercialization;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to develop, acquire or in-license additional technologies or product candidates;

- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- variations in our financial results or those of companies that are perceived to be similar to us;
- rumors or announcements regarding transactions involving our company or product candidates;
- proposed changes to healthcare laws in the United States or foreign jurisdictions, or speculation regarding such changes;
- market conditions or trends in the pharmaceutical and biotechnology sectors;
- the societal and economic impact of public health epidemics;
- general economic, industry and market conditions; and
- the other events or factors, including those described in this "Risk Factors" section.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

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

We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make any related party transaction disclosures. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

We are a non-accelerated filer. For so long as we remain a non-accelerated filer, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act. An independent assessment of the effectiveness of our internal controls could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

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

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

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 pharmaceutical 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.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about us, our business or our market, our stock price and/or trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not control these analysts or the content and opinions or financial models included in their reports. If additional securities analysts do not provide research coverage of our company, or if analysts cease coverage of us, the trading price for our common stock could be negatively affected. If one or more of the analysts who cover us downgrade our common stock or publish 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 fail 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.

General Risk Factors

An active trading market for our common stock may not be sustained.

Although our common stock is listed on the Nasdaq Global Select Market, an active trading market for our shares may not be sustained. If an active market for our stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or to sell their shares at all. An inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

We incur substantial costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

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

The global credit and financial markets have experienced extreme volatility and disruptions in the past. These disruptions can result in severely diminished liquidity and credit availability, increase in inflation, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment, higher inflation, bank failures, or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Our portfolio of corporate and government bonds could also be adversely impacted. Failure to secure any necessary financing in a timely manner and on favorable terms, or the inability to access our existing capital in the event of a failure in the U.S. banking system, could have a material adverse effect on our operations, growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn or rising inflation, which could directly affect our ability to attain our operating goals on schedule and on budget.

Other international and geo-political events could also have a serious adverse impact on our business. For instance, in February 2022 Russia initiated military action against Ukraine. In response, the United States and certain other countries imposed significant sanctions and trade actions against Russia and could impose further sanctions, trade restrictions, and other retaliatory actions. While we cannot predict the broader consequences, the conflict and retaliatory and counter-retaliatory actions could materially adversely affect global trade, currency exchange rates, inflation, regional economies, and the global economy, which in turn may increase our costs, disrupt our supply chain, impair our ability to raise or access additional capital when needed on acceptable terms, if at all, or otherwise adversely affect our business, financial condition, and results of operations.

Our business could be negatively impacted by environmental, social and corporate governance (ESG) matters or our reporting of such matters.

There is an increasing focus from certain investors, employees, partners, and other stakeholders concerning ESG matters. We may be, or be perceived to be, not acting responsibly in connection with these matters, which could negatively impact us. For instance, the SEC has recently proposed climate change and ESG reporting requirements, which, if approved, would significantly increase our costs. In addition, we currently do not report our environmental emissions, and lack of reporting or future reporting could result in certain investors declining to invest in our common stock.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our corporate headquarters are located in San Mateo, California, where we lease office space pursuant to a lease agreement which commenced on August 1, 2018. On February 8, 2021, we amended our lease agreement and, on July 1, 2021, we relocated to a larger area in the same building comprising approximately 17,340 square feet of office space. The amendment extended the expiration date of the lease from April 30, 2025 to the earlier of the last day of the 60th calendar month following the commencement of the relocation or August 31, 2026. We also lease approximately 40,514 square feet of office and laboratory space in Cambridge, Massachusetts pursuant to a lease agreement which was entered into on February 28, 2020 and expires on February 28, 2031. We have completed the build out of this facility, which we began to occupy on November 24, 2020. We believe that our existing facilities are adequate for the foreseeable future. As we expand, we believe that suitable additional alternative spaces will be available in the future on commercially reasonable terms, if required.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. We are not currently a party to any material legal proceedings. Regardless of outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II.

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market for Our Common Stock

Our common stock began trading on The Nasdaq Global Select Market under the symbol "KRON" on October 9, 2020. Prior to that date, there was no public trading market for our common stock.

Holders of Common Stock

As of March 10, 2023, there were approximately 56 holders of record for our common stock.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

None.

Use of Proceeds from our Initial Public Offering of Common Stock

In October 2020, we completed our initial public offering, pursuant to which we sold 15,131,579 shares of our common stock at a price to the public of $19.00 per share, including 1,973,684 shares sold pursuant to the full exercise of the underwriters' option to purchase additional shares. The shares were registered pursuant to a registration statement on Form S-1 (File No. 333-248925) that was declared effective on October 8, 2020. As a result of our IPO, we raised a total of approximately $263.7 million in net proceeds after deducting underwriting discounts and commissions of $20.1 million and offering expenses of approximately $3.7 million. Goldman Sachs & Co. LLC, Jefferies LLC, Cowen and Company, LLC and Piper Sandler & Co. acted as joint book-running managers for our IPO.

Upon receipt, the net proceeds from our IPO were held in cash, cash equivalents and investments. As of December 31, 2022, we have used $19.4 million of the net proceeds from our IPO for working capital purposes.

We expect to use the net proceeds from our IPO as described under "Use of Proceeds" in the final prospectus for the IPO, as filed with the SEC on October 9, 2020, except funds that would have been directed to our registrational clinical trial of entospletinib are now expected to be directed to development activities related to lanraplenib and KB-0742, to discovery and preclinical development of additional product candidates, and to headcount costs, working capital and other general corporate purposes. We cannot predict with certainty all of the particular uses for the net proceeds from our IPO, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual use of the net proceeds will vary depending on numerous factors, including our ability to access additional financing, the relative success and cost of our research, preclinical and clinical development programs and whether we are able to enter into future licensing arrangements. As a result, our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds from our IPO.

ITEM 6. [Reserved]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis should be read in conjunction with our financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that reflect our plans, estimates and beliefs and involve numerous risks and uncertainties, including but not limited to those described in the "Risk Factors" section of this Annual Report. Actual results may differ materially from those contained in any forward-looking statements. You should carefully read "Forward-Looking Statements" and "Risk Factors."

Overview

We are an integrated discovery through clinical development biopharmaceutical company, with a focus on developing therapeutics that target the dysregulated transcription that causes cancer and other serious diseases. We are enrolling patients in clinical trials for two compounds. Our product engine, which includes our proprietary small molecule microarray (SMM) screening platform, provides us with the capability to map and target transcription regulatory networks (TRNs) in a differentiated manner to enable discovery of novel compounds and improve our ability to discover and optimize clinical development candidates. In addition to our own internal preclinical programs, we have entered into a collaboration agreement with Genentech, Inc., a member of the Roche Group (Genentech).

We are developing KB-0742, our internally discovered, oral cyclin dependent kinase 9 (CDK9) inhibitor, for the treatment of MYC-amplified and other transcriptionally addicted solid tumors. We have initiated the Phase 2 portion of our Phase 1/2 clinical trial. KB-0742 was generated from our optimization of a compound that was identified using our SMM platform.

We are also developing lanraplenib, our next generation orally-administered SYK inhibitor, and are in the dose escalation stage of our Phase 1b/2 clinical trial. This clinical trial will evaluate lanraplenib in combination with gilteritinib in patients with relapsed or refractory FLT3- mutated AML. Lanraplenib has multiple advantages over our first-generation SYK inhibitor, entospletinib. In November 2022, we announced the decision to close enrollment of our Phase 3 clinical trial of entospletinib in combination with intensive chemotherapy in patients with newly diagnosed NPM-1 mutated AML for strategic reasons, and study closure is anticipated in mid-2023.

In our research efforts, we are leveraging our product engine to drive multiple oncology discovery programs targeting dysregulated transcription factors and their associated TRNs. Some of the most powerful oncogenes in all of human cancer encode transcription factors: proteins that bind to specific DNA sequences on the genome and control how sets of genes are turned on and off. Transcription factors historically have been difficult to target in drug development because they are typically intrinsically disordered, adopting a functional structure only when assembled with a complex of cofactors in the nucleus on the genome. Transcription factors with aberrant expression or activity result in dysregulated TRNs, which are frequently responsible for reprogramming healthy cells into cancerous tumor cells. Therapeutically modulating dysregulated transcription factors requires a sophisticated and holistic approach due to their complexity and their regulation of complex TRNs in a context-dependent manner. Based on this work, in November 2021, we announced the advancement of two programs, one focused on the MYC TRN and one focused on the androgen receptor (AR) TRN, which we are continuing to advance.

In addition, in January 2023, we entered into a research collaboration with Genentech, focused on discovering and developing small-molecule drugs that modulate transcription factor targets selected by Genentech. Under the collaboration, we will leverage our proprietary drug discovery platform, including the small molecule microarray, for hit finding, to build upon research conducted by Genentech.

Since our formation, we have incurred significant operating losses, primarily from costs incurred in connection with research and development activities and general and administrative costs associated with our operations. Our net losses were $133.2 million and $151.1 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $396.2 million. As of December 31, 2022, we had $247.9 million of cash, cash equivalents and investments. We expect to continue to incur net losses for the foreseeable future, and we expect to continue to make significant investments in research and development, general and administrative and capital expenditures.

Strategic Agreements

Genentech Collaboration Agreement

On January 6, 2023, we entered into a Collaboration and License Agreement with Genentech, a member of the Roche Group. Pursuant to the agreement, the parties have agreed to initially collaborate on two discovery research programs in oncology, each focused on a designated transcription factor, to discover small-molecule GLP-Tox-ready candidates that modulate transcription factor targets selected by Genentech. Each discovery research program will primarily consist of (i) a mapping phase with the goal of identifying the transcription regulatory network for such designated transcription factor, and (ii) a screening phase having the goal of identifying and characterizing multiple screening hits suitable for nomination as a preclinical development program.

We will lead discovery and research activities under the discovery research programs and will use our proprietary drug discovery platform, including our SMM, for hit finding. Following the completion of initial discovery and research activities, Genentech will have the exclusive right to pursue further preclinical and clinical development and commercialization of compounds identified in the discovery research programs and designated by Genentech (each, a Hit Program).

In connection with the agreement, we received an upfront payment of $20.0 million from Genentech. In addition, we are eligible for additional milestone payments upon achievement of certain preclinical, clinical and regulatory (including first-sale) milestones, totaling up to $177.0 million for the first development candidate per hit program, and are eligible to receive net sales milestones of up to $100.0 million for the first licensed product per hit program. We are also eligible to receive tiered royalties in the low- to high-single digits on any products that are commercialized by Genentech as a result of the collaboration.

The term of the discovery research programs will be up to 24 months, which may be extended by six months at our option subject to satisfying certain conditions.

Tempus R&D Services Agreement

In October 2021, we entered into an agreement for research and development services (Tempus Agreement) with Tempus Labs, Inc. (Tempus), pursuant to which Tempus agreed to provide us with research and development services for a period of three years. The three primary services are analytical services, data licensing, and organoid services. We intend to utilize the services contemplated under the Tempus Agreement to advance the development of KB-0742 and lanraplenib.

In consideration for the access to the services throughout the term of the Tempus Agreement, we have agreed to pay an annual minimum commitment of $1.5 million in year one, $2.0 million in year two, and $2.5 million in year three. Payments are made in quarterly installments. As of December 31, 2022, we have paid $1.1 million under the Tempus Agreement.

In addition, we are required to make milestone payments upon successful achievement of certain regulatory milestones for KB-0742, lanraplenib, and other discovery pipeline compounds up to a combined maximum of $22.4 million. For each milestone payment that becomes due, we have the right to pay up to 50% of such milestone payment amount in shares of our common stock as long as certain regulatory requirements are met.

Gilead Asset Purchase Agreement

In July 2020, we entered into the Gilead Asset Purchase Agreement, pursuant to which we acquired certain assets from and assumed certain liabilities of Gilead related to lanraplenib or entospletinib, and patents and other intellectual property covering or related to the development, manufacture and commercialization of lanraplenib or entospletinib.

In consideration for such assets, on the date of the Gilead Asset Purchase Agreement, we made a $3.0 million upfront cash payment and issued a $3.0 million principal amount convertible promissory note, which was settled in exchange for 188,567 shares of common stock in connection with the closing of our IPO at a settlement price of $16.15 per share. We also made a $0.7 million payment to reimburse Gilead for certain liabilities we assumed pursuant to the Gilead Asset Purchase Agreement. In addition, we are required to make milestone payments upon successful achievement of certain regulatory and sales milestones for lanraplenib, entospletinib and other SYK inhibitor compounds covered by the patent rights acquired pursuant to the Gilead Asset Purchase Agreement and developed by us as a back-up to entospletinib or lanraplenib (Other Compounds). Upon successful completion of certain regulatory milestones in the United States, European Union and United Kingdom for lanraplenib, entospletinib and any Other Compounds, across up to two distinct indications, we will be required to pay to Gilead an aggregate total of $51.3 million. Upon achieving certain thresholds for the aggregate annual net sales of lanraplenib, entospletinib, and any Other Compounds combined, we would owe to Gilead potential milestone payments totaling $115.0 million. For the year ended December 31, 2022, there have been no milestone payments made to Gilead. As of December 31, 2021, we made a $29.0 million milestone payment to Gilead which became payable upon initiation of our registrational Phase 3 clinical trial of entospletinib in combination with induction chemotherapy in acute myeloid leukemia patients with NPM1 mutations.

Gilead is also eligible to receive (i) tiered marginal royalties ranging from high-single digits to the mid-teens on annual worldwide net sales of lanraplenib, (ii) tiered marginal royalties ranging from the very low-teens to high-teens on annual worldwide net sales of entospletinib, and (iii) tiered marginal royalties ranging from the low single digits to mid-single digits on annual worldwide net sales of any Other Compounds. The royalties in the foregoing clauses are subject to reduction, on a country-by-country basis, for products not covered by certain claims within the assigned patents, for generic entry and, in the case of lanraplenib and entospletinib, for any royalties paid for future licenses of third-party intellectual property required to develop or commercialize lanraplenib or entospletinib. Our royalty obligation with respect to a given product in a given country begins upon the first commercial sale of such product in such country and ends on the latest of (i) expiration of the last claim of a defined set of the assigned patent rights covering such product in such country, (ii) loss of exclusive data or marketing rights to such product in such country or (iii) 10 years from the first commercial sale of such product in such country.

Under the Gilead Asset Purchase Agreement, we are required to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize either lanraplenib or entospletinib.

Harvard License Agreement

In January 2018, we entered into a license agreement with President and Fellows of Harvard College (Harvard), pursuant to which Harvard granted us a non-exclusive, worldwide, royalty-free license to certain patent rights covering aspects of our SMM platform. We paid a one-time license fee in the amount of $10,000 on the date of the agreement and an annual license maintenance fee of $20,000 on each of the first two anniversaries. We are required to pay $25,000 on each subsequent anniversary until the last to expire of any valid claim included in the licensed patents.

Components of Our Results of Operations

Operating Expenses

Our operating expenses consisted of research and development expenses and general and administrative expenses.

Research and Development Expenses

Our research and development expenses consist primarily of direct and indirect costs incurred in connection with our therapeutic discovery efforts and the preclinical and clinical development of our product candidates, as well as the development of our product engine.

Direct costs include:

- expenses incurred under agreements with contract research organizations (CROs) and other vendors that conduct our clinical trials and preclinical activities;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- costs of acquiring, developing, and manufacturing clinical trial materials and lab supplies; and
- payments made under third-party strategic agreements.

Indirect costs include:

- personnel costs, which include salaries, benefits, and other employee related costs, including stock-based compensation, for personnel engaged in research and development functions;
- costs related to compliance with regulatory requirements; and
- facilities costs, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies.

We expense research and development costs as the services are performed or the goods are received. We recognize costs for certain development activities based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our internal management. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as prepaid or accrued research and development expenses.

Because we are working on multiple research and development programs at any one time, we intend to track our direct costs by the stage of program, clinical or preclinical. However, our internal costs, employees and infrastructure are not directly tied to any one program and are deployed across multiple programs. As such, we do not track indirect costs on a specific program basis.

Our research and development expenses may vary significantly based on a variety of factors, such as:

- the scope, rate of progress, and results of our preclinical development activities;
- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the number of patients that participate in the trials;
- the countries in which the trials are conducted;
- uncertainties in clinical trial design and patient enrollment or drop out or discontinuation rates;
- potential additional safety monitoring requested by regulatory agencies;

- the duration of patient participation in the trials and follow-up;
- the safety and efficacy of our product candidates;
- the timing, receipt, and terms of any approvals from applicable regulatory authorities including the FDA and non-U.S. regulators;
- significant and changing government regulation and regulatory guidance;
- potential additional trials requested by regulatory agencies;
- establishing clinical and commercial manufacturing capabilities or making arrangements with third-party manufacturers in order to ensure that we or our third-party manufacturers are able to make product successfully;
- the extent to which we establish additional strategic collaborations or other arrangements;
- the impact of any business interruptions to our operations or to those of the third parties with whom we work; and
- maintaining a continued acceptable safety profile of our product candidates following approval, if any, of our product candidates.

A change in the outcome of any of these variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate.

We expect to continue to make significant investments into research and development for the foreseeable future as we continue to identify and develop additional product candidates and as more of our product candidates move into later stages of clinical development, which typically have higher development costs than those in earlier stages of clinical development due to the increased size and duration of later-stage clinical trials.

The process of conducting the necessary preclinical and clinical research to obtain regulatory approval is costly and time-consuming. The actual probability of success for our product candidates may be affected by a variety of factors. We may never succeed in achieving regulatory approval for any of our product candidates. Further, a number of factors, including those outside of our control, could adversely impact the timing and duration of our product candidates' development, which could increase our research and development expenses.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel costs, which include salaries, benefits and other employee related costs, such as stock-based compensation, for personnel in our executive, finance, corporate and business development, and administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; recruiting costs; travel expenses; and facilities-related costs.

We expect to maintain the general and administrative function for the foreseeable future to support personnel in research and development and to support our operations generally as we execute on our research and development activities. We also expect to continue to incur expenses associated with operating as a public company, including 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.

Interest and Other Income, Net

Interest and other income, net primarily consists of interest earned on our cash, cash equivalents and investments.

Results of Operations

Comparison of Years Ended December 31, 2022 and 2021

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

	Year Ended December 31,		Change
	2022	2021	2022 vs 2021
		(in thousands)	
Operating expenses:			
Research and development	$ 93,715	$ 112,903	$ (19,188)
General and administrative	43,400	38,495	4,905
Total operating expenses	137,115	151,398	(14,283)
Loss from operations	(137,115)	(151,398)	14,283
Other income (expense), net:			
Interest and other income, net	3,911	320	3,591
Total other income (expense), net	3,911	320	3,591
Net loss	$ (133,204)	$ (151,078)	$ 17,874

Research and Development Expenses

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

	Year Ended December 31,		Change
	2022	2021	2022 vs 2021
		(in thousands)	
Direct Costs[(1)]	$ 50,142	$ 74,640	$ (24,498)
Indirect Costs:			
Personnel	35,734	30,819	4,915
Facilities, depreciation and other expenses[(1)]	7,839	7,444	395
Total research and development expenses	$ 93,715	$ 112,903	$ (19,188)

[(1)] Certain costs have been reclassified from Facilities, depreciation and other expenses to Direct Costs, and the prior period amounts have been adjusted by $6.1 million for comparison purposes.

Research and development expenses were $93.7 million for the year ended December 31, 2022, compared to $112.9 million for the year ended December 31, 2021. The decrease of $19.2 million was primarily due to a decrease in Direct Costs related to a $29.0 million milestone payment in prior year with no associated milestone payment in the current year, partially offset by an increase in outside and consulting research expenses of $5.0 million related to an increase in research and development activities and increases in personnel costs of $3.2 million and stock-based compensation of $1.8 million, both of which are primarily attributable to increased research and development personnel headcount.

General and Administrative Expenses

General and administrative expenses were $43.4 million for the year ended December 31, 2022 compared to $38.5 million for the year ended December 31, 2021. The increase of $4.9 million was primarily due to an increase in stock-based compensation of $3.1 million and an increase of $2.4 million in personnel costs, both of which are primarily attributable to increased general and administrative personnel headcount. The increase in general and administrative expenses was partially offset by a decrease of $0.9 million in professional fees, primarily attributable to lower insurance, legal and outside consultant costs.

Interest and Other Income, Net

Interest and other income, net was $3.9 million and $0.3 million for the years ended December 31, 2022 and 2021, respectively. The $3.6 million increase was due to higher interest rates during the twelve months ended December 31, 2022.

Liquidity and Capital Resources

Sources of Liquidity

To date, we have incurred significant operating losses and negative cash flows from operations. We have not yet commercialized any products and we do not expect to generate revenue from sales of any product candidates for several years, if ever. Prior to our IPO, our operations were financed primarily by net proceeds from the sale and issuance of our convertible preferred stock and convertible notes, totaling aggregate gross proceeds of $278.2 million. Upon completion of our IPO on October 14, 2020, we sold an aggregate of 15,131,579 shares of our common stock including 1,973,684 shares of common stock sold pursuant to the full exercise of the underwriters' option to purchase additional shares at a price of $19.00 per share and received approximately $263.7 million in net proceeds after deducting underwriting discounts and commissions and offering expenses.

As of December 31, 2022, we had cash, cash equivalents and investments of $247.9 million. We expect that our cash, cash equivalents and investments as of December 31, 2022, will enable us to fund our planned operating expenses and capital expenditure requirements into the second half of 2025.

Material Cash Requirements

Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures related KB-0742 and lanraplenib, the wind-down of the entospletinib trial and our other research efforts, and to a lesser extent, general and administrative expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Our product candidates are still in the early stages of clinical and preclinical development, and the outcomes of these efforts are uncertain. Accordingly, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates or whether, or when, we may achieve profitability. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity or debt financings and collaboration agreements. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our existing stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we are unable to raise capital when needed, we will need to delay, reduce or terminate planned activities to reduce costs. Doing so will likely harm our ability to execute our business plans.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Cash used in operating activities	$ (90,926)	$ (117,924)
Cash provided by (used in) investing activities	(32,222)	63,724
Cash provided by financing activities	851	4,460
Net decrease in cash and cash equivalents	$ (122,297)	$ (49,740)

Operating Activities

During the year ended December 31, 2022, cash used in operating activities was $90.9 million, which was primarily attributable to our net loss of $133.2 million and $6.2 million net cash provided by changes in our operating assets and liabilities, partially offset by non-cash charges of $36.1 million. The non-cash charges consisted of $31.1 million of stock-based compensation, $2.2 million of noncash lease expense, $2.3 million of depreciation and amortization, and $1.0 million change in accrued interest on marketable securities, partially offset by a decrease related to net amortization and accretion of investment securities of $0.5 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2022 consisted of a decrease of $2.7 million in right of use assets and liabilities, a decrease of $1.1 million in other long term assets, partially offset by, an increase of $1.6 million in prepaid and other current assets and an increase in accounts payable and accrued expenses of $8.2 million. The decrease in right of use assets was the result of regular amortization. The increase in accounts payable and accrued expenses was primarily due to increases in accrued compensation and external research and development costs.

During the year ended December 31, 2021, cash used in operating activities was $117.9 million, which was primarily attributable to our net loss of $151.1 million, partially offset by non-cash charges of $34.8 million. The non-cash charges primarily consisted of $26.2 million in stock-based compensation, net amortization and accretion of investment securities of $4.0 million, noncash lease expense of $2.1 million, depreciation and amortization of $2.0 million, and cash used by changes in our operating assets and liabilities of $1.6 million. Net cash used by changes in our operating assets and liabilities of $1.6 million during the year ended December 31, 2021 consisted of a decrease of $2.3 million in other liabilities and a decrease of $1.0 million in prepaid and other current assets partially offset by a net increase in accounts payable and accrued expenses of $1.6 million and an increase of $0.1 million in other assets. The decrease in other liabilities was primarily the result of an decrease in the unvested early exercised share liability. The net increase in accounts payable and accrued expenses was largely due to increases in accrued compensation and external research and development costs

Investing Activities

During the year ended December 31, 2022, cash used in investing activities was $32.2 million, consisting of $366.6 million of net purchases of marketable securities and $0.6 million of purchases of property and equipment, partially offset by $335.0 million in maturities of marketable securities.

During the year ended December 31, 2021, cash provided by investing activities was $63.7 million, consisting of $226.2 million in maturities of marketable securities, partially offset by net investment purchases of $158.3 million and $4.3 million for the purchase of property and equipment.

Financing Activities

During the year ended December 31, 2022, net cash provided by financing activities was $0.9 million, consisting primarily of net proceeds from the issuance of common stock upon vesting and exercise of options of $0.5 million and issuance of common stock under the employee stock purchase plan of $0.4 million.

During the year ended December 31, 2021, net cash provided by financing activities was $4.5 million, consisting primarily of net proceeds from the issuance of common stock upon vesting and exercise of options of $3.1 million and issuance of common stock under the employee stock purchase of $1.3 million.

Contractual Obligations and Commitments

In March 2020, we entered into a lease agreement for our research and development operations facility at 301 Binney Street, Cambridge, Massachusetts (Cambridge facility). The initial annual base rent was $4.1 million with rent payments escalating 3.0% annually after the initial 12 payments. As discussed in Note 2, we executed a letter of credit for $2.0 million in connection with the lease. The remaining lease term is 8.2 years.

In February 2021, we entered into a new lease agreement for our office space in San Mateo, California, in order to move from our former suites to a single, larger suite totaling 17,340 square-feet, and relocated in the third quarter of 2021. We accounted for this change in lease term of the original suites as a modification of the originally amended lease.

The initial annual base rent for the San Mateo facility was $1.2 million, and such amount will increase by 3% annually on each anniversary of the new premises commencement date. In connection with the larger space leased, we also made an additional one-time cash security deposit in the amount of $59,000, bringing our total security deposit to $0.1 million. The new lease commenced in April 2021 while tenant improvements were being made and the new lease agreement extended the termination date from April 30, 2025 to August 31, 2026.

Pursuant to the Gilead Asset Purchase Agreement, we are obligated to make milestone payments upon the achievement of specified regulatory and clinical milestones as well as royalty payments. The payment obligations under this agreement are contingent upon future events, such as our achievement of specified milestones or generating product sales. We are currently unable to estimate the timing or likelihood of achieving these milestones or generating future product sales. See the subsection titled “—Strategic Agreements—Gilead Asset Purchase Agreement” above.

Pursuant to the Tempus Agreement, we are obligated to make milestone payments upon the achievement of specified regulatory milestones as well as annual minimum commitments in quarterly installments. Some payment obligations under this agreement are contingent upon future events, such as our achievement of specified milestones. We are currently unable to estimate the timing or likelihood of achieving these milestones. See the subsection titled “—Strategic Agreements—Tempus R&D Services Agreement” above.

We enter into contracts in the ordinary course of business with CROs for clinical trials, preclinical and clinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts do not contain any minimum purchase commitments and are generally terminable by us upon prior notice. Payments due upon termination generally consist only of payments for services provided and expenses incurred up to the date of termination and certain wind down costs that may be associated with the termination of a contract or clinical trial program.

Critical Accounting Policies and Estimates

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

While our significant accounting policies and estimates are described in more detail in the notes to our financial statements included elsewhere in this Annual Report on Form 10-K, we consider the assumptions and estimates associated with accrued research and development expenditures and stock-based compensation to have the most significant impact on our financial statements and therefore we consider these to be our critical accounting policies and estimates.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development and manufacturing expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research activities on our behalf and conducting preclinical studies and clinical trials on our behalf;
- investigative sites or other service providers in connection with clinical trials;
- vendors in connection with preclinical and clinical development activities; and
- vendors related to product manufacturing and development and distribution of preclinical and clinical supplies.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CROs that conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation and vary from contract to contract, which may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the completion of scientific milestones. In accruing 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 amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We measure stock options and other stock-based awards granted to employees, directors, and non-employees based on their fair value on the date of grant and recognize stock-based compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. We recognize the impact of forfeitures on stock-based compensation expense as forfeitures occur. We apply the straight-line method of expense recognition to all awards with only service-based vesting conditions.

We estimate the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model. This model requires the use of highly subjective assumptions to determine the fair value of stock-based awards, including:

- *Fair Value of Common Stock*—For grants before the completion of our IPO in October 2020 when we were a privately held company with no public market for our common stock, the fair value of our common stock underlying share-based awards was estimated on each grant date by our Board of Directors. In order to determine the fair value of our common stock underlying option grants, our Board of Directors considered, among other things, valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accounts Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. For all grants subsequent to our IPO in October 2020, the fair value of common stock was determined by taking the closing price per share of common stock as reported on the Nasdaq Stock Market.

- *Expected Term*—The expected term represents the period that the stock-based awards are expected to be outstanding. We use the simplified method to determine the expected term, which is based on the average of the time-to-vesting and the contractual life of the options.

- *Expected Volatility*—The expected volatility for the years ended December 31, 2022 and 2021 is estimated based on the average historical volatilities of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants. The comparable companies are chosen based on their size, stage in the product development cycle or area of specialty. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

- *Risk-Free Interest Rate*—The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the expected term of the awards.

- *Expected Dividend*—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

See Note 9 to our financial statements included elsewhere in this Annual Report to Form 10-K for information concerning certain of the specific assumptions we used in applying the Black-Scholes option-pricing model to determine the estimated fair value of our stock options granted in the years ended December 31, 2022 and 2021.

Recently Issued and Adopted Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is provided in Note 2 to our financial statements included elsewhere in Item 8 of Part II of this Annual Report on Form 10-K.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

Our cash equivalents and investments as of December 31, 2022 consist of money market funds and available-for-sale securities. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant for us. A one percent change in the interest rates in effect on December 31, 2022, would not have had a material effect on the fair market value of our cash equivalents and investments.

Foreign Currency Exchange Risk

All of our employees and our operations are currently located in the United States and our expenses are generally denominated in U.S. dollars. However, we have entered into a limited number of contracts with vendors for research and development services that permit us to satisfy our payment obligations in U.S. dollars (at prevailing exchange rates) but have underlying payment obligations denominated in foreign currencies, primarily including the Euro and GBP. We are subject to foreign currency transaction gains or losses on our contracts denominated in foreign currencies. To date, foreign currency transaction gains and losses have not been material to our financial statements, and we have not had a formal hedging program with respect to foreign currency. A one percent increase or decrease in exchange rates at December 31, 2022 would not have had a material effect on our financial statements.

Inflation Risk

Inflation generally affects us by increasing our costs of labor, goods, and services. We do not believe that inflation had, or that an immediate one percent change in inflation would have had, a material effect on our financial statements included in Item 8 of Part II of this Annual Report on Form 10-K.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Kronos Bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Kronos Bio, Inc., (the Company) as of December 31, 2022 and 2021, the related statements of operations and comprehensive loss, 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 "financial statements"). In our opinion, the 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.

Critical Audit Matter

Critical audit matters are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements, and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2019.
San Mateo, California
March 15, 2023

KRONOS BIO, INC.
Balance Sheets
(in thousands, except share and per share amounts)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 75,973	$ 198,270
Short-term investments	162,212	141,239
Prepaid expenses and other current assets	6,106	8,045
Total current assets	244,291	347,554
Long-term investments	9,762	—
Property and equipment, net	12,985	14,880
Operating lease right-of-use assets	24,707	26,904
Restricted cash	2,026	2,026
Other noncurrent assets	1,167	112
Total assets	$ 294,938	$ 391,476
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 5,047	$ 998
Accrued expenses	12,963	9,063
Current portion of operating lease liabilities	2,347	2,109
Current portion of other liabilities	1,129	1,456
Total current liabilities	21,486	13,626
Noncurrent operating lease liabilities	28,744	31,653
Other noncurrent liabilities	209	1,100
Total liabilities	50,439	46,379
Commitments and contingencies (Note 13)		
Stockholder's equity (deficit):		
Preferred stock, $0.001 par value; 10,000,000 authorized; no shares issued and outstanding		
Common stock, $0.001 par value, 200,000,000 shares authorized as of December 31, 2022 and 2021; 56,967,436 and 55,703,327 shares issued and outstanding as of December 31, 2022 and 2021, respectively.	57	56
Additional paid-in capital	641,422	608,064
Accumulated deficit	(396,188)	(262,984)
Accumulated other comprehensive income (loss)	(792)	(39)
Total stockholders' equity (deficit)	244,499	345,097
Total liabilities and stockholders’ equity (deficit)	$ 294,938	$ 391,476

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

KRONOS BIO, INC.
Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Years Ended December 31,	
	2022	2021
Operating expenses:		
Research and development	$ 93,715	$ 112,903
General and administrative	43,400	38,495
Total operating expenses	137,115	151,398
Loss from operations	(137,115)	(151,398)
Other income (expense), net:		
Interest and other income, net	3,911	320
Total other income (expense), net	3,911	320
Net loss	(133,204)	(151,078)
Other comprehensive income (loss):		
Net unrealized gain (loss) on available-for-sale securities	(753)	(20)
Net comprehensive loss	$ (133,957)	$ (151,098)
Net loss per share, basic and diluted	$ (2.37)	$ (2.76)
Weighted-average number of shares used to compute net loss per share, basic and diluted	56,201,398	54,753,599

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

KRONOS BIO, INC.
Statement of Stockholders' Equity (Deficit)
(in thousands, except share and per share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balance at December 31, 2020	54,073,901	$ 54	$ 577,390	$ (19)	$ (111,906)	$ 465,519
Issuance of common stock upon vesting and exercise of options and vesting of restricted stock	1,533,703	2	3,125	—	—	3,127
Stock-based compensation expense	—	—	26,211	—	—	26,211
Employee stock purchase plan	95,723	—	1,338	—	—	1,338
Net unrealized gain (loss) on available-for-sale securities	—	—	—	(20)	—	(20)
Net loss	—	—	—	—	(151,078)	(151,078)
Balance at December 31, 2021	55,703,327	$ 56	$ 608,064	$ (39)	$ (262,984)	$ 345,097
Issuance of common stock upon vesting and exercise of options and vesting of restricted stock	1,003,344	1	1,833	—	—	1,834
Stock-based compensation expense	—	—	31,145	—	—	31,145
Employee stock purchase plan	260,765	—	380	—	—	380
Net unrealized gain (loss) on available-for-sale securities	—	—	—	(753)	—	(753)
Net loss	—	—	—	—	(133,204)	(133,204)
Balance at December 31, 2022	56,967,436	$ 57	$ 641,422	$ (792)	$ (396,188)	$ 244,499

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

KRONOS BIO, INC.
Statements of Cash Flows
(in thousands)

	Years Ended December 31,	
	2022	2021
Cash flows from operating activities:		
Net loss	$ (133,204)	$ (151,078)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation and amortization	2,266	1,977
Net amortization/accretion on available-for-sale securities	(533)	3,997
Change in accrued interest on available-for-sale securities	1,025	485
Stock-based compensation expense	31,145	26,211
Noncash lease expense	2,197	2,104
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,605	(975)
Other long-term assets	(1,055)	54
Accounts payable	4,025	(3,195)
Accrued expenses	4,130	4,786
Right-of-use operating assets and liabilities, net	(2,671)	19
Other liabilities	144	(2,309)
Net cash provided by (used in) operating activities	(90,926)	(117,924)
Cash flows from investing activities:		
Purchase of property and equipment	(577)	(4,260)
Purchase of marketable securities	(367,124)	(177,734)
Maturities of marketable securities	334,979	226,245
Sale of marketable securities	500	19,473
Net cash provided by (used in) investing activities	(32,222)	63,724
Cash flows from financing activities:		
Principal payments on finance lease	—	(5)
Proceeds from issuance of common stock upon exercise of stock options	471	3,127
Proceeds from issuance of common stock under the employee stock purchase plan	380	1,338
Net cash provided by (used in) financing activities	851	4,460
Net increase (decrease) in cash and cash equivalents	(122,297)	(49,740)
Cash, cash equivalents and restricted cash at beginning of period	200,296	250,036
Cash, cash equivalents and restricted cash at end of period	$ 77,999	$ 200,296
Supplemental disclosures of non-cash activities:		
Property and equipment additions included in accounts payable and accrued expenses	$ 20	$ 226
Reduction of right-of-use asset due to modification	$ —	$ (1,741)
Right-of-use asset obtained in exchange for operating lease liability	$ —	$ 3,764
Cash and cash equivalents at end of period	$ 75,973	$ 198,270
Restricted cash at end of period	2,026	2,026
Cash, cash equivalents and restricted cash at end of period	$ 77,999	$ 200,296

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

1. NATURE OF OPERATIONS AND BASIS OF PRESENTATION

Kronos Bio, Inc. (Kronos or the Company), a Delaware corporation, was incorporated on June 2, 2017. The Company is an integrated discovery through clinical development biopharmaceutical company, with a focus on developing therapeutics that target the dysregulated transcription that causes cancer and other serious diseases.

The Company operates in one business segment, the development of biopharmaceutical products.

Basis of Presentation

The accompanying financial statements have been prepared in accordance with the rules and regulations of the Securities and Exchange Commission (SEC) and accounting principles generally accepted in the United States of America (GAAP).

Initial Public Offering

In October 2020, the Company completed an initial public offering (IPO) of its common stock. In connection with its IPO, the Company issued and sold 15,131,579 shares of its common stock, which included 1,973,684 shares of its common stock issued and sold pursuant to the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $19.00 per share. As a result of the IPO, the Company received $263.7 million in net proceeds, after deducting underwriting discounts and commissions of $20.1 million and offering expenses of $3.7 million payable by the Company. At the closing of the IPO, all then outstanding shares of convertible preferred stock were automatically converted into 22,687,625 shares of common stock. Following the IPO, there were no shares of convertible preferred stock outstanding.

Need for Additional Capital

The Company has incurred net losses since its inception and expects to continue to generate net losses for the foreseeable future. The Company's ultimate success depends on the outcome of its research and development activities. The Company had cash, cash equivalents and investments of $247.9 million as of December 31, 2022. Since inception through December 31, 2022, the Company has incurred a cumulative net operating loss of $396.2 million. Management expects to incur additional losses in the future to fund its operations and conduct product research and development and recognizes the need to raise additional capital.

The Company intends to raise additional capital through the issuance of equity securities, debt financings or other sources in order to continue its operations. However, if such financing is not available when needed and at adequate levels, the Company will need to reevaluate its operating plan and may be required to delay the development of its product candidates. The Company expects that its cash and cash equivalents and investments will be sufficient to fund its operations for a period of at least one year from the date the accompanying financial statements are filed with the Securities and Exchange Commission (SEC).

The future viability of the Company is dependent on its ability to generate cash from operating activities or to raise additional capital to finance its operations. The Company's failure to raise capital as and when needed could have a material adverse effect on its financial condition and ability to pursue business strategies. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaboration arrangements or obtain government grants. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. If the Company is unable to obtain funding, the Company could be forced to delay, reduce, or eliminate its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects. In the event that the Company requires additional funding, there can be no assurance that it will be successful in obtaining sufficient funding on terms acceptable to the Company to fund its continuing operations, if at all.

2. SIGNIFICANT ACCOUNTING POLICIES, ESTIMATES AND JUDGMENTS

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these financial statements include, but are not limited to, the accrual of research and development expenses, the fair value of investments, income tax uncertainties, the valuation of equity instruments and the incremental borrowing rate for determining the operating lease assets and liabilities. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ from the Company's estimates.

Research and Development Expenses

Research and development (R&D) expenses consist primarily of personnel costs, including salaries, benefits and stock-based compensation, discovery and development research performed by contract research organizations (CROs), investigator grants, materials and supplies, licenses and fees and overhead allocations consisting of various support and facility-related costs. The Company expenses R&D costs as the services are performed or the goods are received.

CRO costs are a significant component of R&D expenses. The Company monitors levels of performance under each significant contract through communications with its CROs. The Company accrues costs for discovery research and development performed by CROs over the service periods specified in the contracts and adjusts its estimates, if required, based upon its ongoing review of the level of effort and costs actually incurred by the CROs. All of the Company's material CRO contracts are terminable by the Company upon written notice and it is generally only liable for actual services completed by the CRO and certain non-cancellable expenses incurred at any point of termination.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents.

Restricted Cash

The Company has deposited cash of $2.0 million as of December 31, 2022 and 2021 to secure a letter of credit in connection with the lease of the Cambridge facility (see Note 13). The Company has classified the restricted cash as a noncurrent asset on its balance sheets.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments, which potentially subject the Company to significant concentrations of credit risk, consist primarily of cash and cash equivalents and investments. The primary objectives for the Company's investment portfolio are the preservation of capital and the maintenance of liquidity. The Company does not enter into any investment transaction for trading or speculative purposes.

The Company's investment policy limits investments to certain types of instruments such as certificates of deposit, money market instruments, obligations issued by the U.S. government and U.S. government agencies as well as corporate debt securities, and places restrictions on maturities and concentration by type and issuer. The Company maintains cash balances in excess of amounts insured by the FDIC and concentrated within a limited number of financial institutions. The accounts are monitored by management and management believes that the financial institutions are financially sound, and, accordingly, minimal credit risk exists with respect to these financial institutions. As of December 31, 2022 and 2021, the Company has not experienced any credit losses in such accounts or investments.

The Company is subject to a number of risks common for biopharmaceutical companies, including, but not limited to, dependency on the clinical and commercial success of its product candidates, ability to obtain regulatory approval of its product candidates, the need for substantial additional financing to achieve its goals, uncertainty of broad adoption of its approved products, if any, by physicians and patients, significant competition, and untested manufacturing capabilities.

Investments

Investments are available-for-sale and are carried at estimated fair value. The Company's valuations of available-for-sale securities are generally derived from independent pricing services based upon quoted prices in active markets for similar securities, with prices adjusted for yield and number of days to maturity, or based on industry models using data inputs, such as interest rates and prices that can be directly observed or corroborated in active markets. Management determines the appropriate classification of its investments in debt securities at the time of purchase. Investments with original maturities beyond three months at the date of purchase and which mature at, or less than 12 months from, the balance sheet date are classified as short-term investments.

Unrealized gains and losses are excluded from earnings and are reported as components of comprehensive loss. The Company periodically evaluates whether declines in fair values of its available-for-sale securities below their book value are other-than-temporary. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss as well as the Company's ability and intent to hold the available-for-sale security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the security or whether it is more likely than not that it will be required to sell any available-for-sale security before recovery of its amortized cost basis. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in interest and other income, net. Interest income on investments is included in interest and other income, net on the Company's statements of operations and comprehensive loss.

Fair Value Measurement

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Observable inputs such as unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2—Inputs (other than quoted prices included in Level 1) are either directly or indirectly observable for the asset or liability. These include quoted prices for similar assets or liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active.

Level 3— Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The fair value estimates are made at a discrete point in time based on relevant market information and information about the financial instruments. Fair value estimates are based on judgments regarding future expected loss experience, current economic conditions, risk characteristics of various financial instruments, and other factors. These estimates are subjective in nature and involve uncertainties and matters of significant judgment and, therefore, cannot be determined with precision. Changes in assumptions could significantly affect the estimates.

As of December 31, 2022 and 2021, the Company recorded financial assets requiring fair value measurement. The financial assets include cash equivalents and investments. There were no financial liabilities requiring fair value measurement as of December 31, 2022 and 2021.

Property and Equipment, Net

Property and equipment is stated at cost less accumulated depreciation and amortization. Depreciation and amortization are recognized using the straight-line method over the estimated useful lives of the respective assets. Leasehold improvements are amortized over the lesser of their useful lives or the remaining life of the lease. When assets are retired or otherwise disposed of, the cost and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gain or loss is reflected in the statements of operations and comprehensive loss in the period realized. Repairs and maintenance costs are expensed as incurred.

Estimated useful lives in years are generally as follows:

Description	Estimated Useful Life
Lab equipment	3 to 7 years
Leasehold improvements	Shorter of useful life or lease term
Furniture and fixtures	5 to 7 years
Computer equipment	3 years

Leases

The Company determines if an arrangement is a lease at inception. Operating leases are included in operating lease right-of-use (ROU) assets, current portion of operating lease liabilities, and noncurrent operating lease liabilities on the Company's balance sheet.

ROU assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. As most of our leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The operating lease ROU asset also includes any lease payments and initial direct costs incurred, net of lease incentives. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise that option. Lease expense for lease payments is recognized on a straight-line basis over the lease term. The Company elected to exclude from its balance sheets recognition of leases having a term of 12 months or less (short-term leases) and elected to not separate lease components and non-lease components for its long-term real-estate leases.

Impairment of Long-Lived Assets

Long-lived assets, including property and equipment, are reviewed for impairment whenever facts or circumstances either internally or externally may suggest that the carrying value of an asset or asset group may not be recoverable. Should there be an indication of impairment, the Company tests for recoverability by comparing the estimated undiscounted future cash flows expected to result from the use of the asset or asset group and its eventual disposition to the carrying amount of the asset or asset group. Any excess of the carrying value of the asset or asset group over its estimated fair value is recognized as an impairment loss.

Stock-Based Compensation

The Company has an equity incentive plan under which various types of equity-based awards are granted, including stock options, restricted stock awards (RSAs), and restricted stock units (RSUs). The Company measures stock-based awards granted to employees and nonemployees based on the fair value on the date of the grant and recognizes stock-based compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. The Company calculates the fair value measurement of stock options using the Black-Scholes option-pricing model. Forfeitures are accounted for as

they occur. The fair value of the RSA and RSUs is equal to the fair value of the Company's common stock on the grant date of the award.

Income Taxes

The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the Company's financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amounts and the tax bases of the assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertainty in income taxes recognized in the financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

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. For the years ended December 31, 2022 and 2021, other comprehensive loss consisted of unrealized gains and losses from available-for-sale securities.

Net Loss Per Share

Basic net loss per share is computed using the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is computed using the sum of the weighted-average number of shares of common stock outstanding during the period and the effect of dilutive securities.

In periods in which the Company reports a net loss, diluted net loss per share is the same as basic net loss per share, since dilutive shares of common stock are not assumed to have been issued if their effect on net loss per share is anti-dilutive.

Recent Accounting Pronouncements

In May 2021, the FASB issued ASU No. 2021-04, *Earnings Per Share (Topic 260), Debt—Modifications and Extinguishments (Subtopic 470-50), Compensation—Stock Compensation (Topic 718), and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options (a consensus of the FASB Emerging Issues Task Force)*, which clarifies and reduces diversity in accounting for modifications or exchanges of freestanding equity-classified written call options (for example, warrants) that remain equity classified after modification or exchange. This guidance was effective for the Company in the first quarter of 2022. The effect on the Company's financial statements and related disclosures was not material.

The Company continues to monitor new accounting pronouncements issued by the FASB and does not believe any accounting pronouncements issued through the date of this report will have a material impact on the Company's consolidated financial statements.

3. FAIR VALUE MEASUREMENTS

The Company follows authoritative accounting guidance, which among other things, defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is an 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.

The Company measures and reports its cash equivalents and investments at fair value.

Money market funds are measured at fair value on a recurring basis using quoted prices and are classified as Level 1. Investments measured at fair value based on inputs other than quoted prices that are derived from observable market data are classified as Level 2.

Financial assets and liabilities subject to fair value measurements on a recurring basis and the level of inputs used in such measurements by major security type as of December 31, 2022 and 2021 were as follows:

	December 31, 2022			
	Level 1	Level 2	Level 3	Fair Value
	(in thousands)			
Financial Assets:				
Money market funds	$ 49,003	$ —	$ —	$ 49,003
Certificates of deposit	490	—	—	490
Commercial paper	—	1,667		1,667
Corporate bonds	—	30,657	—	30,657
U.S. agency securities	—	13,000	—	13,000
U.S. treasury securities	138,734	—	—	138,734
Total financial assets	$ 188,227	$ 45,324	$ —	$ 233,551

	December 31, 2021			
	Level 1	Level 2	Level 3	Fair Value
	(in thousands)			
Financial Assets:				
Money market funds	$ 188,923	$ —	$ —	$ 188,923
Corporate bonds	—	63,620	—	63,620
U.S. treasury securities	79,394	—	—	79,394
Total financial assets	$ 268,317	$ 63,620	$ —	$ 331,937

The carrying amounts of accounts payable and accrued expenses approximate their fair values due to their short-term maturities. The Company's Level 2 securities are valued using third-party pricing sources. The pricing services utilize industry standard valuation models, including both income- and market-based approaches, for which all significant inputs are observable, either directly or indirectly.

The Company did not have any financial assets or liabilities as of December 31, 2022 and 2021 that required Level 3 inputs.

4. INVESTMENTS

The fair value and amortized cost of available-for-sale securities by major security type as of December 31, 2022 and 2021 were as follows:

	December 31, 2022			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(in thousands)			
Money market funds	$ 49,003	$ —	$ —	$ 49,003
Certificates of deposit	490	—	—	490
Commercial paper	1,667	—	—	1,667
Corporate bonds	30,683	3	(29)	30,657
U.S. agency securities	13,024	—	(24)	13,000
U.S. treasury securities	139,477	4	(747)	138,734
Total cash equivalents and investments	$ 234,344	$ 7	$ (800)	$ 233,551

	December 31, 2021			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(in thousands)			
Money market funds	$ 188,923	$ —	$ —	$ 188,923
Corporate bonds	63,647	2	(29)	63,620
U.S. treasury securities	79,406	—	(12)	79,394
Total cash equivalents and investments	$ 331,976	$ 2	$ (41)	$ 331,937

Marketable securities that had been in unrealized loss positions as of December 31, 2022 and 2021 were in an unrealized loss position for less than twelve months.

These available-for-sale debt securities were classified on the Company's balance sheets as of December 31, 2022 and 2021 as:

	Fair Value	
	December 31,	
	2022	2021
	(in thousands)	
Cash equivalents	$ 61,577	$ 190,698
Short-term investments	162,212	141,239
Long-term investments	9,762	—
Total cash equivalents and investments	$ 233,551	$ 331,937

The fair values of available-for-sale securities by contractual maturity as of December 31, 2022 and 2021 were as follows:

	December 31,	
	2022	2021
	(in thousands)	
Due in 1 year or less	$ 174,786	$ 143,014
Due in 1 to 2 years	9,762	—
Total	$ 184,548	$ 143,014

As of December 31, 2022 and 2021, the remaining contractual maturities of available-for-sale securities were less than two years, respectively. There have been no significant realized losses on available-for-sale securities for any of the periods presented in the accompanying financial statements. As of December 31, 2022 and 2021, unrealized losses on available-for-sale securities are not attributed to credit risk. The Company believes that it is more likely than not that investments in an unrealized loss position will be held until maturity and all interest and principal will be received. The Company believes that an allowance for credit losses is unnecessary because the unrealized losses on certain of the Company's available-for-sale securities are due to market factors. To date, the Company has not recorded any impairment charges on available-for-sale securities.

5. PREPAID EXPENSES AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets consisted of the following as of December 31, 2022 and 2021:

	December 31,	
	2022	2021
	(in thousands)	
Accrued interest on short-term available-for-sale securities	$ 572	$ 816
Prepaid equipment service contracts	289	360
Prepaid external research and development and outside services	2,276	3,074
Prepaid software	905	624
Prepaid insurance	1,630	2,644
Other prepaid expenses	434	527
Total prepaid expenses and other current assets	$ 6,106	$ 8,045

6. PROPERTY AND EQUIPMENT, NET

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

	December 31,	
	2022	2021
	(in thousands)	
Property and equipment:		
Lab equipment	$ 8,475	$ 8,164
Leasehold improvements	9,348	9,335
Furniture and fixtures	619	596
Computer equipment	58	44
Total property and equipment	18,500	18,139
Less: Accumulated depreciation and amortization	(5,515)	(3,259)
Total property and equipment, net	$ 12,985	$ 14,880

Depreciation and amortization expense was $2.3 million and $2.0 million for the years ended December 31, 2022 and 2021, respectively.

7. ACCRUED EXPENSES AND CURRENT PORTION OF OTHER LIABILITIES

Accrued expenses consisted of the following as of December 31, 2022 and 2021:

	December 31,	
	2022	2021
	(in thousands)	
Accrued compensation	$ 4,277	$ 4,570
External research and development	7,694	2,655
Accrued outside services	945	1,598
Accrued taxes	40	—
Other accrued expenses	7	240
Total accrued expenses	$ 12,963	$ 9,063

Current portion of other liabilities consist of the following as of December 31, 2022 and 2021:

	December 31,	
	2022	2021
	(in thousands)	
Current portion of unvested early exercised share liability	891	1,364
ESPP withholdings	238	92
Total current portion of other liabilities	$ 1,129	$ 1,456

8. STOCKHOLDERS' EQUITY (DEFICIT)

Preferred Stock

Pursuant to the Amended and Restated Certificate of Incorporation filed on October 14, 2020, as amended, the Company is authorized to issue a total of 10,000,000 shares of undesignated preferred stock, par value $0.001, of which no shares were issued or outstanding as of December 31, 2022 and 2021.

Common Stock

Pursuant to the Company's amended and restated certificate of incorporation filed on October 14, 2020, as amended, the Company is authorized to issue a total of 200,000,000 shares of its common stock, par value

$0.001. As of December 31, 2022 and 2021, there were 56,967,436 and 55,703,327 shares issued and outstanding, respectively.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Subject to the rights of the Preferred Stock, holders of the Company's common stock are entitled to receive dividends, as may be declared by the Board of Directors. As of December 31, 2022, no dividends have been declared to date.

9. STOCK-BASED COMPENSATION

2020 Equity Incentive Plan

In October 2020, the Company adopted its 2020 Equity Incentive Plan (the 2020 Plan) which replaced the 2017 Equity Incentive Plan (Prior Plan) upon completion of the IPO. The 2020 Plan provides for the grant of incentive stock options or nonqualified stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance awards and other forms of awards to employees, directors, and consultants of the Company. Under the 2020 Plan, the maximum number of shares of common stock that may be issued increased to 11,938,152 shares. The number of shares of common stock reserved for issuance under the 2020 Plan will automatically increase each year for a period of ten years, beginning in 2021 and continuing through 2030, in an amount equal to (1) 5.0% of the total numbers of shares of the Company's common stock outstanding on December 31st of the immediately preceding year, or (2) a lesser number of shares determined by the Board of Directors no later than December 31st of the immediately preceding year. As a result of the automatic annual increases, the maximum number of shares of common stock that may be issued under the 2020 Plan as of December 31, 2022 was 17,568,821 shares.

Under the 2020 Plan, the exercise prices, vesting, and other restrictions are determined at the discretion of the Board of Directors, or a designated committee thereof, 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 and the term of stock option may not be greater than 10 years. The Company recognizes the impact of forfeitures on stock-based compensation expense as forfeitures occur. The Company applies the straight-line method of expense recognition to all awards with only service-based vesting conditions. Vesting periods are determined at the discretion of the Board of Directors. Stock options typically vest over four years. The maximum contractual term is 10 years.

As of December 31, 2022 and 2021, there were 4,098,939 and 4,647,580 shares, respectively, reserved by the Company under the 2020 Plan for the future issuance of equity awards.

Stock Option Valuation

The Company estimates the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model. This model requires the use of assumptions to determine the fair value of stock-based awards, including:

- ***Fair Value of Common Stock***—For grants before the completion of the IPO in October 2020 when the Company was a privately held company with no public market for its common stock, the fair value of its common stock underlying share-based awards was estimated on each grant date by its Board of Directors. In order to determine the fair value of our common stock underlying option grants, the Company's Board of Directors considered, among other things, valuations of its common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accounts Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. For all grants subsequent to our IPO in October 2020, the fair value of common stock was determined by taking the closing price per share of common stock as reported on the Nasdaq Stock Market.

- ***Expected Term***—The expected term represents the period that the stock-based awards are expected to be outstanding. The Company uses the simplified method to determine the expected term, which is based on the average of the time-to-vesting and the contractual life of the options.

- ***Expected Volatility***—The expected volatility for the years ended December 31, 2022 and 2021 is estimated based on the average historical volatilities of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants. The comparable companies are chosen based on their size, stage in the product development cycle or area of specialty. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.
- ***Risk-Free Interest Rate***—The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the expected term of the awards.
- ***Expected Dividend***—The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

The Black-Scholes option-pricing model assumptions that the Company used to determine the grant-date fair value of stock options for the years ended December 31, 2022 and 2021 were as follows, presented on a weighted-average basis:

	Year Ended December 31,	
	2022	2021
Fair value of common stock per share	$ 6.48	$ 25.99
Expected term (in years)	5.91	6.01
Expected volatility	78.21%	85.26%
Risk-free interest rate	2.28%	0.90%
Expected dividend	—%	—%

The weighted-average grant-date fair value per share of stock options granted, using the assumptions listed above, was $5.57 and $18.52, during the years ended December 31, 2022 and 2021, respectively.

Stock Options

Stock option activity under the 2020 Plan as of December 31, 2022 is summarized as follows:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
			(in years)	(in thousands)
Balance at December 31, 2021	6,590,400	$ 14.33		
Granted	2,730,338	6.48		
Forfeited	(1,192,074)	18.54		
Exercised	(673,999)	2.72		
Balance at December 31, 2022	7,454,665	$ 11.83	7.69	$ 54
Exercisable at December 31, 2022	3,394,398	$ 11.94	7.38	$ 53
Unvested and expected to vest at December 31, 2022	4,060,267	$ 11.75	7.94	$ 1

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the closing price of the Company's common stock on the Nasdaq Global Select Market on December 31, 2022. The intrinsic value of options exercised for the years ended December 31, 2022 and 2021 was $2.0 million and $23.8 million, respectively,

determined as of the applicable date of exercise. There was no future tax benefit related to options exercised, as the Company had accumulated net operating losses as of December 31, 2022 and December 31, 2021.

For the years ended December 31, 2022 and 2021 total stock-based compensation related to stock options was classified in the Company's statements of operations and comprehensive loss as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Research and development expenses	$ 8,464	$ 7,753
General and administrative expenses	10,414	8,406
Total stock-based compensation expense	$ 18,878	$ 16,159

As of December 31, 2022 and 2021, there was $35.4 million and $49.9 million of unrecognized stock-based compensation related to stock options, respectively, which is expected to be recognized over a weighted average period of 2.25 and 2.93 years, respectively.

2020 Employee Stock Purchase Plan

In October 2020, the Company adopted its 2020 Employee Stock Purchase Plan (ESPP), which initially reserved 688,000 shares of the Company's common stock for employee purchase under terms and provisions established by the Board of Directors. The number of shares of our common stock reserved for issuance under the ESPP automatically increases in 2021 and continuing through 2030, by the lesser of (i) 1.0% of the total number of shares of common stock outstanding on December 31st of the immediately preceding year, and (ii) 1,376,000 shares, except before the date of any increase, the Board of Directors may determine that such increase will be less than the amount set forth in clauses (i) and (ii). Effective January 1, 2022 and 2021, the number of shares authorized under the ESPP for employee purchases increased by 565,798 and 560,335 shares, respectively. The ESPP is intended to qualify as an 'employee stock purchase plan' under Section 423 of the Internal Revenue Code. Under the current offering adopted pursuant the ESPP, each offering period shall not exceed 27 months, with shorter duration purchase periods within each offering. Employees are eligible to participate if they are employed by the Company for at least 20 hours per week and more than five months of the year. The Company issued and sold 260,765 and 95,723 shares of common stock under the ESPP during the years ended December 31, 2022 and 2021. The Company has 1,553,368 shares reserved for future issuance under the ESPP as of December 31, 2022.

Under the ESPP, employees may purchase common stock through payroll deductions at a price equal to 85% of the lower of the fair market value of common stock on the first trading day of each offering period or on the purchase date. The initial offering period commenced on October 8, 2020, the date of the underwriting agreement related to the Company's IPO. A new offering (Subsequent Offering) automatically began in 2021, and a new offering will begin every six months thereafter over the term of the ESPP. Each Subsequent Offering will be approximately 24 months long and will consist of four purchase periods (with the purchase dates occurring on June 30 and December 31 each year during the term of the Subsequent Offering). Contributions under the ESPP are limited to a maximum of 15% of an employee's eligible compensation.

The fair values of the rights granted under the ESPP were calculated using the following assumptions:

	Year Ended December 31,	
	2022	2021
Expected term (in years)	0.49 - 2.00	0.50 - 2.00
Expected volatility	56.55% - 87.15%	71.67% - 94.85%
Risk-free interest rate	0.22% - 2.84%	0.05% - 0.25%
Dividend yield	—%	—%

For the years ended December 31, 2022 and 2021, total stock-based compensation related to the ESPP was $1.1 million and $1.4 million, respectively, with $0.3 million and $0.3 million, respectively, recorded in general and administrative expenses and $0.8 million and $1.1 million, respectively, recorded in research and development expenses in the statements of operations and comprehensive loss.

Restricted Stock

Restricted stock awards and units as of December 31, 2022 are summarized as follows:

	Number of Restricted Stock	Weighted-Average Grant Date Fair Value	Weighted-Average Remaining Vesting Life	Aggregate Intrinsic Value
			(in years)	(in thousands)
Unvested at December 31, 2021	787,719	$ 26.88		
Granted - restricted stock units	2,061,081	5.50		
Vested and converted to shares	(329,345)	27.51		
Forfeited	(221,710)	11.50		
Unvested at December 31, 2022	2,297,745	$ 9.18	1.58	$ 3,722
Vested and expected to vest at December 31, 2022	2,297,745	$ 9.18	1.58	$ 3,722

The Company recorded stock-based compensation expense for the RSAs of $0.1 million and $0.1 million in general and administrative expenses and zero and $5,000 in research and development expenses in the statements of operations and comprehensive loss for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, there was $0.2 million of unrecognized stock-based compensation related to RSAs, which is expected to be recognized over a weighted average period of 1.58 years.

The total grant date fair value for RSAs vested during the years ended December 31, 2022 and 2021 was $0.1 million and $0.2 million, respectively.

For the years ended December 31, 2022 and 2021, the Company issued 2,061,081 and 347,267, restricted stock units (RSUs), respectively, to executive officers and non-executive employees pursuant to the 2020 Plan. These RSUs have a three year vest period and in order to vest, the holder is required to provide service to the Company.

The Company recognized $11.0 million of stock-based compensation expense related to the RSUs for the year ended December 31, 2022, of which $5.7 million and $5.3 million are recorded in research and development and general and administrative expenses, respectively, in the current year statement of operations and comprehensive loss. The Company recognized $8.5 million of stock-based compensation expense related to the RSUs for the year ended December 31, 2021, of which $4.1 million and $4.4 million are recorded in research and development and general and administrative expenses, respectively, in the current year statement of operations and comprehensive loss.

As of December 31, 2022, there was $15.7 million of unrecognized stock-based compensation related to RSUs, which is expected to be recognized over a weighted average period of 1.32 years. As of December 31, 2022 and 2021, 295,053 and 188,470 RSUs have vested, respectively.

Stock-Based Compensation Summary

Total stock-based compensation expense was classified in the Company's statements of operations and comprehensive loss for the years ended December 31, 2022 and 2021 as follows for stock options, RSAs, RSUs, and ESPP:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Research and development expenses	$ 14,974	$ 12,961
General and administrative expenses	16,171	13,250
Total stock-based compensation expense	$ 31,145	$ 26,211

Early Exercised Options

The terms of certain stock options granted under the Prior Plan allow the holder to exercise options prior to vesting. The shares related to early exercised stock options are subject to the Company's lapsing repurchase right upon termination of employment or service on the Board of Directors at the lesser of the original purchase price or fair market value at the time of repurchase. In order to vest, the holders are required to provide continued service to the Company. The early exercise by an employee or consultant of a stock option is not considered to be a substantive exercise for accounting purposes, and therefore the payment received by the employer for the exercise price is recognized as a liability. For accounting purposes, unvested early exercised shares are not considered issued and outstanding and therefore are not reflected as issued and outstanding in the accompanying statements of convertible preferred stock and stockholders' equity (deficit) until the awards vest.

The deposits received are initially recorded in current portion of other liabilities and other noncurrent liabilities for the noncurrent portion. The liabilities are reclassified to common stock and paid-in capital as the repurchase right lapses. During the years ended December 31, 2022 and 2021, there have been no early exercised options. At December 31, 2022 and 2021, there was $0.9 million and $1.4 million recorded in current portion of other liabilities, and $0.2 million and $1.1 million recorded in other noncurrent liabilities, respectively, related to shares held by employees and nonemployees that were subject to repurchase.

10. INCOME TAXES

The Company recorded a small amount of income tax expense related to state minimum taxes for the year ended December 31, 2022 and did not record any income tax expense for the years ended December 31, 2021. The Company has incurred net operating losses for all the periods presented and has not reflected any benefit of such net operating loss carryforwards in the accompanying financial statements. The Company has recorded a full valuation allowance against all of its deferred tax assets as it is not more likely than not that such assets will be realized in the near future.

Reconciliation of the income tax expense calculated at the statutory rate to our zero expense for income taxes for the years ended December 31, 2022 and 2021 were as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Tax benefit at federal statutory rate	$ (27,973)	$ (31,726)
State taxes	(5,017)	(7,138)
Research tax credits	(15,012)	(597)
Change in valuation allowance	42,664	38,846
Stock based compensation	5,181	1,212
Other	157	(597)
Expense/(Benefit) for income taxes	$ —	$ —

The Company's deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets or liabilities for financial reporting purposes and the amounts used for income tax purposes as of December 31, 2022 and 2021. Significant components of the Company's deferred tax assets and liabilities are as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Deferred tax assets:		
Lease liabilities	$ 7,948	$ 8,750
Stock-based compensation	4,755	2,777
Accrued compensation	1,093	1,320
Net operating loss carryforwards	58,628	52,052
Tax credit carryforwards	15,963	1,296
Capitalized Research and Development Cost	18,857	—
Other	17	—
Total deferred tax assets	107,261	66,195
Valuation allowance	(100,656)	(58,713)
Net deferred tax assets	6,605	7,482
Deferred tax liabilities:		
Right-of-use assets	(6,316)	(6,973)
Fixed assets and intangibles	(289)	(509)
Total deferred tax liabilities	(6,605)	(7,482)
Net deferred tax assets	$ —	$ —

The Company records a valuation allowance for certain temporary differences for which it is more likely than not that it will not receive future tax benefits. The Company assesses its past earnings history, income tax planning and projections of future net income when determining whether it is more likely than not future tax benefits will be realized. Based on the Company's history of losses, the Company has maintained a full valuation allowance of approximately $100.7 million and $58.7 million for the years ended December 31, 2022 and 2021, respectively. The change in valuation allowance of $41.9 million is due to increases in net operating losses and other deferred tax assets due to current year activity.

The following table sets forth the Company's federal and state net operating loss and research credit carryforwards as of December 31, 2022:

	Amount	Expiration
	(in thousands)	
Net operating losses, federal	$ 229,617	Indefinite
Net operating losses, federal	$ 601	2037
Net operating losses, state	$ 162,694	2037-2042
Tax credits, federal	$ 13,775	2037-2042
Tax credits, state	6,358	2037

Current federal and state tax laws include substantial restrictions on the utilization of net operating loss and tax credit carryforwards in the event of an ownership change as defined under Section 382 of the Internal Revenue Code of 1986, as amended. Accordingly, the Company's ability to use these carryforward attributes may be limited as a result of such ownership change.

The Company applies the provisions of ASC Topic 740 to account for uncertain income tax positions. A reconciliation of the beginning and ending amount of unrecognized tax benefits were as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Balance at beginning of the year	$ 246	$ 141
Additions based on tax positions related to the current year	1,993	105
Additions to tax positions of prior years	796	—
Balance at the end of the year	$ 3,035	$ 246

It is the Company's policy to record penalties and interest related to income taxes as a component of income tax expense. The Company has not recorded any interest or penalties related to income taxes during the years ended December 31, 2022 and 2021. Unrecognized tax benefits are not expected to change during the next 12 months. The reversal of the unrecognized tax benefits would not affect the effective tax rate. The Company is subject to examination by U.S. federal and state tax authorities for all years since its inception.

Beginning January 1, 2022, the Tax Cuts and Jobs Act enacted in 2017, eliminates the option to deduct research and development expenditures in the current year and requires taxpayers to capitalize and amortize pursuant to IRC Section 174. As a result, we recognized an increase in our deferred tax assets due to the capitalization of $73.8 million. Given such amount was offset by our valuation allowance there were no material impacts to the financial statements outside of the deferred tax table.

During August 2022, the CHIPS and Science Act ("CHIPS Act") and Inflation Reduction Act ("IRA") were enacted, neither of which are expected to have a material impact to our financial statements.

The American Rescue Plan Act ("ARA") was signed into law on March 11, 2021. We do not expect the ARA to have a material impact on our financial statements but given potential changes to IRC Section 162(m) will take place in 2027, we will continue to monitor and assess.

The following table shows the change in the deferred tax valuation as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Beginning Balance, January 1	$ 58,713	$ 20,797
Change charged to expense/(income)	$ 41,943	$ 37,916
Ending Balance, December 31	$ 100,656	$ 58,713

11. NET LOSS PER SHARE

The following table summarizes the computation of basic and diluted net loss per share of the Company for the years ended December 31, 2022 and 2021:

	Year Ended December 31,	
	2022	2021
	(in thousands, except share and per share amounts)	
Net loss	$ (133,204)	$ (151,078)
Weighted-average common stock outstanding, basic and diluted	56,201,398	54,753,599
Net loss per share, basic and diluted	$ (2.37)	$ (2.76)

The Company's potentially dilutive securities, which include options to purchase shares of the Company's common stock and restricted stock awards subject to future vesting, 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 is the same. The Company excluded the following potential shares of common stock, presented based on amounts outstanding at each stated period end, from the computation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2022	2021
Stock options to purchase common stock	7,150,339	5,802,435
Early exercised stock options subject to future vesting	304,326	787,965
Restricted stock awards subject to future vesting	54,297	88,589
Restricted stock units subject to future vesting	2,243,448	699,129
Total	9,752,410	7,378,118

In addition to the potentially dilutive securities noted above, the Company also has the option under its agreement with Tempus to issue common shares upon the achievement of specified milestones (see Note 12). Because the necessary conditions for issuance of the shares had not been met as of December 31, 2022, the Company excluded these shares from the table above and from the calculation of diluted net loss per share for the year ended December 31, 2022.

12. COMMITMENTS AND CONTINGENCIES

R&D Services Agreement

In October 2021, the Company entered into an agreement for research and development services (Tempus Agreement) with Tempus Labs, Inc. (Tempus), pursuant to which Tempus agreed to provide the Company with research and development services for a period of three years. The three primary services are analytical services, data licensing, and organoid services. The Company intends to utilize the services contemplated under the Tempus Agreement to advance the development of KB-0742 and lanraplenib.

In consideration for the access to the services throughout the term of the Tempus Agreement, the Company has agreed to pay an annual minimum commitment of $1.5 million in year one, $2.0 million in year two, and $2.5 million in year three. Payments are made in quarterly installments. As of December 31, 2022, the Company has paid $1.1 million under the Tempus Agreement. As of December 31, 2021, the Company had not made any payments under the Tempus Agreement.

In addition, the Company is required to make milestone payments upon successful achievement of certain regulatory milestones for KB-0742, lanraplenib, and other discovery pipeline compounds up to a combined maximum of $22.4 million. For each milestone payment that becomes due, the Company has the right to pay up

to 50% of such milestone payment amount in shares of its common stock as long as certain regulatory requirements are met.

Asset Purchase Agreement

In July 2020, the Company entered into the Gilead Asset Purchase Agreement with Gilead Sciences, Inc. (Gilead), pursuant to which the Company acquired certain assets from and assumed certain liabilities of Gilead related to lanraplenib or entospletinib, and patents and other intellectual property covering or related to the development, manufacture and commercialization of lanraplenib or entospletinib.

In consideration for such assets, on the date of the Gilead Asset Purchase Agreement, the Company made a $3.0 million upfront cash payment and issued a $3.0 million principal amount convertible promissory note, which was settled in exchange for 188,567 shares of common stock in connection with the closing of the Company's IPO at a settlement price of $16.15 per share. The Company also made a $0.7 million payment to reimburse Gilead for certain liabilities assumed by the Company pursuant to the Gilead Asset Purchase Agreement. In addition, the Company is required to make milestone payments upon successful achievement of certain regulatory and sales milestones for lanraplenib, entospletinib, and other SYK inhibitor compounds covered by the patent rights acquired pursuant to the Gilead Asset Purchase Agreement and developed by the Company as a back-up to entospletinib or lanraplenib (Other Compounds). Upon initiation of the Company’s registrational Phase 3 clinical trial of entospletinib in combination with induction chemotherapy in acute myeloid leukemia patients with NPM1 mutations in December 2021, the Company paid a milestone payment to Gilead of $29.0 million. Upon successful completion of certain other regulatory milestones in the United States, European Union and United Kingdom for lanraplenib, entospletinib and any Other Compounds, across up to two distinct indications, the Company will be required to pay to Gilead an aggregate total of $51.3 million. Upon achieving certain thresholds for the aggregate annual net sales of lanraplenib, entospletinib and any Other Compounds combined, the Company would owe to Gilead potential milestone payments totaling $115.0 million.

Gilead is also eligible to receive (i) tiered marginal royalties ranging from high-single digits to the mid-teens on annual worldwide net sales of lanraplenib, (ii) tiered marginal royalties ranging from the very low-teens to high-teens on annual worldwide net sales of entospletinib, and (iii) tiered marginal royalties ranging from low single digits to mid-single digits on annual worldwide net sales of any Other Compounds. The royalties in the foregoing clauses are subject to reduction, on a country-by-country basis, for products not covered by certain claims within the assigned patents, for generic entry and, in the case of lanraplenib and entospletinib, for any royalties paid for future licenses of third party intellectual property required to develop or commercialize lanraplenib or entospletinib. The Company’s royalty obligation with respect to a given product in a given country begins upon the first commercial sale of such product in such country and ends on the latest of (i) expiration of the last claim of a defined set of the assigned patent rights covering such product in such country; (ii) loss of exclusive data or marketing rights to such product in such country; or (iii) 10 years from the first commercial sale of such product in such country.

Under the Gilead Asset Purchase Agreement, the Company is required to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize either lanraplenib or entospletinib.

Purchase Commitments

In the normal course of business, the Company enters into contracts with CROs for preclinical and clinical studies and other vendors for other services and products. These agreements generally provide for termination or cancellation, other than for costs already incurred and certain wind down costs that may be associated with the termination of a contract or clinical trial program.

Contingencies

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for general indemnifications. The Company’s exposure under these agreements is unknown, because it involves claims that may be made against the Company in the future, but have not yet been made. The Company accrues a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated.

Indemnification

In accordance with the Company's amended and restated certificate of incorporation and amended and restated bylaws, the Company has indemnification obligations to its officers and directors for certain events or occurrences, subject to certain limits, while they are serving in such capacity. There have been no claims to date, and the Company has a directors and officers liability insurance policy that may enable it to recover a portion of any amounts paid for future claims.

13. LEASES

In March 2020, the Company entered into an 11-year lease agreement to move its research and development operations from 21 Erie Street, Cambridge, Massachusetts, to a 40,514 square-feet facility at 301 Binney Street, Cambridge, Massachusetts (Cambridge facility). The lease commenced on February 28, 2020 with an initial annual base rent of $4.1 million and payments. The initial rent payment was paid as of September 30, 2020, with rent payments escalating 3.0% annually after the initial 12 payments. As discussed in Note 2, the Company executed a letter of credit for $2.0 million in connection with the lease. The lease includes $3.7 million in certain tenant improvement allowances, which the Company included in its calculation of the right-of-use asset in the lease at commencement. As of December 31, 2022, $3.7 million in improvement costs incurred by the Company were reimbursed by the lessor are now included within the total lease liability. In connection with the lease, the Company recognized an operating lease right-of-use asset of $21.9 million and an aggregate lease liability of $28.0 million on the December 31, 2022 balance sheet. The remaining lease term is 8.2 years, and the estimated incremental borrowing rate is 8.50%.

In February 2021, the Company entered into a new lease agreement for its office space in San Mateo, California to move from its current suites, totaling 8,075 square-feet, to a larger suite totaling 17,340 square-feet, and a lease commencement date in the second quarter of 2021. The Company accounted for this change in lease term of the original suites as a modification of the originally amended lease. As a result of the modification, the operating right-of-use asset and lease liability were remeasured as of the modification date.

The new 17,340 square foot suite will be treated as a separate lease for accounting purposes. The initial annual base rent for the new space will be $1.2 million, and such amount will increase by 3% annually on each anniversary of the new premises commencement date. In connection with the larger space leased, the Company has also made an additional one-time cash security deposit in the amount of $59,000. The new lease commenced in April 2021 and the new lease agreement extends the termination date from April 30, 2025 to June 1, 2026. In connection with the lease, the Company recognized an operating lease right-of-use asset of $2.8 million and $3.3 million an aggregate lease liability of $3.7 million and $4.1 million as of December 31, 2022 and December 31, 2021. The remaining lease term is 3.5 years, and the estimated incremental borrowing rate is 11.18%.

The following table summarizes the presentation of the Company's operating leases in its balance sheets as of December 31, 2022 and 2021:

Balance Sheet Caption	December 31, 2022	December 31, 2021
	(in thousands)	
Assets:		
Operating lease assets	$ 24,707	$ 26,904
Liabilities:		
Current portion of operating lease liabilities	$ 2,347	$ 2,109
Noncurrent operating lease liabilities	28,744	31,653
Total operating lease liabilities	$ 31,091	$ 33,762

The following table summarizes the effect of operating lease costs in the Company's statements of operations and comprehensive loss for the years ended December 31, 2022 and 2021:

Statement of Operations and Comprehensive Loss Caption	Year Ended December 31, 2022	Year Ended December 31, 2021
	(in thousands)	
Research and development	$ 3,068	$ 3,308
General and administrative	2,043	2,015
Total operating lease cost	$ 5,111	$ 5,323

The Company made cash payments of $5.7 million and $4.4 million under the lease agreements during the years ended December 31, 2022 and 2021, respectively.

The undiscounted future non-cancellable lease payments under the Company's operating leases as of December 31, 2022 for the next five years and thereafter is expected to be as follows:

Period Ending December 31,	Amount
	(in thousands)
2023	$ 5,130
2024	5,749
2025	5,921
2026	5,405
2027 and thereafter	21,298
Total undiscounted lease payments	43,503
Less: Present value adjustment	(12,412)
Present value of operating lease liabilities	$ 31,091

14. RELATED PARTIES

On December 1, 2017, the Company entered into a services agreement with Two River Consulting, LLC (Two River) to provide various clinical development, operational, managerial, accounting and financial, and administrative services to the Company. On December 31, 2021, the Company amended the agreement to limit the scope to accounting and managerial consulting services. Arie Belldegrun, M.D., FACS, the Chair of the Board of Directors, is the Chair of Two River. Mr. Joshua Kazam and Mr. David Tanen, each a director of the Company, are each partners of Two River. Mr. Christopher Wilfong, a strategic advisor to the Company, is an Operating Partner of Two River and Mr. Sean Algeo, serving as a financial consultant to the Company, is the Chief Financial

Officer of Two River. During the years ended December 31, 2022 and 2021, the Company incurred expenses of $0.1 million and $0.3 million, respectively, for these services.

In 2019, the Company entered into a consulting agreement with Bellco Capital, LLC (Bellco) to provide various executive services to the Company. Arie Belldegrun, M.D., FACS, the Chair of the Board of Directors, is the Chairman of Bellco. Rebecka Belldegrun, M.D., who served as a director of the Company through January 25, 2021, is the President and Chief Executive Officer of Bellco. During the years ended December 31, 2022 and 2021, the Company incurred expenses of $25,200 and $129,000, respectively, for these services.

15. SUBSEQUENT EVENTS

On January 6, 2023 (the "Effective Date"), the Company entered into a Collaboration and License Agreement (the "Agreement") with Genentech, Inc., a member of the Roche Group ("Genentech"). Pursuant to the Agreement, the parties have agreed to initially collaborate on two discovery research programs in oncology, each focused on a designated transcription factor, to discover small-molecule GLP-Tox-ready candidates that modulate transcription factor targets selected by Genentech. Each discovery research program will primarily consist of (i) a mapping phase with the goal of identifying the transcription regulatory network for such designated transcription factor, and (ii) a screening phase having the goal of identifying and characterizing multiple screening hits suitable for nomination as a preclinical development program.

The Company will lead discovery and research activities under the discovery research programs and will use its proprietary drug discovery platform, including the small molecule microarray (SMM), for hit finding. Following the completion of initial discovery and research activities, Genentech will have the exclusive right to pursue further preclinical and clinical development and commercialization of compounds identified in the discovery research programs and designated by Genentech (each, a "Hit Program").

Pursuant to the Agreement, the Company received an upfront payment of $20.0 million from Genentech. In addition, the Company is eligible for additional milestone payments upon achievement of certain preclinical, clinical and regulatory (including first-sale) milestones, totaling up to $177 million for the first development candidate per Hit Program, and is eligible to receive net sales milestones of up to $100 million for the first licensed product per Hit Program. The Company is also eligible to receive tiered royalties in the low- to high-single digits on any products that are commercialized by Genentech as a result of the collaboration.

The term of the discovery research programs under the Agreement will be up to 24 months, which may be extended by six months at the Company's option subject to satisfying certain conditions.

Unless earlier terminated, the Agreement will remain in effect for each product licensed under the Agreement until expiration of the royalty term for such licensed product. Genentech has the right to terminate this Agreement in its entirety, or with respect to a particular discovery research program or Hit Program, in its sole discretion, at any time by providing 60 days' advance written notice to the Company. Each party may also terminate the Agreement upon the other party's material breach that remains uncured for 90 days (or 45 days in the event of nonpayment), or in the event of certain insolvency events involving the other party.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURES

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to provide reasonable assurance that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and our Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based, in part, upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Our management, with the participation and supervision of our Chief Executive Officer and our Chief Financial Officer, has evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on that evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that, as of the end of the period covered by this Annual Report on Form 10-K, our disclosure controls and procedures were effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Rule 13a-15(f) of the Exchange Act. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of 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 or procedures may deteriorate.

Management has assessed the effectiveness of our internal control over financial reporting based on the framework set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013 framework). Based on our evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2022.

Changes in Internal Control over Financial Reporting

An evaluation was performed under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of any change in our internal control over financial reporting that occurred during our last fiscal year and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. During the quarter ended December 31, 2022, there were no changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item and not set forth below will be set forth in the section headed "—Election of Directors" and "Information Regarding the Board of Directors and Corporate Governance" in our definitive Proxy Statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC (our Proxy Statement) on or before May 1, 2023 and is incorporated in this Annual Report by reference.

Our Executive Officers

Norbert Bischofberger, Ph.D., 67, has served as our President and Chief Executive Officer since August 2018 and as a member of our Board of Directors since April 2018. From August 1990 to August 2018, Dr. Bischofberger held various positions at Gilead Sciences, Inc. ("Gilead"), a public biopharmaceutical company, and most recently served as Executive Vice President, Research and Development and Chief Scientific Officer of Gilead. During his 28-year tenure at Gilead, he presided over the development and approval of more than 25 medicines for a range of serious conditions. Prior to joining Gilead, Dr. Bischofberger served as a Senior Scientist in the DNA Synthesis group at Genentech, Inc., a biotechnology company, from 1986 to 1990. Dr. Bischofberger serves on the Supervisory Board of Bayer AG and board of directors of Morphic Therapeutic, a public biopharmaceutical company. Dr. Bischofberger received a Ph.D. in Organic Chemistry from the Eidgenossische Technische Hochschule in Zurich, Switzerland and an M.S. in Chemistry from the University of Innsbruck. We believe Dr. Bischofberger is qualified to serve on our Board due to his expertise and experience in the life sciences industry, including his work as a senior executive, and his educational background.

Yasir Al-Wakeel, BM BCh, 41, has served as our Chief Financial Officer and Head of Corporate Development since August 2020. Prior to joining our company, Dr. Al-Wakeel served as the Chief Financial Officer of Neon Therapeutics, Inc. from July 2017 to May 2020. Previously, Dr. Al-Wakeel served as the Chief Financial Officer and Head of Corporate Development at Merrimack Pharmaceuticals, Inc. from August 2015 until July 2017. Prior to that, Dr. Al-Wakeel served in various capacities at Credit Suisse, an investment banking firm, from 2008 to 2015. While at Credit Suisse, Dr. Al-Wakeel was Director of Healthcare Investment Banking, focused on biotechnology, and, prior to that role, he was an Equity Research Analyst covering the biotechnology and specialty pharmaceuticals sectors. Before joining Credit Suisse, Dr. Al-Wakeel was a practicing physician, holding both clinical and academic medical posts. Dr. Al-Wakeel has served on the Maxcyte, Inc. Board of Directors since June 2021. Dr. Al-Wakeel received his BM BCh (Doctor of Medicine and Surgery) from Oxford University and his M.A. in theology from Cambridge University.

Jorge DiMartino, M.D., Ph.D., 59, has served as our Chief Medical Officer and Executive Vice President, Clinical Development since December 2019. Prior to joining us, Dr. DiMartino served as Vice President, Translational Development Oncology at Celgene Corp., a global biopharmaceutical company acquired by Bristol Myers Squibb, from July 2014 to December 2019, where he led early-stage oncology clinical programs and directed the Translational Research Laboratories. During that time, he also served as the Head of Celgene's Epigenetics Thematic Center of Excellence, a fully integrated unit driving drug discovery through clinical proof of concept efforts around epigenetic targets. From April 2011 to July 2014, Dr. DiMartino served as Executive Director, Translational Development Oncology at Celgene. Prior to joining Celgene from December 2005 to April 2011, Dr. DiMartino was Group Medical Director at Genentech in the Oncology Exploratory Clinical Development group. Dr. DiMartino received his Ph.D. in Immunology from Cornell University Graduate School of Medical Sciences, and his M.D. from University of California San Diego. He completed a residency in Pediatrics and a fellowship in Pediatric Hematology/Oncology, both at Stanford University School of Medicine.

Christopher Dinsmore, Ph.D., 57, has served as our Chief Scientific Officer since June 2020. Prior to joining us, Dr. Dinsmore served as an Entrepreneur-in-Residence at Third Rock Ventures from June 2019 to June 2020, where he focused on discovering and launching new innovative therapeutic companies. Previously, he served as Vice President and Head of Chemistry at Forma Therapeutics, a biopharmaceutical company, from December 2013 to June 2019, where he applied an array of discovery chemistry platforms and approaches to target classes in epigenetics and protein homeostasis. Earlier, Dr. Dinsmore served at Merck Research Laboratories for 19 years, where he held various positions in medicinal chemistry. His project experiences in discovery and development have been in therapeutic categories that include cancer, hematology, sickle cell disease, neurodegeneration, asthma, and rheumatoid arthritis, leading to the advancement of numerous development

compounds into clinical trials. Dr. Dinsmore also serves on the scientific advisory board for Stablix, Inc. and on the advisory board for WARF Therapeutics. Dr. Dinsmore received his B.A. in Chemistry and Art from Bowdoin College and his Ph.D. in Synthetic Organic Chemistry from the University of Minnesota in Minneapolis, and then conducted postdoctoral research in chemical synthesis at Harvard University.

Barbara Kosacz, 65, has served as our Chief Operating Officer and General Counsel since July 2020. Prior to joining us, Ms. Kosacz was a Partner at Cooley LLP from January 1997 to December 2000, and again from February 2002 until July 2020, where she led the international Life Sciences Practice. Ms. Kosacz has more than 25 years of experience in counseling clients in the life sciences arena, ranging from early-stage startups to larger public companies, venture funds, investment banks, and non-profit institutions. She has served as a member of the BIO Emerging Companies' Section Governing board, is a member of the board of Trustees of the Keck Graduate Institute, an advisory board member of Locust Walk Partners, and has been a speaker at multiple life sciences-related conferences, as well as guest lecturer at the University of California, Berkeley, Stanford University, the University of Pennsylvania and Columbia University about biotechnology law, biotech business models, corporate partnering negotiations and deal structures, and bioethics. Recognized by Best Lawyers in America since 2008 and most recently as Biotechnology Lawyer of the Year in 2018, Ms. Kosacz was listed as a "leading lawyer" for healthcare and life sciences in the 2018 Legal 500, as a "Band 1" attorney in the 2018 edition of Chambers USA: America's Leading Lawyers for Business and recognized as a "highly recommended transactions" lawyer by IAM Patent 1000 for her "nearly three decades advising diverse companies in the industry at a deeply strategic and commercial level and overseeing their most complex and profitable deals." Ms. Kosacz is currently senior counsel at Cooley LLP and a member of the boards of directors of XOMA Corp., a biotechnology royalty aggregator company, Athira Pharma, a clinical-stage company focused on developing therapies for neurodegenerative diseases, and Phoenix Biotech Acquisition Corp., a blank check company formed for the purpose of acquiring or merging with one or more businesses. Ms. Kosacz received her B.A. from Stanford University and her J.D. from the University of California, Berkeley School of Law.

Our Board of Directors

Set forth is the biographical information for each member of our Board of Directors other than Dr. Bischofberger, whose biographical information is set forth above.

Arie S. Belldegrun, M.D., FACS, 73, has served as Chair of our Board of Directors since November 2017. Dr. Belldegrun is a co-founder of Allogene Therapeutics, a public biopharmaceutical company, and has served as Executive Chair of its board of directors since November 2017. From March 2014 to October 2017, Dr. Belldegrun served as the President and Chief Executive Officer of Kite Pharma, Inc. and as a member of its board of directors from June 2009 to October 2017. Dr. Belldegrun currently serves as Chair of Bellco Capital LLC, a position he has held since 2004; Chair of UroGen Pharma Ltd., a position he has held since December 2012; as Chair and Partner of Two River Group, a position he has held since June 2009; and as a director of Ginkgo Bioworks, a position he has held since September 2021.Since November 2017, Dr. Belldegrun also serves as Senior Managing Director of Vida Ventures, LLC. Dr. Belldegrun previously served as a director of Teva Pharmaceutical Industries Ltd. from March 2013 to January 2017, Chair of Arno Therapeutics, Inc. from March 2008 to January 2017, a director of Capricor Therapeutics, Inc. from September 2009 to November 2013, and a director of SonaCare Medical, LLC from October 2009 to October 2014. In 1996, he founded Agensys, Inc., a biotechnology company, where he served as its founding Chair from 1996 to 2001, and continued to serve on the board until 2007 when it was acquired by Astellas Pharma Inc. Dr. Belldegrun was also the Founding Vice-Chair of the board of directors and Chair of the scientific advisory board of Cougar Biotechnology, Inc., a biotechnology company, from 2003 to 2009, when it was acquired by Johnson & Johnson. He is certified by the American Board of Urology and the American Association of Genitourinary Surgeons. Dr. Belldegrun is Research Professor, holds the Roy and Carol Doumani Chair in Urologic Oncology, and Director of the Institute of Urologic Oncology at the David Geffen School of Medicine at the University of California, Los Angeles. Prior to joining UCLA in October of 1988, he was a research fellow at NCI/NIH in surgical oncology and immunotherapy from July 1985 to August 1988 under Dr. Steven Rosenberg. Dr. Belldegrun received his M.D. from the Hebrew University Hadassah Medical School in Jerusalem before completing his post graduate studies in Immunology at the Weizmann Institute of Science and his residency in Urologic Surgery at Harvard Medical School. We believe Dr. Belldegrun is qualified to serve on our Board due to his experience as a senior executive and as a director of several life sciences companies, and because of his knowledge of our industry.

Roshawn Blunt, 48, has served as a member of our Board since November 2021. She has more than 25 years of experience in the biopharmaceutical and medical device industries and founded and has served as managing director of 1798, LLC., a national health care consulting firm that specializes in healthcare compliance, reimbursement, health policy and patient access issues in 2010. She served as a on the board of directors of Adamis Pharmaceuticals from 2019 to 2021. From 2007 to 2010 Ms. Blunt was a managing director of the Aequitas Group, a healthcare advisory firm, where she led the health economics and reimbursement consultancy. Prior to that, Ms. Blunt worked at Johnson & Johnson, a public pharmaceutical company, from 2005 to 2007, and from 2000 to 2005 she was part of the global government affairs organization at Amgen, Inc., a public biopharmaceutical company. Prior to founding 1798 LLC, Ms. Blunt was vice president of strategy, planning, and communication at Long Beach Memorial Center and Miller Children's Hospital. Ms. Blunt graduated from Princeton University, where she earned her A.B. from the Princeton School of Public and International Affairs. She earned her MBA from Kellogg School of Management at Northwestern University. We believe Ms. Blunt is qualified to serve on our Board due to her experience running a national health care consulting firm, the depth of her knowledge around reimbursement and patient access and her prior experience working in the biopharmaceutical industry.

Marianne De Backer, Ph.D., 55, joined our Board of Directors in January 2021. In January 2023, Vir Biotechnology announced her appointment as Chief Executive Officer as of April 3, 2023. She most recently served as Executive Vice President, Head of Strategy, Global Business Development & Licensing and Open Innovation, and a member of the Executive Committee of the Pharmaceuticals Division of Bayer AG ("Bayer"). She joined Bayer in 2019. On From 1991 through 2019, she was at Johnson & Johnson, where she most recently held global Business and Corporate Development roles, including the position of Vice President of M&A Operations and Divestitures globally for the Pharmaceuticals Group and head of Infectious Diseases & Vaccines Business Development. Prior to that she led a commercial business unit in Europe as well as drug discovery research in both Europe and the United States. During her tenure with Johnson & Johnson, Dr. De Backer had direct accountability for more than 200 strategic alliances. Since December 2019, she has served on the board of Arrowhead Pharmaceuticals. Dr. De Backer received a MSc in Molecular Biology from the University of Brussels, Belgium, and a master's degree in Engineering and Biochemistry and a Ph.D. in Biotechnology from the University of Ghent, Belgium, and an MBA from Rotterdam School of Management, Erasmus University, The Netherlands. We believe Dr. De Backer is qualified to serve on our Board due to her expertise and experience in the life sciences industry and her educational background.

Joshua Kazam, 46, has served as a member of our Board since our founding in June 2017. Mr. Kazam currently serves on the board of directors of Allogene Therapeutics, Inc., a public biopharmaceutical company, and served as its President from November 2017 until June 2018. He was a founder of Kite Pharma, Inc. and served as a member of its board of directors from its inception in June 2009 until October 2017. In June 2009, Mr. Kazam co-founded Two River Consulting, LLC, a life science consulting and investment firm. He has served on the board of Flying Eagle Acquisition Corp. since February 2020. Mr. Kazam previously served as a director of Diamond Eagle Acquisition Corp. from January 2019 until April 2020, Capricor Therapeutics, Inc. from May 2005 until May 2019 and Platinum Eagle Acquisition Corp. from January 2018 to March 2019. Platinum Eagle Acquisition Corp., Diamond Eagle Acquisition Corp. and Flying Eagle Acquisition Corp. are blank check companies formed for the purpose of effecting a business combination with one or more businesses. Mr. Kazam has served as the President of Desert Flower Foundation since June 2016. Mr. Kazam received his B.A. in Entrepreneurial Management from the Wharton School of the University of Pennsylvania and is a member of the Wharton School's Undergraduate Executive Board. We believe Mr. Kazam is qualified to serve on our Board due to his experience serving on the boards of directors of clinical-stage life sciences companies, and because of his investment experience in the life sciences industry.

Elena H. Ridloff, CFA, 43, has served as a member of our Board of Directors since September 2020. Since September 2021, Ms. Ridloff has been serving as the Chief Financial Officer of Sionna Therapeutics, Inc., a private biotechnology company. Previously, she held multiple roles at Acadia Pharmaceuticals, Inc. (Acadia), a public biopharmaceutical company, including Senior Vice President, Investor Relations from April 2018 to March 2019; interim Chief Financial Officer from October 2018 to March 2019; and Executive Vice President and Chief Financial Officer of Acadia from March 2019 to September 2021. Previously, Ms. Ridloff held various roles at Alexion Pharmaceuticals, Inc. (Alexion), a public biopharmaceutical company, including Executive Director, Investor Relations from April 2014 to January 2016, and Vice President, Investor Relations from January 2016 to March 2018. Ms. Ridloff also served as a member of Alexion's Operating Committee. While at Alexion, Ms. Ridloff

was responsible for building and leading an investor relations function. Prior to joining Alexion, Ms. Ridloff served as the Chief Executive Officer and Managing Member of BIOVISIO, an independent consulting firm providing strategic, financial and investor relations counsel to the life sciences industry, from January 2012 to April 2014. Ms. Ridloff also served as Managing Director at Maverick Capital, a hedge fund responsible for investments in the biotechnology, pharmaceutical, medical device and life science sectors, from July 2005 to January 2012. Ms. Ridloff received her B.A. in History and Sociology of Science from the University of Pennsylvania, and is a Chartered Financial Analyst. We believe Ms. Ridloff is qualified to serve on our Board due to her financial and accounting expertise and her experience in the finance and life sciences industries.

Otello Stampacchia, Ph.D., 54, has served as a member of our Board since May 2018. Dr. Stampacchia has served as founder and Managing Director of Omega Funds since January 2004. Previously, he was in charge of life sciences direct investments at AlpInvest Partners B.V. from November 2001 to December 2003, and he was the portfolio manager of the Lombard Odier Immunology Fund from January 2001 to November 2001. Prior to that, Dr. Stampacchia was a member of the healthcare corporate finance and mergers and acquisitions team at Goldman Sachs Group, Inc. from 1997 to 2000. Before joining Goldman Sachs, Dr. Stampacchia helped co-found the healthcare investment activities at Index Securities, now Index Ventures, Inc. Dr. Stampacchia is currently a member of the boards of directors of Ikena Oncology, Inc., a public biotechnology company, and Omega Alpha SPAC, a public special purpose acquisition corporation. Dr. Stampacchia also serves on the board of directors of seven private companies and previously served on the boards of the following public companies: ESSA Pharma, Inc., Gossamer Bio, Inc., Morphic Therapeutic, Inc. and Replimune Group, Inc. Dr. Stampacchia received his M.S. in Genetics from Universa' degli Studi di Pavia, his Ph.D. in Molecular Biology from the University of Geneva and a European Ph.D. in Biotechnology (EDBT) from the European Association for Higher Education in Biotechnology. We believe Dr. Stampacchia is qualified to serve on our Board due to his investment experience in the life sciences industry and his prior experience as a director of life sciences companies.

David M. Tanen, 51, has served as a member of our Board since our inception in June 2017. Mr. Tanen is a co-founder Two River, LLC, a life-science consulting and investment firm, and has served as a partner since September 2004. He has served as an advisor to Vida Ventures, a life science investment firm, since November 2018. Prior to founding Two River, Mr. Tanen served as General Counsel for a life science-focused venture capital firm. Mr. Tanen is also a co-founder of Kite Pharma, Inc., where he served as Corporate Secretary and General Counsel from June 2009 until its acquisition by Gilead Sciences in 2017. He is a co-founder of Allogene Therapeutics, and has served as its Corporate Secretary since its inception in December 2017. Mr. Tanen also serves as an officer and director of Neogene Therapeutics, Inc. and 76Bio, Inc., two privately held life science companies focused on developing treatments for cancer. Mr. Tanen received his B.A. from The George Washington University and his J.D. from Fordham University School of Law, where he has served on the Dean’s Planning Council since 2009.We believe Mr. Tanen is qualified to serve on our Board due to his experience serving as an officer and a member of the boards of directors of clinical-stage life sciences companies, and because of his investment experience in the life sciences industry.

Taiyin Yang, 69, joined our board of directors in March 2021 and is the former Executive Vice President of Pharmaceutical Development and Manufacturing at Gilead Sciences, Inc. until July 2022. She directed operations of chemical and biologics process development, device and formulation development, manufacturing, packaging, analytical operations, laboratory information systems, data science, quality assurance, CMC regulatory affairs, program management, supply chain management and site operations for all the company’s small molecules, biologics and antibody-drug conjugates of investigational compounds and marketed products. Under her leadership, Gilead developed the world’s first HIV single table regimen and advanced more than 25 compounds from early-stage development to market, reaching millions of people around the world. Prior to joining Gilead in 1993, Dr. Yang worked at Syntex Corporation from 1980 where she contributed to the development and Commercialization of more than 10 medicines. Dr. Yang is a member of the Expert Scientific Advisory Committee of Medicines for Malaria Venture, and the scientific advisory board of Sionna Therapeutics. Dr. Yang also serves on the Board of Directors of Kodiak Sciences and Brii Biosciences. Dr. Yang received her bachelor’s degree in chemistry from National Taiwan University and her Ph.D. in organic chemistry from the University of Southern California. Dr. Yang was elected a Fellow of the American Institute for Medical and Biological Engineering (2021) and a member of the National Academy of Engineering (2022).We believe Dr. Yang is qualified to serve on our Board due to her expertise and experience in the life sciences industry and her educational background.

We have adopted a code of ethics for directors, officers (including our principal executive officer, principal financial officer and principal accounting officer) and employees, known as the Code of Business Conduct and

Ethics. The Code of Business Conduct and Ethics is available on our website at www.kronosbio.com under the Corporate Governance section of our Investors and Media page. We will promptly disclose on our website (i) the nature of any amendment to the policy that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of the policy that is granted to one of these specified individuals, the name of such person who is granted the waiver and the date of the waiver. Shareholders may request a free copy of the Code of Business Conduct and Ethics from our Assistant General Counsel, c/o Kronos Bio, 1300 So. El Camino Real, Suite 400, San Mateo, California 94402.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item will be set forth in the section headed “Executive Compensation” in our Proxy Statement and is incorporated in this Annual Report by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNER AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item will be set forth in the section headed “Security Ownership of Certain Beneficial Owners and Management” in our Proxy Statement and is incorporated in this Annual Report by reference.

Information regarding our equity compensation plans will be set forth in the sections headed “Executive Compensation” and “Director Compensation” in our Proxy Statement and is incorporated in this Annual Report by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item will be set forth in the sections headed “Transactions With Related Persons” and “Information Regarding the Board of Directors and Corporate Governance” in our Proxy Statement and is incorporated in this Annual Report by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item will be set forth in the section headed “— Ratification of Selection of Independent Registered Public Accounting Firm” in our Proxy Statement and is incorporated in this Annual Report by reference.

PART IV.

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

1. Financial Statements.

The response to this portion of Item 15 is set forth under Part II, Item 8 above.

2. Financial Statement Schedules.

All schedules have been omitted because they are not required or because the required information is given in the financial statements or notes thereto set forth under Part II, Item 8 above.

3. Exhibits.

The exhibits listed below are filed or incorporated by reference as part of this Annual Report.

Exhibit Number	Description Of Document
2.1‡*	Asset Purchase Agreement, by and between the registrant and Gilead Sciences, Inc., dated July 14, 2020 (incorporated by reference to Exhibit 2.1 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on September 18, 2020).
3.1	Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the registrant's Current Report on Form 8-K, filed with the SEC on October 14, 2020).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the registrant's Current Report on Form 8-K, filed with the SEC on October 14, 2020).
4.1	Reference is made to Exhibits 3.1 and 3.2.
4.2	Form of Common Stock Certificate of the registrant (incorporated by reference to Exhibit 4.1 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on October 5, 2020).
4.3	Amended and Restated Investors' Rights Agreement, by and among the registrant and certain of its stockholders, dated July 1, 2019, as amended on August 20, 2020 (incorporated by reference to Exhibit 4.2 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on September 18, 2020).
4.4	Description of Registrant's Common Stock (incorporated by reference to Exhibit 4.4 to the registrant's Annual Report on Form 10-K (File No. 001-39592), filed with the SEC on February 24, 2022).
10.1+	Form of Indemnity Agreement, by and between the registrant and its directors and officers (incorporated by reference to Exhibit 10.1 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on October 5, 2020).
10.2+	Kronos Bio, Inc. 2017 Equity Incentive Plan, as amended, and Forms of Option Agreement, Notice of Exercise, Notice of Early Exercise, Restricted Stock Grant Notice and Restricted Stock Award Agreement thereunder (incorporated by reference to Exhibit 10.2 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on September 18, 2020).
10.3+	Kronos Bio, Inc. 2020 Equity Incentive Plan, and Forms of Option Grant Notice, Option Agreement, Notice of Exercise, Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement thereunder (incorporated by reference to Exhibit 10.3 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on October 5, 2020).
10.4+	Kronos Bio, Inc. 2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.4 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on October 5, 2020).
10.5+	Kronos Bio, Inc. Severance and Change in Control Plan with amended form of Participation Agreement thereunder (incorporated by reference to Exhibit 10.3 to the registrant's Quarterly Report on Form 10-Q/A (File No. 001-39592), filed with the SEC on September 9, 2022).

10.6+	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.1 to the registrant's Quarterly report on form 10-Q/A (File No 001-39592), filed with the SEC on September 9, 2022).
10.7+‡	Letter Agreement, by and between the registrant and Norbert Bischofberger, Ph.D., dated April 30, 2018, as amended (incorporated by reference to Exhibit 10.5 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on October 5, 2020).
10.8+‡	Letter Agreement, by and between the registrant and Jorge DiMartino, M.D., Ph.D., dated September 4, 2019 (incorporated by reference to Exhibit 10.6 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on September 18, 2020).
10.9+‡	Letter of Agreement, by and between the registrant and Barbara Kosacz, dated July 15, 2020 (incorporated by reference to Exhibit 10.1 to the registrant's Quarterly Report on Form 10-Q, filed with the SEC on November 18, 2020).
10.10+‡	Letter Agreement, by and between the registrant and Yasir Al-Wakeel, dated August 16, 2020 (incorporated by reference to Exhibit 10.8 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on September 18, 2020).
10.11‡	Letter of Agreement, by and between the registrant and Christopher Dinsmore, Ph.D., dated May 29, 2020 (incorporated by reference to Exhibit 10.13 to the registrant's Annual Report on Form 10-K (File No. 001-39592), filed with the SEC on March 23, 2021).
10.12	Office Lease, by and between the registrant and MPVCA SAN MATEO LLC, a California limited liability company (as successor in interest to DWF IV 1300 S El Camino LLC), dated July 19, 2018, as amended (incorporated by reference to Exhibit 10.9 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on September 18, 2020).
10.13	Second Amendment to Office Lease, dated February 8, 2021, by and between the registrant and MPVCA San Mateo LLC (incorporated by reference to Exhibit 10.1 to the registrant's Quarterly Report on Form 10-Q (File No. 001-39592), filed with the SEC on May 11, 2021).
10.14	Lease, by and between the registrant and BMR-Rogers Street LLC, dated February 28, 2020 (incorporated by reference to Exhibit 10.10 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on September 18, 2020).
10.15‡	License Agreement, by and between the registrant and President and Fellows of Harvard College, dated January 16, 2018 (incorporated by reference to Exhibit 10.11 to the registrant's Registration Statement on Form S-1 (File No. 333-248925), as amended, filed with the SEC on September 18, 2020).
10.16*‡	Collaboration and License Agreement between the registrant and Genentech, Inc. and F. Hoffmann-La Roche Ltd., dated January 6, 2023.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney. Reference is made to the signature page hereto.
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act.
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act.
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rule 13a-14(b) of the Exchange Act, and 18 U.S.C. Section 1350.
101.INS	Inline XBRL Instance Document (this document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document).
101.SCH	Inline XBRL Taxonomy Extension Schema Document.
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

‡ Schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The registrant undertakes to furnish supplemental copies of any of the omitted schedules upon request by the SEC.

\+ Indicates management contract or compensatory plan.

* Certain portions of this exhibit are omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

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

KRONOS BIO, INC.

Date: March 15, 2023

By: /s/ Norbert Bischofberger
Norbert Bischofberger, Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Norbert Bischofberger, Ph.D., and Barbara Kosacz, and each of them, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them full power and authority to do and perform each and every fact and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or share might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact 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 Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the Registrant in the capacities and of the dates indicated.

Signature	Title	Date
/s/ Norbert Bischofberger Norbert Bischofberger, Ph.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 15, 2023
/s/ Yasir Al-Wakeel Yasir Al-Wakeel, BM BCh	Chief Financial Officer and Head of Corporate Development *(Principal Financial and Accounting Officer)*	March 15, 2023
/s/ Arie Belldegrun Arie Belldegrun, M.D. FACS	Chair of the Board of Directors	March 15, 2023
/s/ Marianne De Backer Marianne De Backer, Ph.D.	Director	March 15, 2023
/s/ Roshawn Blunt Roshawn Blunt	Director	March 15, 2023
/s/ Joshua Kazam Joshua Kazam	Director	March 15, 2023
/s/ Elena Ridloff Elena Ridloff, CFA	Director	March 15, 2023
/s/ Otello Stampacchia Otello Stampacchia, Ph.D.	Director	March 15, 2023
/s/ David Tanen David Tanen	Director	March 15, 2023
/s/ Taiyin Yang Taiyin Yang, Ph.D.	Director	March 15, 2023