ikena™ ONCOLOGY

Ikena Oncology Annual Report 2023

ikenaoncology.com

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, 2023

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 001-40287

IKENA ONCOLOGY, INC.

(Exact name of Registrant as specified in its charter)

Delaware	**81-1697316**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
645 Summer Street, Suite 101 Boston, MA	**02210**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (857) 273-8343

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on June 30, 2023 was $178.5 million.

The number of shares of Registrant's Common Stock outstanding as of March 5, 2024 was 48,258,111.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's proxy statement for the 2024 annual meeting of stockholders to be filed pursuant to Regulation 14A within 120 days after the Registrant's fiscal year ended December 31, 2023, are incorporated by reference in Part III of this Form 10-K.

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Table of Contents

Summary of the Material and Other Risks Associated with Our Business

Our business is subject to numerous material and other risks and uncertainties that you should be aware of in evaluating our business. These risks include, but are not limited to, the following:

- We are a targeted oncology company with a limited operating history.
- We have incurred significant net losses since our inception and anticipate that we will continue to incur losses for the foreseeable future.
- We have no products approved for commercial sale and have not generated any revenue from product sales.
- We will require additional capital to finance our operations, which may not be available on acceptable terms, or at all. If we are unable to raise capital when needed or on terms acceptable to us, we would be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts.
- Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.
- We have never successfully completed any clinical trials for our target oncology programs, and we may be unable to do so for any of our current product candidates.
- Our programs are focused on the development of oncology therapeutics for patients with genetically defined or biomarker-driven cancers, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs is novel and may never lead to approved or marketable products.
- Clinical product development involves a lengthy and expensive process, with an uncertain outcome.
- Pandemics, epidemics, or any outbreak of an infectious disease, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- If the market opportunities for our programs and product candidates are smaller than we estimate or if any regulatory approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.
- We rely on third parties to conduct our clinical trials, as well as investigator-sponsored clinical trials of our product candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.
- We have entered into collaborations and may enter into additional collaborations in the future, and we might not realize the anticipated benefits of such collaborations.
- If we are unable to obtain and maintain patent and other intellectual property protection for our technology and product candidates or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired.
- 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.
- Our future success depends on our ability to retain key executives and experienced scientists and to attract, retain and motivate qualified personnel.
- The dual class structure of our common stock may limit your ability to influence corporate matters and may limit your visibility with respect to certain transactions.

The material and other risks summarized above should be read together with the text of the full risk factors below and with the other information set forth in this Annual Report, including our consolidated financial statements and the related notes, as well as with other documents that we file with the United States Securities and Exchange Commission ("SEC"). If any such material and other risks and uncertainties actually occur, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks summarized above, or described in full below, are not the only risks that we face. Additional risks and uncertainties not currently known to us, or that we currently deem to be immaterial may also materially adversely affect our business, prospects, financial condition and results of operations.

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains express or implied forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements involve risks, uncertainties, and other factors that may cause actual results, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the initiation, timing, progress, results, and cost of our research and development programs and our current and future nonclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs;
- our ability and the potential to successfully manufacture our drug substances and product candidates for preclinical use, for clinical trials, and on a larger scale, for commercial use, if approved;
- the ability and willingness of our third-party strategic collaborators to continue research and development activities relating to our development candidates and product candidates;
- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our ability to commercialize our products, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, and strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- estimates of our future expenses, revenue, capital requirements, and our needs for additional financing;
- the potential benefits of strategic collaboration agreements, our ability to enter into strategic collaborations or arrangements, and our ability to attract collaborators with development, regulatory and commercialization expertise;
- future agreements with third parties in connection with the commercialization of product candidates and any other approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our financial performance;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States and relevant foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our ability to produce our products or product candidates with advantages in turnaround times or manufacturing cost;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the impact of laws and regulations;
- our use of proceeds from our initial public offering and underwritten registered offering;

- developments relating to our competitors and our industry;
- the effect of pandemics, epidemics or any outbreak of an infectious disease, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and clinical trials and any future studies or trials;
- the impact of global economic and political developments on our business, including rising inflation and capital market disruptions, economic sanctions, bank failures, regional conflicts around the world, and economic slowdowns or recessions that may result from such developments which could harm our research and development efforts as well as the value of our common stock and our ability to access capital markets; and
- other risks and uncertainties, including those under the caption “Risk Factors.”

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the “Risk Factors” section, which could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or into which we may enter.

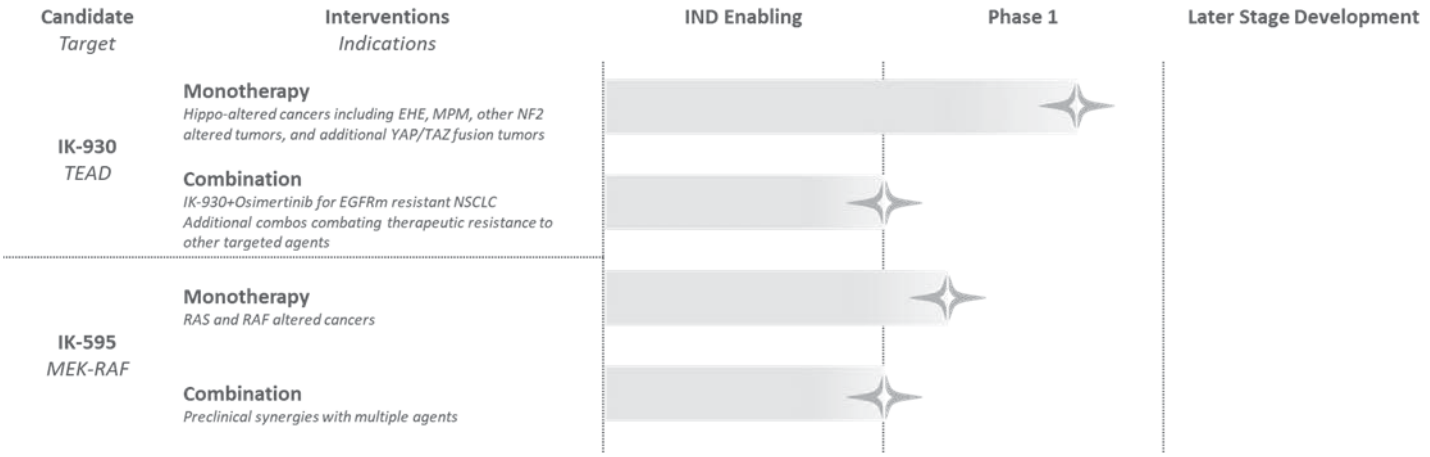
You should read this Annual Report on Form 10-K and the documents that we reference herein and have filed or incorporated by reference as exhibits hereto completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PART I

ITEM 1. BUSINESS

Overview

We are a clinical stage, targeted oncology company, focused on developing differentiated therapies for patients in need that target nodes of cancer growth, spread, and therapeutic resistance in the Hippo and RAS onco-signaling network. Our approach in each of our programs is to target both cancer-driving targets and mechanisms of resistance to other therapies. Our most advanced program, IK-930, is a selective inhibitor of the transcriptional enhanced associate domain 1 ("TEAD1"). The TEAD transcription factors (TEAD 1-4) execute the ultimate step in the Hippo signaling pathway, a known oncogenic pathway that also drives resistance to multiple targeted and chemo therapies. Our program in the RAS pathway, IK-595, is a molecular glue designed to trap MEK and RAF in an inactive complex, more completely inhibiting RAS signals than existing inhibitors. Since we commenced operations in 2016, we have advanced multiple product candidates into clinical development. Across the entirety of our pipeline, shown below, we aim to utilize our depth of institutional knowledge and breadth of tools to efficiently develop the right drug using the right modality for the right patient.



Our most advanced targeted oncology product candidate, IK-930, is an oral, TEAD1-selective, small molecule inhibitor of the Hippo signaling pathway. The Hippo pathway is genetically altered in approximately 10% of human cancers and is widely accepted as a prevalent driver of cancer pathogenesis and a mediator of poor outcomes for patients. In our ongoing first-in-human Phase 1 clinical trial, we are focusing on indications that provide the potential to achieve rapid proof-of-concept, such as NF2 deficient mesothelioma and solid tumors with YAP1 or TAZ gene fusions, including epithelioid hemangioendothelioma ("EHE"). Approximately 40% of mesothelioma patients are genetically deficient for the tumor suppressor NF2 and 100% of EHE patients have oncogenic YAP1 or TAZ gene fusions. In October 2021, our Investigational New Drug Application ("IND") for IK-930 was cleared by the United States Food and Drug Administration (the "FDA") and we subsequently initiated a first-in-human Phase 1 clinical trial to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity of IK-930 as a monotherapy in patients with advanced solid tumors with or without gene alterations in the Hippo pathway. IK-930 received orphan drug designation from the FDA for the treatment of mesothelioma and EHE in March 2022 and December 2023, respectively. IK-930 was granted fast track designation from the FDA for the treatment of unresectable NF2-deficient mesothelioma in June 2022. In November 2023, we shared initial dose escalation safety data and initial anti-tumor activity data from EHE patients enrolled in the dose escalation monotherapy portion of the trial. In addition to the monotherapy approach, we plan to assess IK-930 in combination with other targeted therapies across several indications with multiple targeted therapies. Based on the role that the Hippo pathway plays in resistance to other targeted therapies, we believe that IK-930 may expand the patient populations that could benefit from therapies like epidermal growth factor ("EGFR") inhibitors, KRAS inhibitors, and MEK inhibitors, among others. We have an established clinical collaboration with AstraZeneca for the evaluation of osimertinib in combination with IK-930 for patients with EGFR-mutant lung cancers as a cohort in the clinical program. Additional data from the monotherapy IK-930 clinical program is expected in the second half of 2024.

In addition to our work in the Hippo pathway, we are developing targeted therapies within the RAS pathway, one of the most highly dysregulated pathways in cancer. The RAS pathway is implicated in at least half a million new cancer diagnoses each year in the United States alone. Our goal is to achieve deep and sustained responses through targeting the pathway on multiple levels and leveraging the biology of known resistance mechanisms in our therapeutic design. We nominated IK-595 as our development candidate in our RAS pathway program in November 2022. IK-595 is designed to robustly inhibit MEK-RAF by gluing MEK and the RAFs (A, B, and C) in an inactive complex, thus more completely inhibiting RAS signals than existing inhibitors. IK-595's potential

ability to complex CRAF, in particular, has been shown in preclinical models to prevent a well-recognized signaling bypass mechanism that cancer cells employ to drive therapeutic resistance to other MEK and RAF drugs in this class. In addition, trapping CRAF in an inactive complex has been shown in preclinical models to prevent the kinase independent anti-apoptotic function in RAS and RAF mutant cancers, a mechanism that cannot be addressed with first generation MEK inhibitors or pan-RAF inhibitors. We are developing IK-595 as an oral therapy, with a half-life designed to enable a pharmacokinetic profile that we believe can be potentially superior to other pathway inhibitors, with the goal of optimizing the therapeutic window for patients. We treated the first patient in the dose escalation Phase 1 study of IK-595 in December 2023.

Our Strategy

We are dedicated to bringing next generation targeted oncology therapies to cancer patients. In order to achieve this goal, we are focused on executing on our clinical programs to evaluate the impact of our product candidates for patients. We will continue to rely on our deep understanding of complex biologic pathways and robust biomarker-driven translational research informing clinical development. The key components of our current strategy are as follows:

- **Rapidly advance IK-930 through monotherapy clinical development.** We are developing IK-930, an oral, TEAD1-selective small molecule inhibitor of the Hippo pathway, to evaluate its potential to bring therapeutic benefit to patients. We plan to continue advancing the ongoing monotherapy Phase 1 clinical trial of IK-930 in tumors harboring genetic mutations in the Hippo signaling pathway. Our clinical development strategy is designed to achieve clinical proof-of-concept in genetically defined subsets of solid tumors where significant unmet medical need exists and to leverage the potential for fast-to-market opportunities in orphan indications.
- **Evaluate the ability of IK-930 to combat therapeutic resistance in combination with other targeted agents.** In addition to our monotherapy strategy, we plan to evaluate the combination of IK-930 with other targeted therapies to address therapeutic resistance, including EGFR inhibitors and inhibitors in the RAS pathway. The first of these planned combinations is supported by our clinical supply collaboration with AstraZeneca evaluating IK-930 impact on osimertinib resistance in EGFR mutated cancers.
- **Continue to advance IK-595 in the clinic.** Our most recent development candidate, IK-595, is a molecular glue designed to trap MEK and RAF in an inactive complex, thereby more completely inhibiting RAS signals than existing inhibitors. We plan to advance IK-595 rapidly through clinical development to evaluate its potential best-in-class capabilities and differentiation for patients. IK-595 is being developed as an oral therapy, with a half-life designed to enable pharmacokinetic profile that we believe has the potential to lead to an optimal therapeutic window for patients relative to other agents in this class.
- **Continue to define unique patient populations and markets that can benefit from our product candidates through robust translational biomarker research.** Each of our programs has potential impacts in both rare, biomarker defined markets, and larger patient populations. Our clinical development strategy allows us to evaluate proof of concept in biomarker defined populations that may represent smaller market opportunities yet have the potential to expand into larger, broader markets, including in combinations combating therapeutic resistance to other targeted oncology agents.
- **Maximize our company's value through exploring potential partnering and business development opportunities.** We hold worldwide development and commercial rights to our targeted oncology programs, and we intend to continue to develop our capabilities in late-stage clinical development and commercialization to maximize the potential value of these programs. In addition to our targeted oncology pipeline advancing in clinical development, we have a portfolio of immune-modulating assets that range from IND ready to Phase 2 ready with favorable safety profiles to date. All of these programs are included in our partnering portfolio and are available for strategic business development, including sale or out-licensing.

Our Programs

IK-930, a TEAD Inhibitor

Our lead program, IK-930, is an internally discovered, oral, TEAD1-selective, small molecule inhibitor of the Hippo pathway. TEAD functions as the ultimate step in the Hippo signal transduction pathway by driving expression of genes involved in cell proliferation and survival. TEAD consists of a family of four paralogs and IK-930 is designed to selectively inhibit one of these isoforms, TEAD1, that we believe has the potential to achieve efficacy and balance potential kidney toxicity associated with TEAD inhibition. The Hippo pathway is widely accepted as a key and prevalent driver of cancer pathogenesis and is genetically altered in approximately 10% of all human cancers. Such genetic alterations are often associated with poor clinical outcomes. The involvement of the Hippo pathway in mechanisms of resistance to other targeted therapies has been well established; the pathway is implicated in resistance to EGFR inhibitors, MEK inhibitors, and others.

IK-930 is a novel inhibitor of TEAD that exploits a binding pocket on TEAD to enable the inhibitory effect upon the Hippo pathway. TEAD activity is dependent on binding of the fatty acid palmitate to a central lipid pocket. IK-930 blocks palmitate from binding TEAD, thereby disrupting TEAD-dependent gene transcription. The mechanism of action of IK-930 is differentiated from historically unsuccessful attempts using either small molecules or cyclic peptides. Using structural biology-guided chemistry, we were able to generate novel TEAD inhibitor compounds across several chemical series directed to this binding pocket in TEAD and profile them using various *in vitro* and *in vivo* assays assessing potency, selectivity, tolerability, and antitumor activity. In addition, considering the potential on-target kidney toxicities associated with the Hippo pathway, it was important to design IK-930 to be paralog-selective in order to drive optimal antitumor activity, while significantly reducing the dose-limiting effects of kidney toxicity. By selecting IK-930 based upon these characteristics, we believe IK-930 has the potential to bring differentiated therapeutic benefit to patients with tumors harboring genetic mutations and alterations in the Hippo signaling pathway. Moreover, activation of the Hippo pathway confers resistance to certain targeted therapies, such as EGFR inhibitors and MEK inhibitors, which supports the potential for IK-930 to be combined with these therapies to overcome therapeutic resistance.

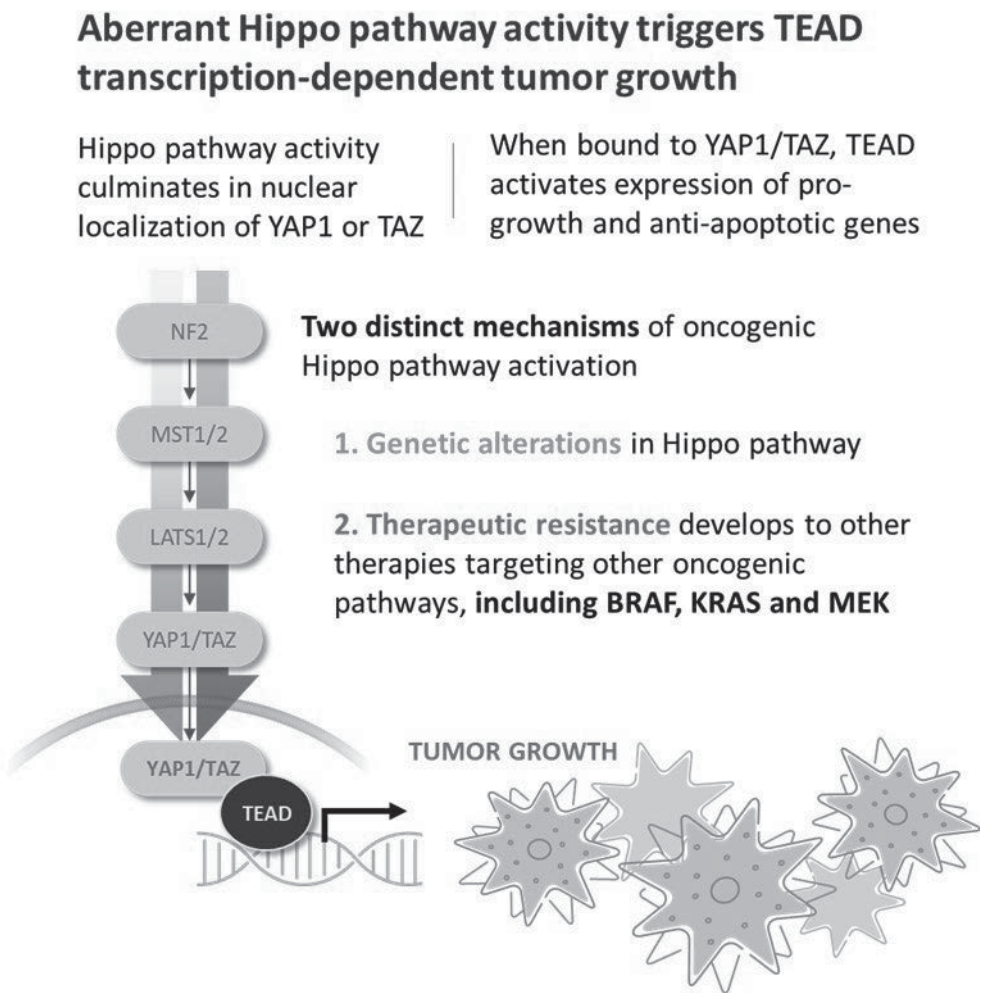
We are currently evaluating IK-930 in a first-in-human Phase 1 clinical trial as a monotherapy. The study aims to evaluate the safety and preliminary antitumor activity of IK-930 in Hippo-mutated cancers in orphan indications such as NF2-deficient malignant pleural mesothelioma and EHE, a rare type of vascular sarcoma. The FDA granted IK-930 both orphan drug and fast track designation for the treatment of mesothelioma in the first half of 2022 and orphan drug designation for the treatment of EHE in the second half of 2023. In addition, we plan to evaluate IK-930 in combination with multiple other targeted agents, with the aim of potentially addressing therapeutic resistance in more prevalent tumor indications characterized by genetic alterations. The first planned combination is IK-930 with osimertinib for patients with EGFR mutant non-small cell lung cancer (“NSCLC”). The Phase 1 clinical trial is currently advancing in monotherapy dose escalation as expected, with multiple dose cohorts cleared.

Role of the Hippo Pathway and TEAD in Oncology

The Hippo pathway is a highly conserved developmental signaling pathway that modulates the regulation of multiple biological processes, including cell proliferation, survival, differentiation, organ size, and tissue homeostasis. Dysregulation of the Hippo pathway is associated with the induction of hyperproliferation, cellular invasion, metastasis, cancer cell maintenance, and therapeutic resistance, and has been linked to other pro-tumorigenic activities, such as activation of regulatory T cells.

The Hippo signaling cascade begins with NF2, a gene that encodes the scaffold protein merlin, which links multiple extracellular cues to an intracellular signaling cascade. Merlin activates the kinases MST1 and MST2 (“MST1/2”) which subsequently phosphorylate and activate the kinases LATS1 and LATS2 (“LATS1/2”). LATS1/2 phosphorylates two key transcriptional coactivators of TEAD: YAP1 and TAZ. When phosphorylated, YAP1 and TAZ are sequestered to the cytoplasm where they are targeted for proteasome-mediated degradation. When the upstream portion of the signaling cascade is inactivated through normal regulation or through inactivating mutations, YAP1 and TAZ are not phosphorylated and can shuttle into the nucleus. Once inside the nucleus, YAP1 and TAZ bind TEAD to enable the transcription of TEAD target genes.

Nuclear YAP1 was observed to lead to increased TEAD activity as measured by higher levels of TEAD gene transcription. Data suggest that the addition of a TEAD inhibitor to an EGFR inhibitor regimen in patients with EGFR resistant tumors may be able to overcome therapeutic resistance to EGFR inhibition. In addition to resistance to EGFR targeting, there are emerging data indicating the Hippo pathway is involved in resistance to other targeted therapies as well, including MEK inhibition inhibitors in BRAF and RAS mutated cancers.



The monotherapy and combination approaches represent two distinct therapeutic strategies. Genetic alterations in the Hippo pathway that drive primary cancers provide a potential opportunity for IK-930 as a monotherapy. Separately, the role of the pathway in therapeutic resistance could open a wide range of patient populations that could benefit from IK-930, including EGFR mutant and KRAS mutant cancers.

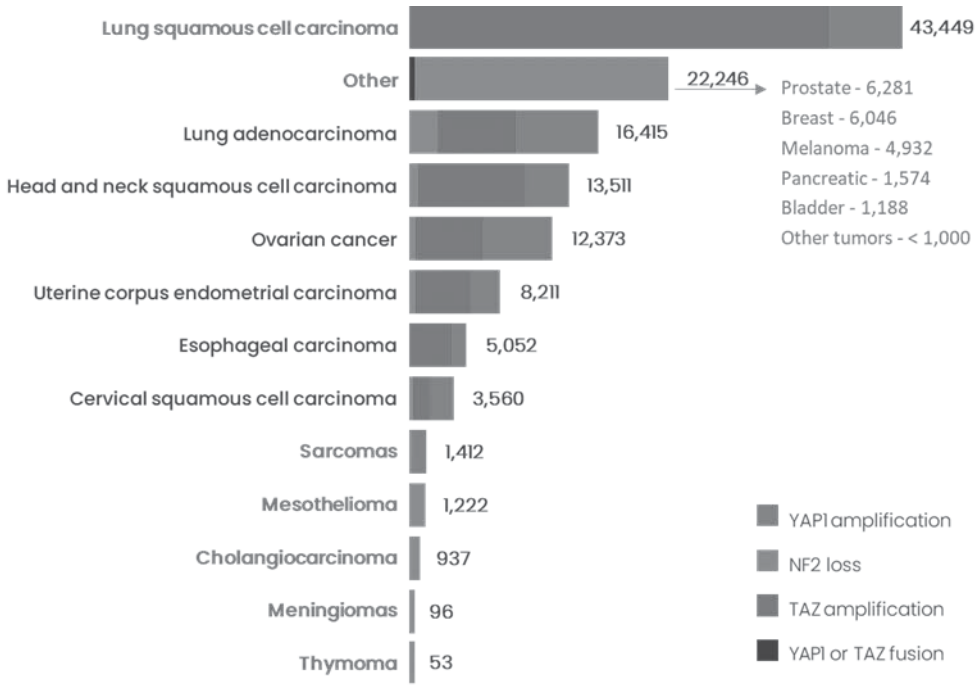
Epidemiology of Hippo Pathway Driven Cancers; Monotherapy Strategy

Published literature suggests that approximately 10% of all solid tumors present with dysregulated Hippo pathway and subsequent activation of TEAD, representing the populations that could potentially benefit from a monotherapy approach with IK-930. Dysregulation can occur at multiple nodes within the pathway. For example, the tumor suppressor gene NF2 can undergo inactivating mutations or YAP1 and TAZ can undergo gene fusion or amplification. These genetic alterations lead to tumor formation in mouse models and therefore are believed to be genetic drivers of cancer.

Based on available epidemiological data, we estimate that approximately 125,000 newly diagnosed cancer patients annually within the United States have tumors which harbor genetic alterations in the Hippo pathway, based on the incidence of cancers with YAP1 and TAZ gene amplification or fusion, as well as NF2 loss.

The figure below illustrates the incidence of individuals with newly diagnosed cancers that harbor Hippo pathway genetic alterations in the United States on an annual basis.

Incidence of Hippo Pathway Genetic Alterations



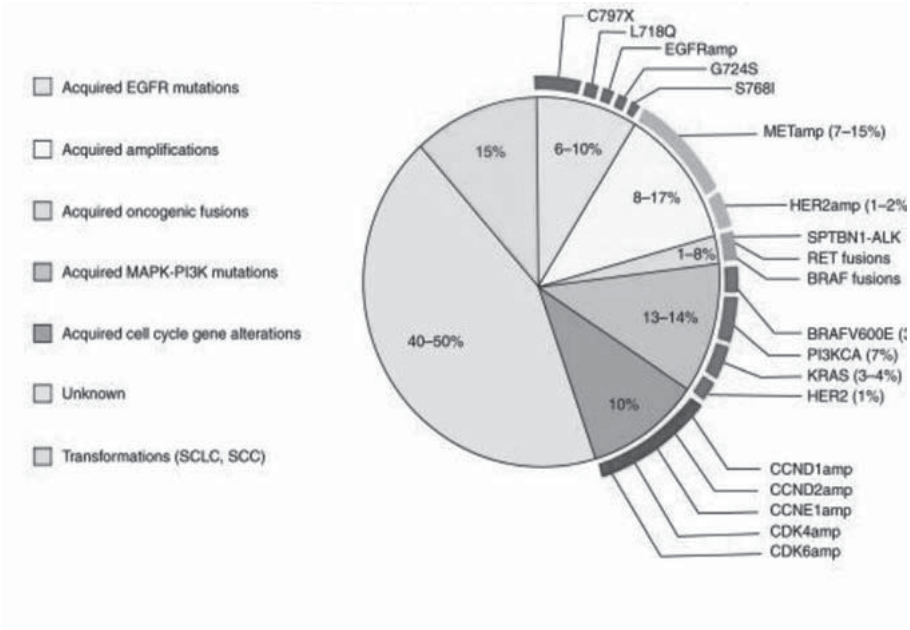
Genetic alterations in the Hippo pathway are present in diverse cancer types, but there are certain cancers, including more prevalent indications, such as lung squamous cell carcinoma, and rarer indications, such as mesothelioma and sarcoma, which are reported to have a particularly high incidence of genetic alterations in the Hippo pathway, where alterations are considered to drive tumor formation and growth, and are associated with a poor patient prognosis:

- Loss of function mutations in NF2 are found in approximately 40% of cases of malignant mesothelioma and are associated with poor prognosis, including a significantly shorter progression free survival and overall survival. IK-930 was granted orphan drug and fast track designation by the FDA for the treatment of mesothelioma.
- All cases of EHE, a form of soft tissue sarcomas, have YAP1 and TAZ gene fusions, where 90% of patients have TAZ-CAMTA1 fusions and the remaining 10% have YAP1-TFE3 fusions, which are directly linked to the etiology of these cancers. The disease is defined by the presence of one of these alterations. IK-930 was granted orphan drug designation by the FDA for the treatment of EHE.
- Meningiomas also exhibit a high frequency of NF2 deficiency accounting for approximately one-third of primary central nervous system (“CNS”) tumors.
- Other solid tumors have exhibited Hippo pathways alteration, including in squamous lung cancer, where YAP1 and TAZ amplifications are found in approximately 6% and 29%, respectively, based on internal analysis of The Cancer Genome Atlas (“TCGA”) using the Genome Data Commons and cBioportal tools.

Hippo-implicated Mechanisms of Therapeutic Resistance; Combination Strategy

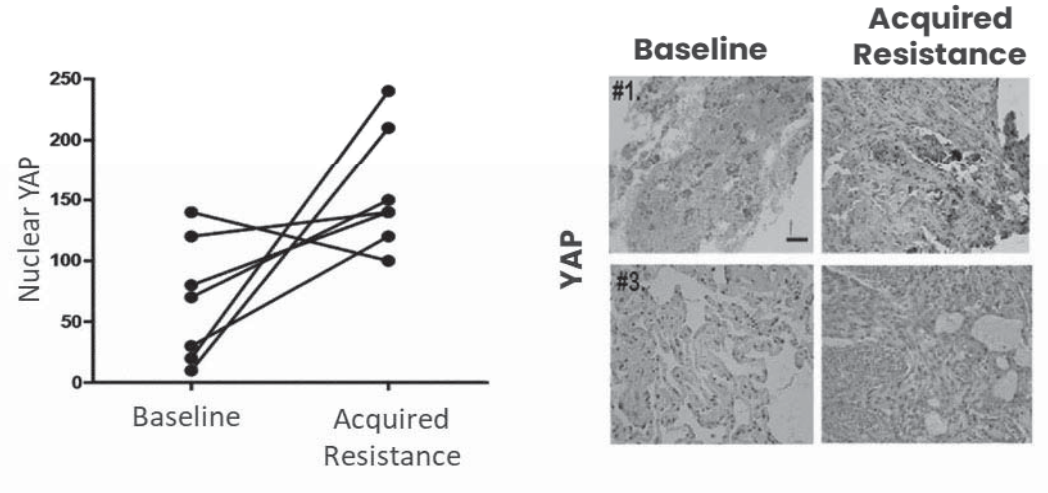
Beyond the role of certain Hippo pathway alterations in driving cancer, several pathway components are known to drive resistance to targeted therapies such as EGFR inhibitors, including osimertinib. Approximately 30% of patients with NSCLC will have EGFR mutations. Osimertinib (Tagrisso™) is an EGFR inhibitor approved for the first-line treatment of patients with NSCLC whose tumors have certain EGFR mutations. Despite the robust clinical activity exerted by osimertinib, patients often develop resistance to this treatment, which poses a significant challenge due to the scarcity of post-osimertinib pharmacological options available to date. A 2019 publication (Leonetti, et al., Br J Cancer, 2019) on EGFR resistance, reported a lack of actionable mutations for 40-50% of first-line osimertinib resistance patients. This is a population in which the Hippo pathway may be conferring resistance.

Resistance Mechanisms to First Line Osimertinib



Leonetti, et al., Br J Cancer, 2019

We believe this population represents a substantial opportunity for TEAD inhibitors. Published data (Lee, et al., BBRC, 2016) from patient tumor samples shows that, upon acquired resistance to EGFR inhibitors, there is an increase in nuclear YAP1 in tumors as compared to tumors collected prior to EGFR inhibitor treatment. In EGFR mutant lung cancer cell lines *in vitro*, the increase in nuclear YAP1 was observed to lead to increased TEAD activity as measured by higher levels of TEAD gene transcription.



Lee, et al., BBRC, 2016

In EGFR mutant lung cancer cell lines *in vitro*, osimertinib leads to increased nuclear YAP1 and activation of TEAD dependent gene expression which can be inhibited by IK-930. In addition, IK-930 combined with osimertinib significantly increased the incidence of apoptosis *in vitro* and anti-tumor activity in mouse xenograft studies in EGFR mutant lung cancer cells. These data suggest that the addition of a TEAD inhibitor to an EGFR inhibitor regimen in patients with EGFR resistant tumors may be able to overcome therapeutic resistance to EGFR inhibition. In addition to EGFR resistance, additional information is emerging from newly marketed and later stage clinical development targeted oncology programs, including suggested resistance to MEK inhibitors. We have generated preclinical data supporting our belief of the clinical opportunity to treat patients with multiple types of genetically-defined tumors and tumors with resistance to other targeted therapies with IK-930.

Disease Overview

The epidemiology findings in mesothelioma, EHE, soft tissue sarcomas, as well as other solid tumors, including meningioma, point to the critical role of the Hippo pathway in tumor formation. In addition to the strong biological rationale for pursuing development of IK-930 in these cancers, we believe that these are areas of high unmet medical need in which IK-930 has the potential to provide meaningful clinical benefit to patients.

Monotherapy Opportunities

- Malignant mesothelioma is a rare cancer in the tissue lining the lungs and is a very aggressive cancer with a poor prognosis. After initial diagnosis, patients are reported to have a median life expectancy of 15 months. Approximately 3,000 people in the United States are diagnosed with mesothelioma each year. On average, about 2,500 mesothelioma-related deaths occur in the United States each year. There are few effective treatment options for advanced unresectable malignant mesothelioma and to date only two treatments have been approved by the FDA for the treatment of this condition. The combination of cisplatin and pemetrexed was the first systemic treatment approved by the FDA in 2004, followed only by the May 2020 FDA approval of nivolumab in combination with ipilimumab. Standard of care in 2023 spanned chemotherapy, immune therapy and a combination of the two, but overall survival for the combination remains approximately 18 months, although three year survival has improved to 25%. IK-930 has FDA orphan drug and fast track designation for the treatment of mesothelioma. Approximately 40% of malignant mesothelioma patients are associated with NF2 deficiency and this genetic alteration has been described to contribute to asbestos-induced mesotheliomagenesis in animal models, showing that NF2 drives the malignant behavior of this subset of mesothelioma cases.
- In addition to mesothelioma, meningioma also has high frequency of NF2 deficiency. Meningioma is the most common CNS tumor, accounting for approximately one-third of primary CNS tumors. Surgery and/or radiation therapy (“RT”) constitute the initial therapeutic approach for meningiomas. Furthermore, surgery and/or RT can control disease in some patients with recurrence. Unfortunately, despite the appropriate use of surgery and RT for initial disease management and management of recurrent disease, there is a subset of patients in whom disease cannot be controlled with local approaches. Experience with systemic treatments is limited and although several agents have been studied, none have an established role in prolonging progression-free survival or overall survival. The outcome of this subset of patients with persistent or recurrent meningiomas continues to be poor, underscoring the substantial need for new therapies.
- Soft tissue sarcomas (“STS”) represent a rare and heterogeneous group of solid tumors derived from mesenchymal progenitor cells and characterized by a variety of genetic alterations. Recent molecular and genetic studies in large cohorts of STS cases have demonstrated an essential role of YAP1/TAZ in sarcomagenesis, implying that a YAP1/TAZ directed therapeutic approach could represent a rational strategy in a selected subgroup of these tumors. STS account for 1% of all adult malignancies. While the clinical outcome of these diseases has improved in the last decade with the use of anthracycline-based chemotherapy and the introduction of novel therapies targeting different cell pathways and the use of immune checkpoints, the prognosis for a significant subgroup of patients with STS is still poor and there is an unmet medical need for these patients. For these reasons, the identification of novel molecular targets is important in these rare malignancies. Recent studies in a large cohort of STS tumors showed that myxoid liposarcomas, synovial sarcomas and angiosarcomas, in addition to EHE, expressed the highest levels of YAP1/TAZ gene expression, potentially driving tumorigenesis in these subsets of STS.
- EHE is a rare STS that grows from the cells that make up the lining of blood vessels with an incidence of one case per million people in which 100% of the cases harbor genetic alterations of Hippo pathway with approximately 90% of the cases harboring a genetic fusion between TAZ and CAMTA1(“TAZ-CAMTA1”) and the other 10% of cases harboring a genetic fusion between YAP1 and TFE3 (“YAP1-TFE3”). EHE is a slow-growing, invasive tumor with no approved treatment options and is challenging to measure due to diffuse infiltration of multiple organs. This cancer can occur anywhere in the body with the most common sites being the liver, lungs, and bone. People with EHE suffer symptoms that relentlessly affect their quality of life and are consistent with the site of the EHE growth, including liver failure, respiratory issues and gastrointestinal symptoms, which are frequently accompanied by severe pain across the body. EHE usually occurs in people between 30 and 50 years of age but can occur in young children and older people. Surgery and radiotherapy have been used as treatment for localized disease and several interventions have been used with palliative intent in the recurrent or metastatic cases, including steroids, interferon, and others, but there is currently no specific targeted therapy approved for the treatment of advanced EHE. IK-930 has FDA orphan drug designation for the treatment of EHE.

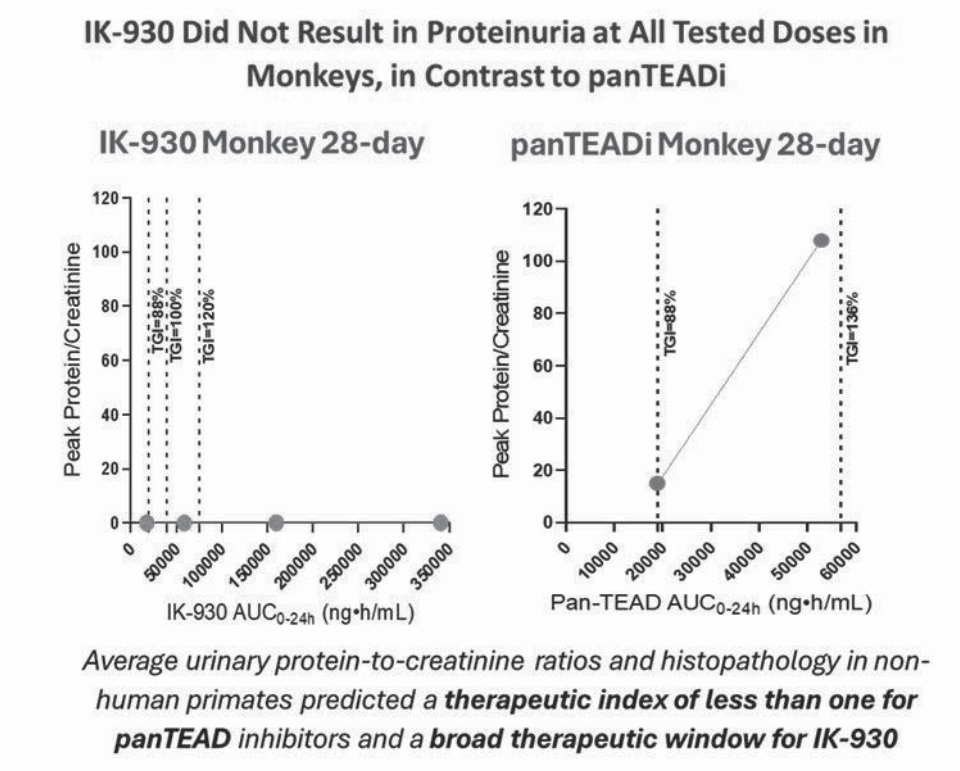
Combination Therapy Opportunities

- Despite the successful expansion of personalized oncology using targeted therapies to selectively treat patients with specific mutations in key oncogenic drivers, intrinsic and acquired resistance to targeted agents is a growing clinical problem. Activation of YAP1/TAZ has been associated with the development of resistance to various targeted agents, including in EGFR mutant NSCLC, and in KRAS mutant tumors such as pancreatic carcinoma, CRC, and NSCLC. In EGFR mutant NSCLC, the successful early use of 3rd generation anti-EGFR inhibitors has improved the clinical outcome for these patients in not only in first line metastatic disease, but also early disease, and has become a new therapeutic paradigm for this patient population. However, the most efficient approach to managing emerging resistance to early use of 3rd generation EGFR inhibitors remains to be determined.

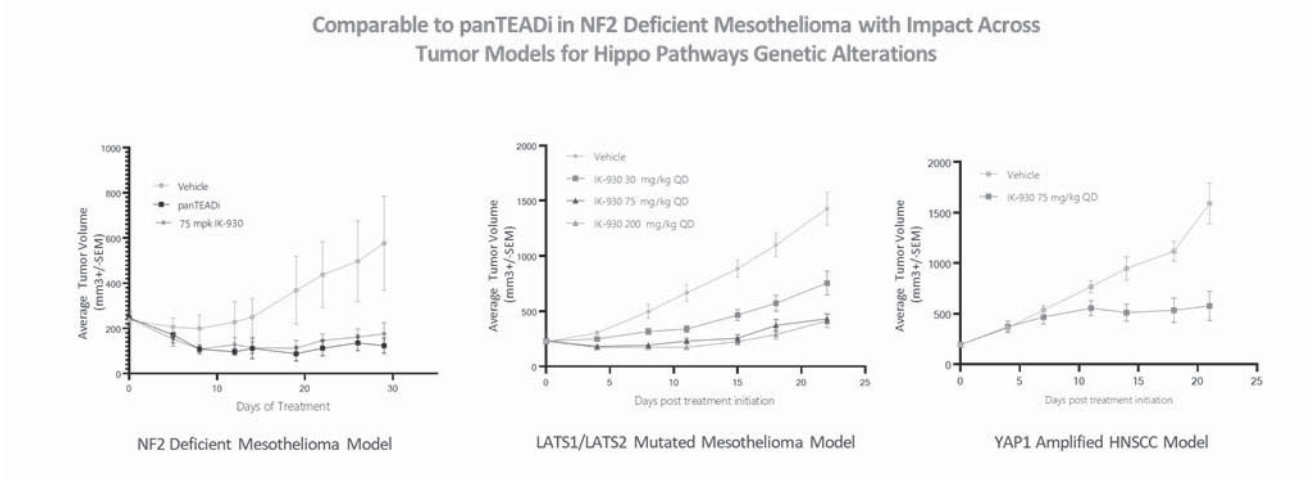
Our Solution, IK-930

IK-930 is an oral, TEAD1-selective, small molecule inhibitor of the Hippo pathway that binds to a lipid binding pocket on TEAD itself. TEAD activity is dependent on binding of the fatty acid palmitate to a central lipid pocket. IK-930 blocks palmitate from binding TEAD, thereby disrupting TEAD-dependent gene transcription. We believe the selectivity of IK-930 and its mechanism in engaging both the activating and suppression states of TEAD provides a differentiated approach to targeting the Hippo pathway, allowing for a potentially wider therapeutic window with continued inhibition of the pathway.

IK-930 was designed to balance antitumor activity and on-target TEAD renal toxicity through leveraging the biology of TEAD1 selectivity and enhancing repressor activity. PanTEAD inhibition has been shown to drive proteinuria and frank kidney toxicity, where the kidney podocytes are impacted. IK-930's selectivity has demonstrated a wider therapeutic window in multiple animal models, while demonstrating equivalent activity in multiple *in vivo* models. In a 28-day monkey study, IK-930 treated animals showed no clinical signs of renal toxicity and no renal changes measured at all tested doses, with no toxicity in other systems. In contrast, panTEAD inhibition showed decreased activity, ataxia and other symptoms in monkeys at both doses tested with the higher doses halted early due to mortality and morbidity.



We conducted multiple studies evaluating IK-930 in preclinical animal models. We observed IK-930 exhibited antitumor activity in *in vivo* models with different genetic alterations leading to constitutively active TEAD transcription status: NCI-H226 (NF2 deficient mesothelioma), MSTO2H11(LATS1/LATS2 mutant mesothelioma) and Detroit 562 (YAP1 amplified head and neck cancer). These studies were conducted utilizing 6-8 animals per group and, in all models, IK-930 dosed animals experienced increased tumor growth inhibition compared to vehicle. These studies demonstrated IK-930 antitumor activity in tumors driven by Hippo pathway signaling (constitutive TEAD activity). In the NF2 deficient mesothelioma model, we also tested a panTEAD inhibitor against which IK-930 showed comparable tumor impact.



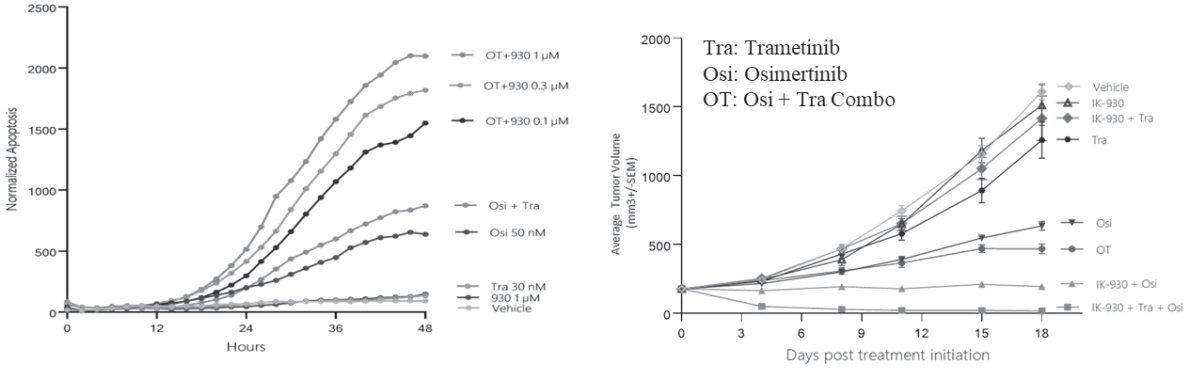
In addition to potential for single agent activity in tumors with genetic alterations in the Hippo pathway, we believe there is an opportunity for IK-930 to be beneficial in combination with other targeted therapies in the therapeutic resistance setting. Alterations in the Hippo pathway have been connected to post-targeted treatment tumor growth or recurrence. For example, YAP1 activation (nuclear localization) has been shown to drive resistance to EGFR targeted therapies. NSCLC patients who develop resistance to EGFR inhibitors have higher levels of nuclear YAP expression in their tumors compared to baseline.

We have conducted extensive preclinical research evaluating IK-930 in combination with other targeted therapies, which has demonstrated IK-930's ability to attenuate EGFR-specific persister cells after treatment with osimertinib.

In addition to these data that highlight the clinical opportunity to treat EGFR resistant patients with IK-930, we observed *in vitro* that inhibitors of EGFR promote YAP1 nuclear localization in EGFR mutant NSCLC cells, which led to an induction of TEAD-dependent gene expression. We observed that IK-930 was able to suppress osimertinib-induced TEAD-dependent gene expression and to significantly enhance apoptosis when combined with osimertinib in EGFR mutant tumors grown *in vitro*. In addition, we observed significantly enhanced antitumor activity when IK-930 was combined with osimertinib in multiple EGFR mutant tumors grown *in vivo*. For example, in the H1975 EGFR mutant lung cancer xenograft mouse model, there was meaningful tumor growth inhibition in the group treated with IK-930 in combination with osimertinib, as well as complete regressions in the group treated with IK-930 in combination with osimertinib and trametinib, a MEK inhibitor, supporting that shutting down the mitogen-activated protein kinase ("MAPK") survival pathway further leads to antitumor activity.

The figure below illustrates *in vitro* apoptosis (left) and *in vivo* antitumor activity (right) in EGFR mutant lung cancer models treated with osimertinib, IK-930, or the combination.

IK-930 in EGFR Mutant Lung Cancer



A clinical supply collaboration with AstraZeneca is in place for osimertinib for evaluation in combination with IK-930 for patients with EGFR mutant NSCLC in our ongoing Phase 1 clinical trial, assessing IK-930's impact on EGFR resistance.

Ongoing Phase 1 Clinical Trail of IK-930

We are currently conducting a Phase 1 clinical trial of IK-930 in multiple tumor types, including cancers with high frequencies of Hippo pathway alterations. The initial monotherapy portion of the trial is evaluating the safety and activity of IK-930 in rare and orphan tumors associated with specific genetic alterations such as NF2 loss. The clinical trial is designed to determine the maximum tolerated dose and the recommended Phase 2 dose. Currently, we are enrolling the monotherapy dose escalation cohorts with patients with tumors known to have high incidence of Hippo pathway alterations, with a particular focus on mesothelioma.

In November 2023, we shared initial dose escalation data from 26 patients as of October 31, 2023. IK-930 demonstrated a favorable tolerability profile in this early data set, with only 3 recorded cases of treatment-related proteinuria, the adverse event of interest for the on target renal toxicity typically associated with TEAD inhibition, all of which were reversible and limited to grade 1 or asymptomatic grade 2. Two EHE patients with significant liver metastases experienced reversible liver enzyme elevation. One of these patients developed treatment-related grade 3 elevation, which was deemed dose limiting and was the only dose limiting toxicity ("DLT") observed. The patient remained on study after dose adjustment. The other patient experienced grade 3-4 elevation that was deemed possibly treatment related.

Maximum tolerated dose ("MTD") had not yet been reached. Additional safety observations in this initial dose escalation population are described in the table below.

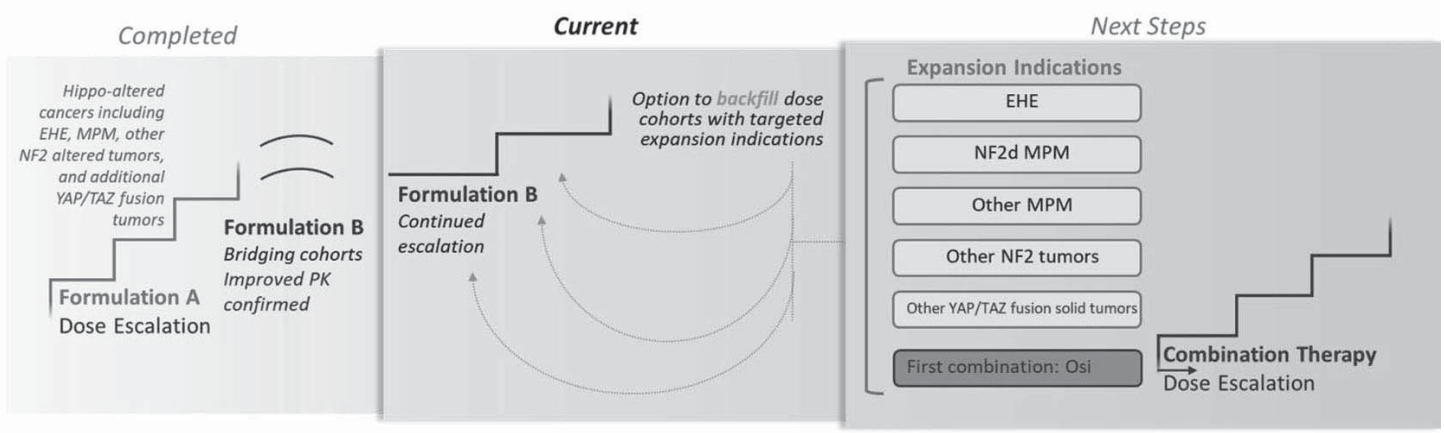
Most Common IK-930 Related Adverse Events and Events of Interest in Dose Escalation as of October 31, 2023

Treatment-Related Adverse Events of Interest	Dose Escalation (n=26)	Grade
Nausea	7	Grade 1-2
Fatigue	5	Grade 1-2
Proteinuria	**3**	**Grade 1-2**
Diarrhea	3	Grade 1-2
LFT Increase*	1 (+1 possibly related)	Grade 3-4 (only DLT reported)

*Two patients developed LFT elevation, both had significant liver metastasis at diagnosis (LFT: Liver function test). Only one of these patients' LFT elevation was reported as a DLT (Grade 3)and the second patient's LFT elevation (Grade 3-4) was reported as possibly related to study drug.

Of the twenty six (26) treated patients in dose escalation, fifteen (15) were treated with doses within the projected efficacious exposure range. Pharmacokinetic data from these fifteen (15) patients showed some variability in exposure; seven (7) out of the 15 patients were determined to reach efficacious exposure. To address variability a twice daily dosing schedule with the original formulation, formulation A, was introduced into dose escalation and a new formulation, formulation B, was introduced and a bridging cohort, was added. The exposure variation seen with formulation A was determined to predominantly be mediated by differences in patient stomach pH, which has been shown to impact IK-930 solubility. Formulation B was designed to overcome differential IK-930 solubility when the tablets are disintegrated in the stomach.

The pharmacokinetic data from the first cohorts treated with formulation B displayed improved exposures with markedly less variability than formulation A. Initial data, which included patients across two dose levels treated with formulation B, indicates that formulation B is suitable to complete the ongoing Phase I study as well as future clinical trials. It is being dosed in current cohorts and will be used for all future cohorts.



In addition to the initial safety data shared in November 2023, initial anti-tumor activity in EHE patients was shared. EHE is a slow-growing, invasive tumor with no approved treatment options and is challenging to measure due to diffuse infiltration of multiple organs. It can occur in multiple areas of the body, including the liver, lungs, bones, and blood vessels. People with EHE suffer symptoms that relentlessly affect their quality of life and are consistent with the site of the EHE growth, including liver failure, respiratory issues and gastrointestinal symptoms, which are frequently accompanied by severe pain across the body. With no approved standard of care, there is substantial need for innovative treatments that can provide clinical benefit and symptom relief and slow or limit the progression of disease.

Seven (7) patients with EHE had been treated with IK-930 in the dose escalation portion of the trial as of October 31, 2023. Seven (7) out of 7 EHE patients reached stable disease as a best response as measured by RECIST and three (3) out of the 7 patients experienced tumor shrinkage in multiple target and non-target lesions. Four (4) out of 7 highly symptomatic EHE patients enrolled across multiple dose levels reported symptomatic improvement and subjective improvement of quality of life such as improved energy, weight gain, and pain control. Three (3) out of the 7 patients continued treatment with time on treatment ranging from eighteen (18) to twenty-six (26) weeks as of October 31, 2023.

EHE Patients Demonstrating Initial Clinical Response as of October 31, 2023
7 out of 7 patients reached **stable disease (SD)**
3 out of 7 patients with SD experienced **tumor shrinkage** in multiple target and non-target lesions
3 out of 7 patients continue on treatment with **time on IK-930** ranging from 18 to 26 weeks and ongoing
4 out of 7 patients had **improvement of clinical symptoms** and subjective improvement of quality of life

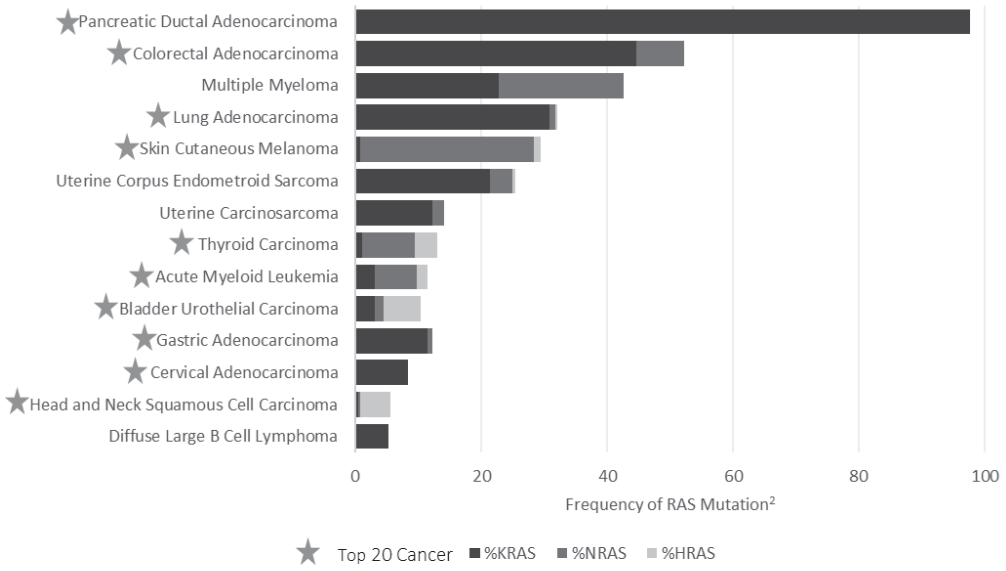
Current recruitment is focused on mesothelioma patients as well as additional EHE patients. We plan to utilize both local testing for NF2 and confirmatory retrospective NF2 testing, in addition to other biomarker testing. Because mesothelioma patients can also experience a loss of NF2 protein or harbor other alterations in the Hippo pathway, we are evaluating the broader patient population while maintaining a keen focus on NF2 deficiency. As dose escalation continues, we plan to identify a recommended phase 2 dose and expand further into the monotherapy target indications, as well as initiate our planned study in combination with osimertinib. A clinical data update for the monotherapy portion of the study is planned for the second half of 2024.

IK-595, a Dual MEK-RAF Inhibitor

Targeting in the RAS Pathway and MEK Inhibition in Cancer

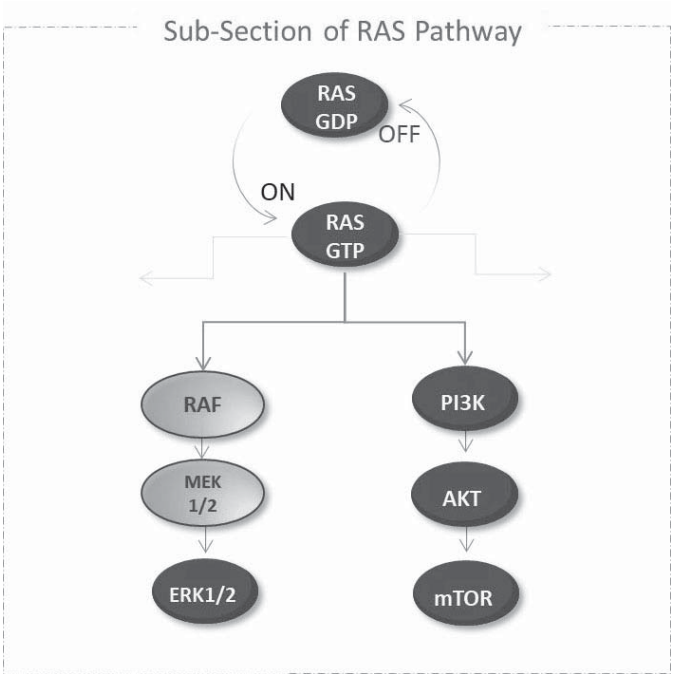
The RAS pathway is implicated in at least half a million new cancer diagnoses each year in the United States alone. Ten (10) of the twenty (20) most common cancers worldwide are associated with RAS pathway mutations, representing a major unmet need for new and innovative approaches in the pathway.

10 of the 20 Most Common Cancers Worldwide are Associated with RAS Pathway Mutations

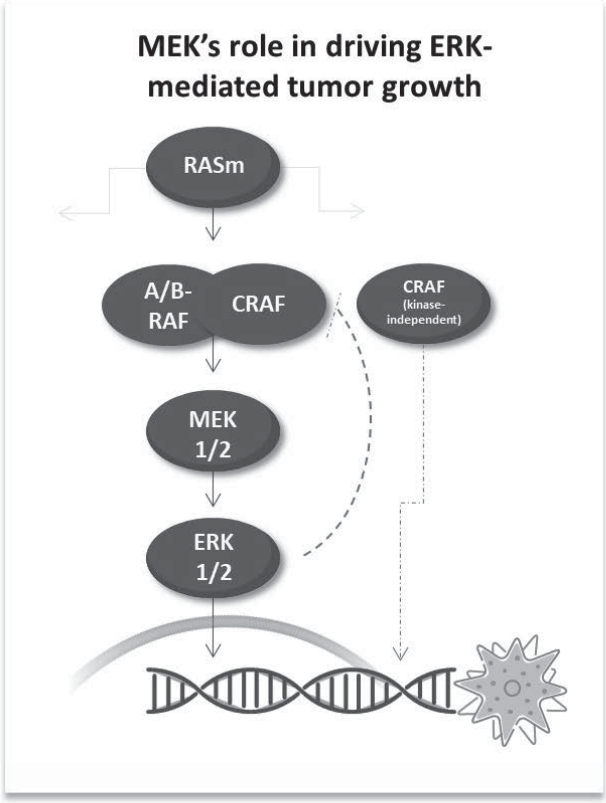


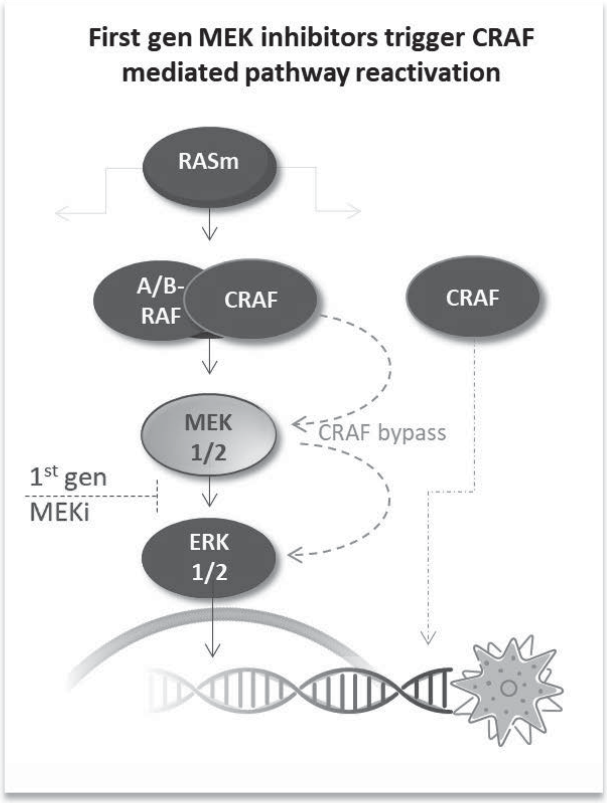
Cox. Nature Reviews Drug Discovery (2014); World Cancer Research Fund International

We aim to target the RAS pathway on multiple levels, including preventing known resistance mechanisms, to achieve deep and sustained responses. Our most recent development candidate and first in the RAS pathway, IK-595, is a dual MEK-RAF inhibitor that is designed to trap MEK and RAF in an inactive complex. The RAS-RAF-MEK-ERK cascade MAPK pathway regulates cell proliferation, differentiation, and survival. Activating mutations in this pathway are known to drive tumorigenesis in a large number of patient populations. Targeting MEK and RAF has the potential to impact patients across a plethora of indications, including RAS and RAF-altered cancers, both in targeting genetic mutations and in targeting escape mechanisms from other targeted therapies, potentially prolonging duration of response for patients.



Existing drugs targeting MEK, classified as kinase inhibitors, are limited by insufficient pathway inhibition and narrow therapeutic window, and are only currently addressing BRAF type I mutant cancer patients and NF1 mutant neurofibroma patients. One of the well-known mechanisms of resistance to existing MEK inhibitors in RAS mutant populations is through CRAF bypass, the reactivation of CRAF through ERK mediated negative feedback control. More recently, CRAF function independent of its kinase activity has also been reported to drive tumor growth, a function that is not addressable through kinase inhibitors, including selective or pan-RAF inhibitors. We believe these two important CRAF roles in tumorigenesis and therapeutic resistance are significant factors in why existing MEK inhibitors, including the four FDA approved therapies, are insufficient for serving the large patient populations with RAS or RAF gene alterations.

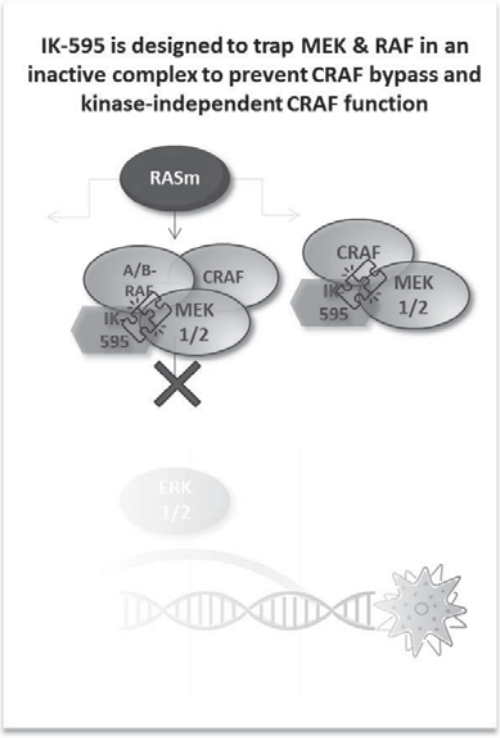




In addition to the approved MEK inhibitors, there are several in development. In many of our preclinical studies, we compared IK-595 to both approved MEK inhibitors and other experimental MEK inhibitors, including avutometinib ("VS-6766"), Verastem's clinical-stage MEK-RAF inhibitor, as a representative of the class of competitor molecules in development. We believe IK-595 has advantages over the class of MEK inhibitors, as it could provide broader, more durable antitumor activity and a better therapeutic window for patients.

Our Solution, IK-595

IK-595 is a clinical stage, potent, oral, small molecule MEK-RAF molecular glue, which is designed to more comprehensively inhibit MAPK signaling than existing treatments, while achieving a broader therapeutic window for patients. Through its ability to stabilize MEK-RAF interaction, including CRAF, IK-595 aims to prevent both CRAF bypass and kinase-independent CRAF activity.



IK-595 is currently being evaluated in a Phase I clinical trial in RAS and RAF mutant cancers. The first patient was treated with IK-595 in December 2023 and the first cohort cleared the initial safety window in January 2024. Dose escalation is ongoing.

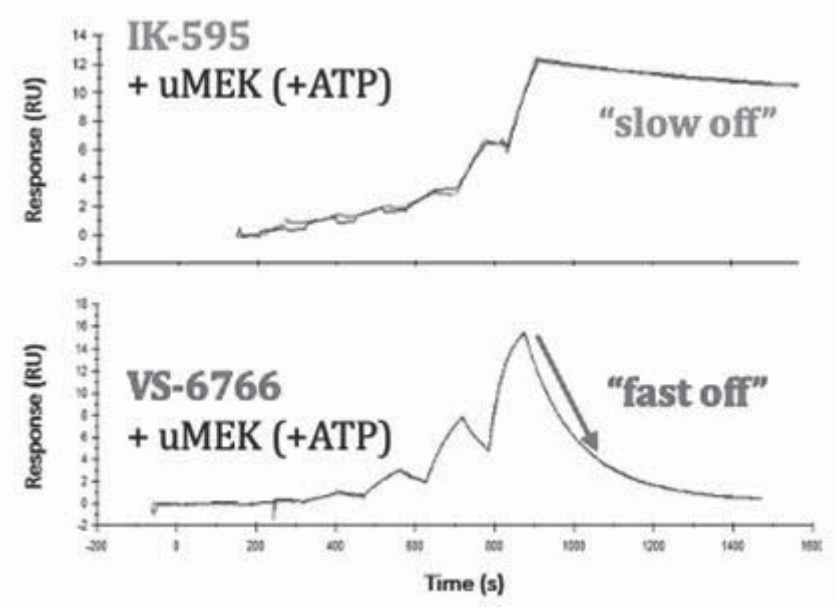
We have generated a robust preclinical dataset supporting IK-595 as a potentially durable therapeutic solution for multiple cancer types linked to the RAS pathway, expanding the potential populations that could benefit from existing MEK inhibitors. These studies demonstrate and include:

- Potent inhibition capabilities of IK-595 through multiple biochemical and cellular potency assays;
- IK-595's ability to stabilize MEK and RAF, including CRAF, which we believe is key to differentiation in the class;
- IK-595's inhibition of phosphorylation, and thus subsequent activation, of MEK and ERK (pMEK and pERK);
- Durability of the inhibition of pERK, and downstream target gene expression;
- IK-595's preclinical efficacy in RAS and RAF altered cancer cell lines;
- Potential synergy of IK-595 in combination with other targeted therapies *in vitro*, including in combination with KRAS G12C inhibitors, EGFR, PI3K, SHP2, and SOS1 inhibitors; and
- Projected pharmacokinetics and pharmacodynamics of IK-595, which has been designed to have shorter half-life in humans to allow for potentially differentiated dosing strategies.

IK-595 demonstrated high potency in a variety of biochemical and cellular assays. IK-595 biochemically inhibited unphosphorylated MEK ("uMEK"). Additionally, in AsPC-1 cells, IK-595 potently blocked cell proliferation and the phosphorylation of ERK and MEK.

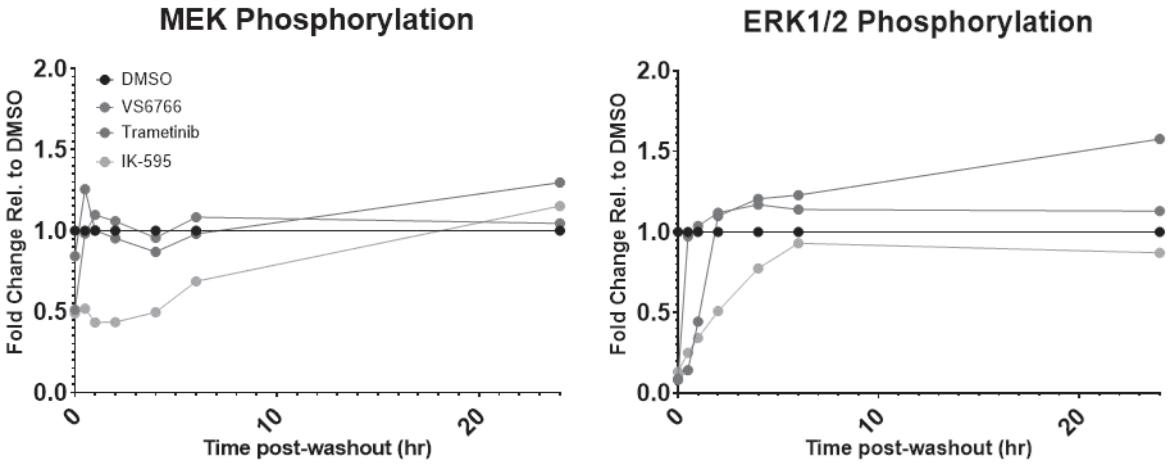
Assay	Cellular pERK IC_{50}	Biochem uMEK IC_{50}	Cellular pMEK 4h / 48h IC_{50}	Proliferation AsPC-1 CTG IC_{50}
IK-595	0.1 nM	3 nM	0.6/1 nM	1.3 nM

We also measured IK-595's ability to tightly bind to MEK and the kinetics of the bind. The binding of IK-595 to unphosphorylated MEK1 was measured by surface plasmon resonance ("SPR"). Biotinylated, unphosphorylated MEK1, IK-595 and VS-6766 were injected over the chip in a single cycle kinetic ("SCK") mode at a flow rate of 30 µL/min and with a 90 second on-time and a 1200 second (IK-595) or 600 second (VS-6766) off-time. In contrast to other MEK inhibitors (VS-6766), IK-595 exhibited considerably slower dissociation kinetics (off-rate) from MEK. The off-rate denotes the duration it takes for IK-595 to separate from MEK following binding. This delayed dissociation significantly impeded the function of MEK for extended time periods.



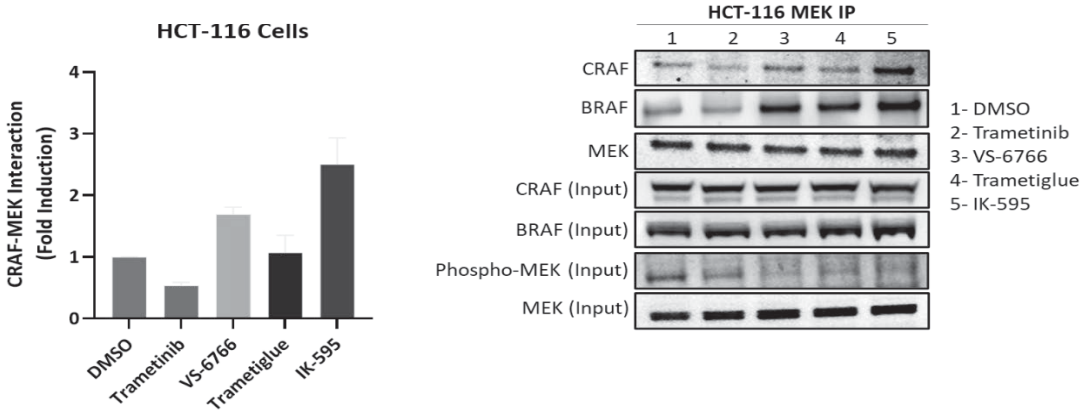
MEK	$k_{on}(M^{-1}s^{-1})$	$k_{off}(s^{-1})$	K_D (nM)
IK-595 (to MEK)	**8.24 E+04**	**6.09 E-04**	**7.39**
VS-6766 (to MEK)	**1.69 E+05**	**7.08 E-03**	**41.83**

In an additional study AsPC-1 cells were treated for 1 hour with DMSO control or one of the following MEK inhibitors: IK-595, trametinib, or VS-6766 at 3 nM, 10 nM, and 30 nM, respectively. Cells were then washed with phosphate-buffered saline (PBS) 5 times and then lysed in radio immunoprecipitation assay ("RIPA") buffer prior to washout or at the following timepoints post-washout: 0.5, 1, 2, 4, 6, and 24 hours. In contrast to other MEK inhibitors (trametinib and VS-6766), IK-595 demonstrated prolonged inhibition of MEK and ERK1/2 phosphorylation following compound washout suggesting that IK-595 has a slower off-rate from MEK.

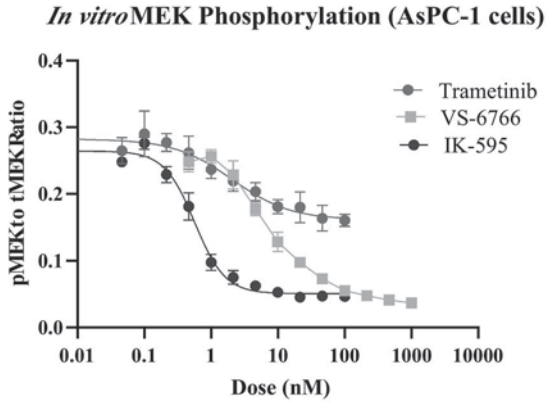


Additionally, western blot quantification of the MEK immunoprecipitates from HCT116 cells showed that IK-595 strongly increased the association of endogenous MEK and CRAF proteins, whereas trametinib decreased the MEK-CRAF interaction, and trametiglue had no effect. VS-6766 also increased MEK-CRAF association, but to a significantly less extent. These data indicate that IK-595 is differentiated from other MEK inhibitors in its potential to stabilize the MEK-CRAF complex.

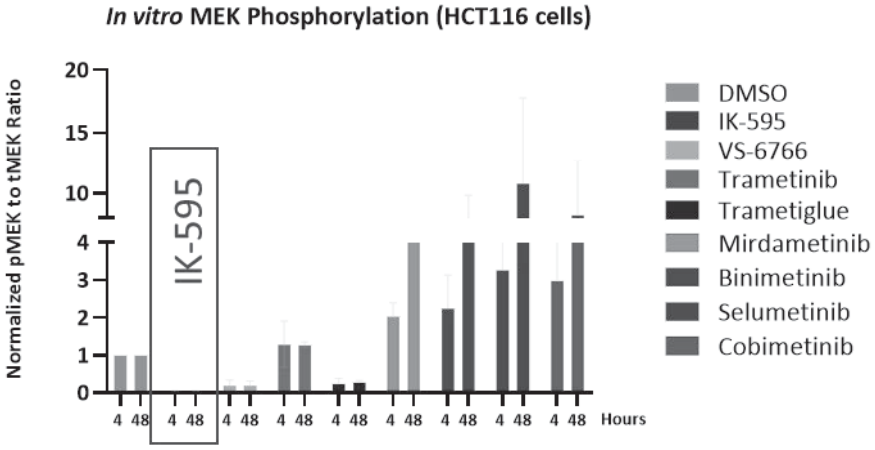
A similar data trend was seen with MEK-BRAF association. These data indicate that IK-595 is differentiated from other MEK inhibitors in its ability to stabilize the MEK-CRAF in a completely inactive complex.



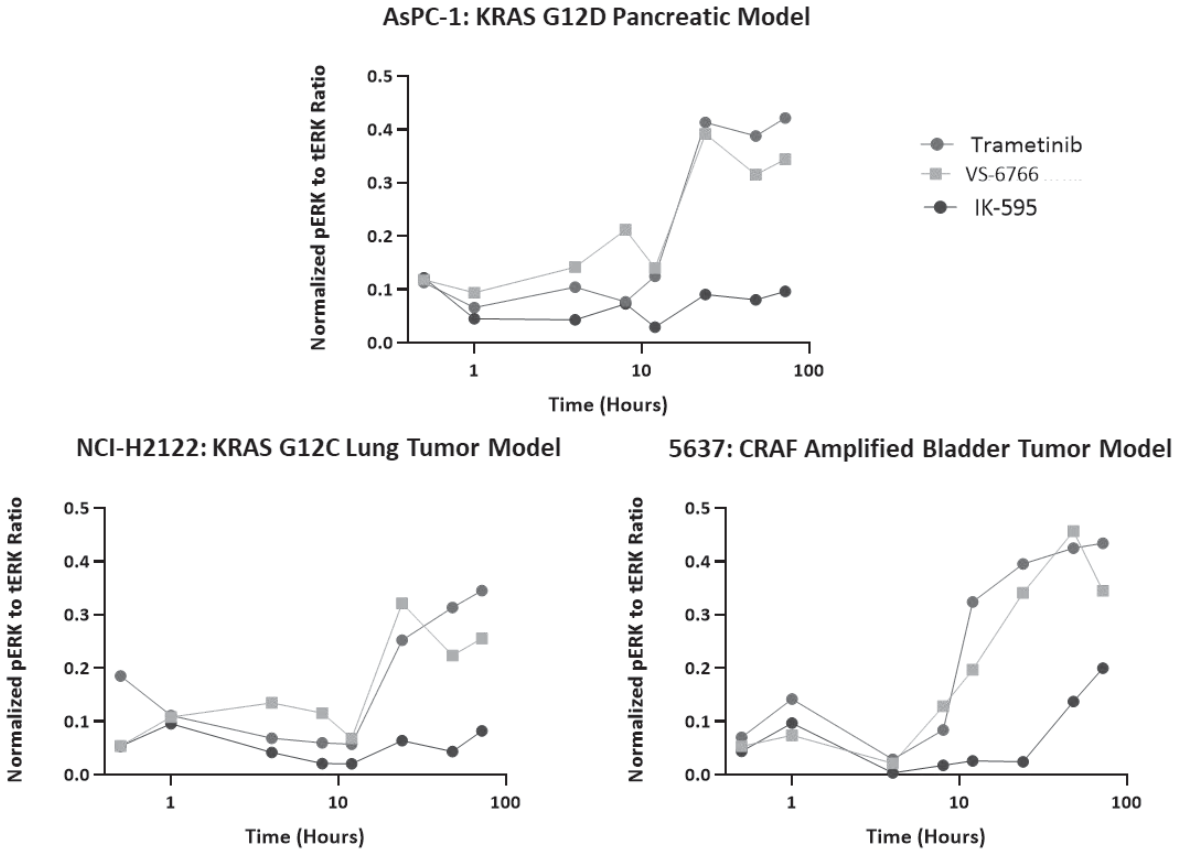
The effect of IK-595 on MEK phosphorylation was measured in KRAS mutant AsPC1 cells, using a Mesoscale Discovery ("MSD") kit detecting total and phosphorylated MEK. In AsPC-1 cells after 4 hours of treatment, IK-595 potently inhibited MEK phosphorylation with an IC50 of 0.6 nM, while VS-6766 was more than 10 fold less potent with an IC50 of 7 nM. Trametinib had little effect on MEK phosphorylation.



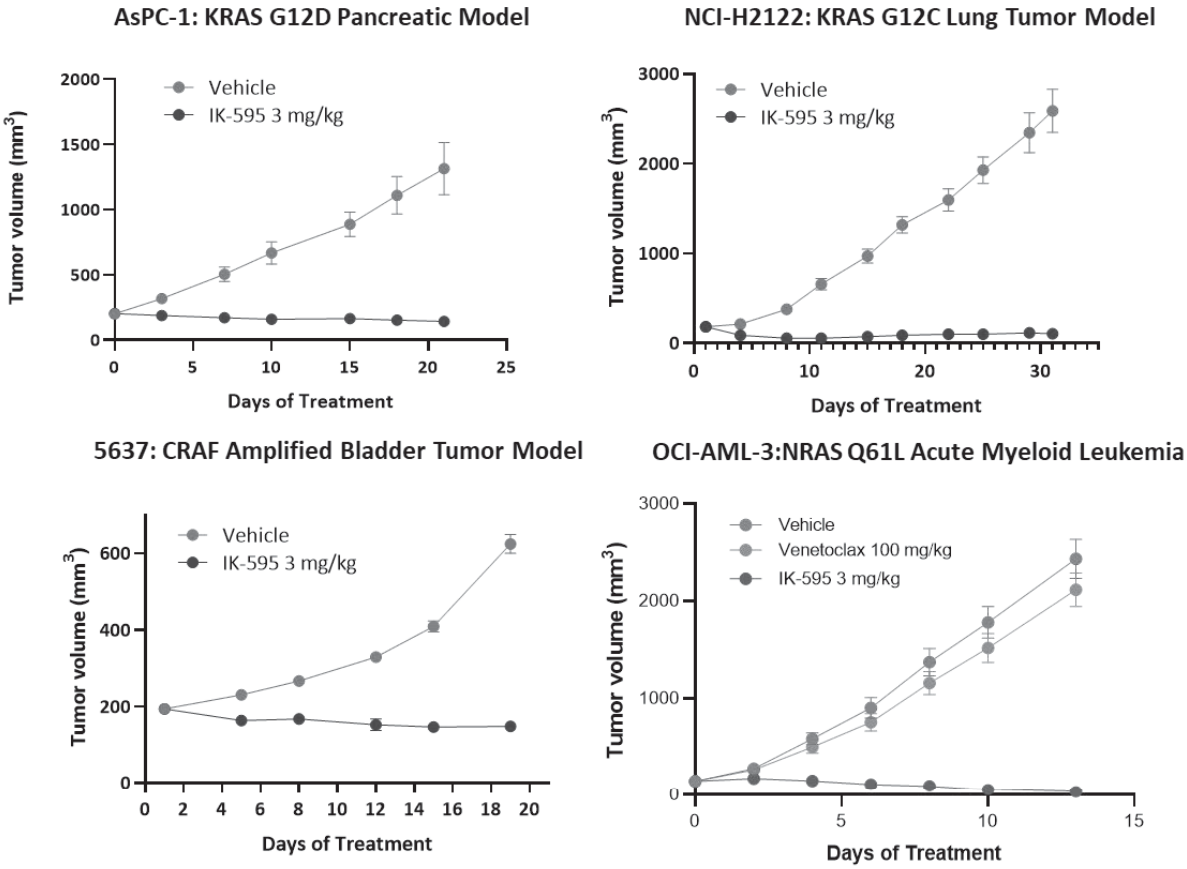
We assessed levels of phosphorylated and total MEK following 4- and 48-hours of treatment of HCT-116 cells with IK-595 compared to seven other MEK inhibitors, displayed below by Western blot analysis. IK-595 was observed to completely block phosphorylation of MEK at both 4 and 48 hours. VS-6766 and trametiglue were also observed to block the phosphorylation of MEK at both 4 and 48 hours. Trametinib had minimal or no effect on MEK phosphorylation at either timepoint, whereas 1st generation MEK inhibitors, namely mirdametinib, binimetinib, selumetinib, and cobimetinib, significantly increased MEK phosphorylation at both 4 and 48 hours. This suggests that IK-595 not only inhibits MEK protein, but also induces an inactive conformation of MEK-RAF protein complex to block RAF mediated MEK phosphorylation and activation.



We measured the ability of IK-595 to inhibit ERK phosphorylation as compared to trametinib and VS-6766 through multiple studies. Levels of phosphorylated and total ERK following the treatment of KRAS mutant AsPC-1 and NCI-H2122 cells as well as CRAF amplified 5637 cells for up to 72 hours with IK-595, trametinib, or VS-6766 were determined by Western blot analysis. IK-595 inhibited ERK phosphorylation for up to 48-72 hours, whereas a rebound in ERK phosphorylation was observed in trametinib and VS-6766 at as early as 12 hours. These data support our belief that IK-595 can achieve more durable inhibition than existing and competitor MEK inhibitors.

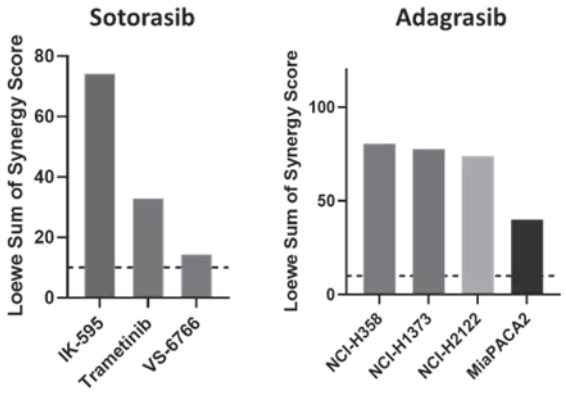


The antitumor activity of IK-595 was evaluated *in vivo* in multiple xenografts models, four of which are shown below having different RAS/MAPK alterations: AsPC-1 (KRAS G12D pancreatic); NCI-H2122 (KRAS G12C non-small cell lung cancer), 5637 (CRAF amplified bladder cancer) and OCI-AML-3 (NRAS Q61L acute myeloid leukemia model that is resistant to standard of care, venetolax). These studies were conducted utilizing 8-10 animals per group. Animals were dosed daily and tumors were measured twice weekly. These studies demonstrated IK-595's robust antitumor activity in tumors driven by alterations in the RAS/MAPK pathway. Similar activity was demonstrated in the AsPC-1 model when IK-595 was dosed intermittently at 6 mg/kg every other day (QOD). In addition, in all models, body weight of the mice was maintained similarly to that of the vehicle group.

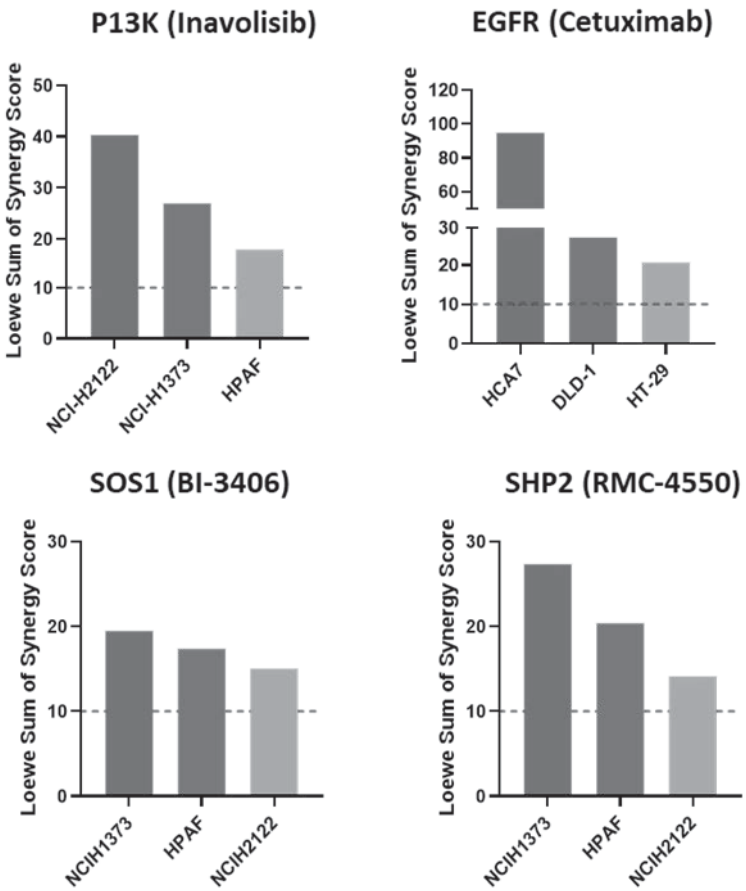


We measured the synergy of IK-595 with multiple potential combination agents. For each agent, we assessed the synergy of IK-595 in combination with the given agent in multiple cell lines, measured cell viability, and calculated Loewe sum of synergy scores. IK-595 demonstrated significantly higher synergy score with AMG510 (sotorasib), a KRAS-G12C inhibitor, over trametinib and VS-6766. Additionally, IK-595 showed significant synergy with other KRAS-G12C inhibitors (adagrasib), as well as P13K, EGFR, SOS1, and SHP2 inhibitors.

IK-595 Synergy with KRAS-G12C Inhibitors

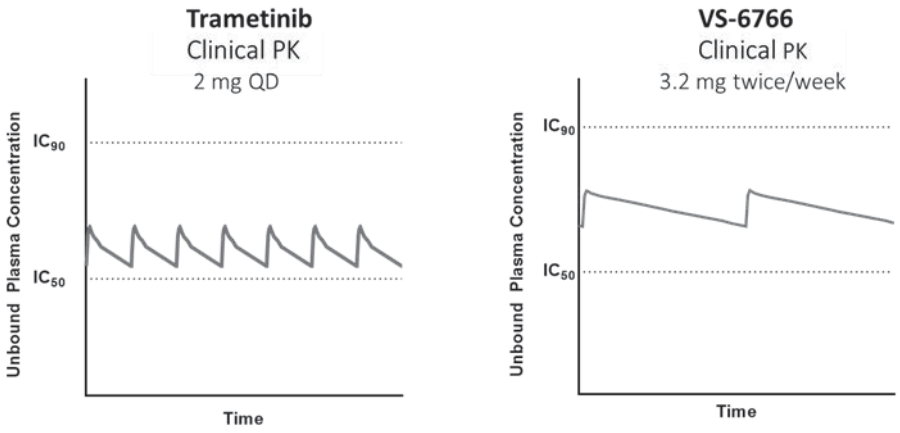


IK-595 Synergy with Multiple Potential Combination Agents

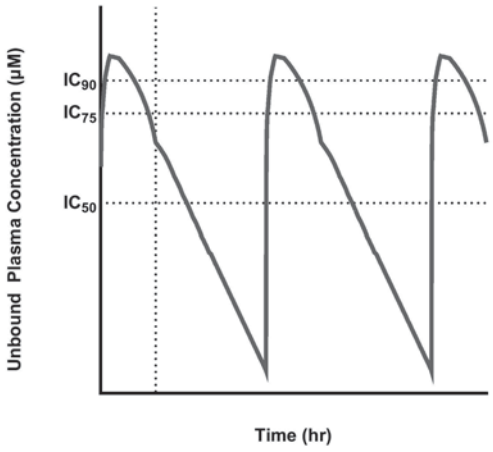


A key consideration for next generation MEK inhibitors is to broaden the therapeutic window that allows for deep inhibition and anti-proliferation effect in cancer cells, but give normal cells sufficient breaks in pathway inhibition to minimize toxic side effects. In order to optimize for tolerability, trametinib and VS-6766's clinical dosing regimens are designed to accommodate their very long half-lives in humans (trametinib 72-120 hours and VS-6766 60-100 hours). Because of this, clinical doses of trametinib and VS-6766 cannot reach concentrations above IC_{75} for pERK inhibition as assessed in KRAS mutant cancer cells, or below IC50 through the entire treatment duration, leading to insufficient antitumor efficacy and poor tolerability. We believe the predicted shorter human half-life of IK-595 will allow for flexibility in dosing schedules and enable transient concentrations above IC_{90} and recovery in normal tissues during periods of low exposure, providing an advantageous therapeutic window for patients.

Trametinib and VS-6766 Pharmacokinetics Based on Actual Clinical Dosing



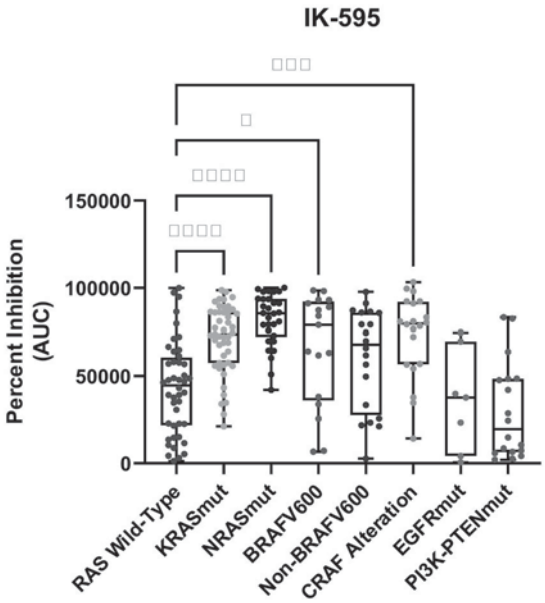
IK-595 Projected Dosing and Pharmacokinetics (Model Only)



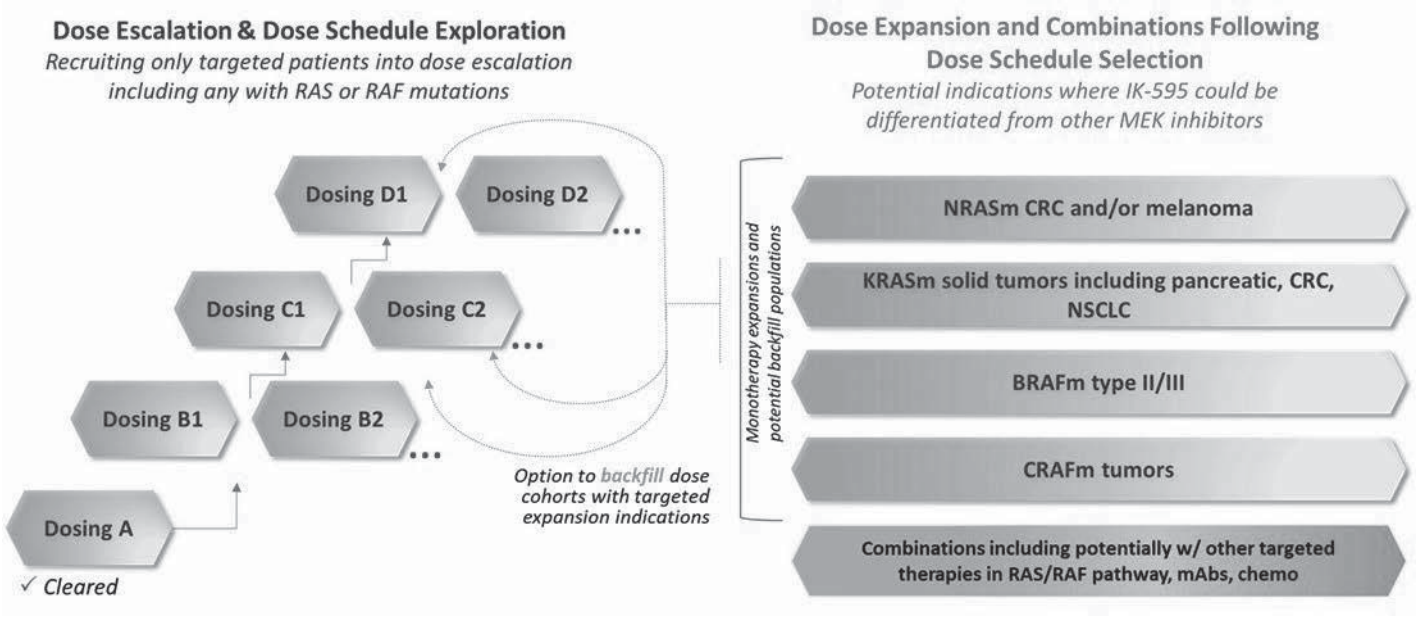
These data combine to support our efforts to advance IK-595 for the treatment of multiple types of RAS and RAF altered cancers. We believe they also demonstrate IK-595's competitive advantages over existing MEK inhibitors and others in development, including ability to trap CRAF in an inactive complex with MEK to avoid CRAF bypass and kinase-independent activity resulting in durable inhibition of the targets, as well as an improved therapeutic window.

IK-595 Translational and Clinical Development Strategy

In planning for clinical development, we have assessed the sensitivity profile of IK-595 in a large number of cancer cell lines harboring different RAS and RAF gene alterations. We plan to initially conduct our clinical program in indications with high prevalence of mutations that demonstrate higher sensitivity to IK-595 and have potential reliance on CRAF function. The ability of IK-595 to inhibit cell proliferation was evaluated by a 5-day cell titer glo ("CTG") assay in ~250 cell lines with genetic alterations that included KRAS, NRAS, BRAF, CRAF alterations, EGFR, PIK3CA, and PTEN mutations. Area under the curve ("AUC") of percent inhibition dose response curves were graphed. IK-595 demonstrated increased sensitivity in NRAS and KRAS mutant, as well as CRAF-altered cell lines compared to RAS wild-type cell lines.



Our ongoing Phase 1 clinical trial of IK-595 is currently recruiting patients in the United States (NCT06270082) with RAS and RAF mutant cancers in dose escalation. We are exploring multiple dosing schedules at each dose level. The trial has the option for backfill and expansion cohorts in multiple indications, such as NRAS, KRAS, and CRAF mutant cancers, as well as BRAF type II and III mutant cancers, as described in the image below. We also plan to explore combination regimens once recommended dosing schedules are identified.



The first patient in the Phase 1 clinical program was dosed in December 2023 and the first cohort cleared its initial safety window in January 2024.

Partnering Portfolio

Our IK-175 aryl hydrocarbon receptor ("AHR") antagonist program that was partnered with Bristol-Myers Squibb Company ("Bristol-Myers Squibb") completed its Phase 1 clinical trial in late 2023. Initial results shared in November 2022 demonstrate encouraging, durable, anti-tumor activity in stage 1 of both the monotherapy and combination arms in urothelial carcinoma patients. In January 2024, we announced that Bristol-Myers Squibb did not opt into the program. We plan to provide a clinical data update in 2024 and pursue strategic alternatives for this program, including sale or outlicensing. Our partnering portfolio also includes several other immune oncology programs that are available for potential sale or outlicensing, including PY314, a Phase 2 ready TREM2 antagonist, PY159, a Phase 2 ready TREM1 antagonist, and PY265, an IND-ready MARCO antagonist.

Competition

The biotechnology and pharmaceutical industries are characterized by rapid innovation of new technologies, fierce competition, and strong defense of intellectual property. While we believe that our pipeline and our knowledge, experience, and scientific resources provide us with competitive advantages, we face competition from major pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and public and private research institutions, among others.

We compete in segments of pharmaceuticals and biotechnology, and there are other companies focusing on structural biology-guided chemistry-based drug design to develop therapies in the fields of cancer and other diseases. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes. Any product candidates that we successfully develop and commercialize will compete with currently approved therapies and new therapies that may become available in the future from segments of the pharmaceutical, biotechnology and other related markets that pursue targeted oncology therapeutics. Key product features that would affect our ability to effectively compete with other therapeutics include the efficacy, safety, and convenience of our products.

We believe principal competitive factors to our business include, among other things, our ability to identify promising biomarkers, our ability to successfully transition research programs into clinical development, our ability to raise capital, and the scalability of our pipeline and business.

Our competitors may obtain regulatory approval of their products more rapidly than we may or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than us in manufacturing and marketing their products.

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

IK-930

Other companies that have publicly disclosed that they are developing TEAD inhibitors are: Vivace Therapeutics, Inc., Novartis International AG (Novartis), Inventiva S.A., Kyowa Hakko Kirin Co., Ltd., SpringWorks Therapeutics, Inc., BridGene Biosceiences, Betta Pharmaceuticals, Beactica Therapeutics, Sporos Biodiscovery, Light Horse Therapeutics, Tasca Therapeutics, Orion Corporation, Merck, Sanofi, and Roche/Genentech. Vivace Therapeutics, Inc., Novartis, and SpringWorks Therapeutics are in Phase 1 clinical trials with their programs. All other programs are in preclinical development.

IK-595

In addition to approved MEK1/2 inhibitors (Mekinist®, Mektovi®, Cotellic®, Koselugo®), we are aware of the following IND-ready and clinical-stage MEK1/2 inhibitors: Nested Therapeutics, SpringWorks' mirdametinib, DayOne Biopharma's pimasertib, KeChow Pharma's tunlametinib (HL-085), Sino Biopharmaceutical's TQB-3234, Fosun Pharma's FCN-159, Recursion's REC-4881, and Lupin's LNP3794. Additional MEK/RAF-targeted agents include Verastem's avutometinib (VS-6766), Immuneering's IMM-1-104, and IMM-6-415. Pan-RAF inhibitors include DayOne Biopharma's tovorafenib (DAY-101), Erasca's naporafenibum (LXH-254), BeiGene's lifirafenib (BGB-283), Genentech's belvarafenib, Kinnate Biopharma's exarafenib (KIN-2787), Jazz Pharma's JZP-815, and Deciphera's DCC-3084.

License and Collaboration Agreements

Master Collaboration Agreement with Bristol-Myers Squibb

In January 2019, we entered into the Bristol-Myers Squibb Collaboration Agreement with Celgene Corporation (which was acquired by Bristol-Myers Squibb in November 2019) under which Bristol-Myers Squibb could elect in its sole discretion to exclusively license rights to develop and commercialize compounds (and products and diagnostic products containing such compounds) that modulate the activity of two collaboration targets, kynurenine and AHR, excluding AHR agonists other than inverse agonists (the "Collaboration Candidates"), known as IK-175 and IK-412. The Bristol-Myers Squibb Collaboration Agreement triggered an upfront payment of $95.0 million, which consisted of approximately $80.5 million in cash and an equity investment of approximately $14.5 million for which we issued 14,545,450 shares of our Series A-1 Preferred Stock pursuant to a separate stock purchase agreement. The series A-1 shares automatically converted into common stock upon the completion of our initial public offering ("IPO").

On a program-by-program basis, through the completion of a Phase 1b clinical trial for each of IK-175 and IK-412, Bristol-Myers Squibb had the exclusive right with respect to such Collaboration Candidate to a worldwide exclusive license with us to develop, commercialize and manufacture the compound (and products and diagnostic products containing such compounds) underlying such Collaboration Candidate. The Collaboration Candidates were eligible for opt-in through early 2024. On January 17, 2024, Bristol-Myers Squibb notified us of its decision not to opt-in on the IK-175 program. In addition, Bristol-Myers Squibb did not provide an opt-in exercise for the IK-412 program. As a result, we have regained full global rights to the IK-175 and IK-412 programs. We will not invest further in the clinical development of IK-175 or IK-412 but will pursue strategic business development opportunities, including out-licensing.

Patent License Agreement with the University of Texas at Austin

In March 2015, we entered into an exclusive patent license agreement (the "License Agreement") with the University of Texas at Austin (the "University"), pursuant to which the University granted us a worldwide license to certain technology and IP rights relating to IK-412, a kynurenine-degrading enzyme.

Pursuant to the License Agreement, we pay a license fee of approximately $40,000 per year. We will also be obligated to make milestone payments to the University of up to an aggregate of $0.7 million upon meeting certain development milestones and up to an aggregate of $4.0 million upon meeting certain regulatory milestones, as well as low single digit royalties based on worldwide annual net sales on any licensed product, subject to specified reductions.

We will be obligated to continue to pay royalties on a licensed product-by-licensed product and country-by-country basis, as long as there is an existing valid claim under the licensed patents in such country. Please see "Business—Intellectual Property—IK-412," for additional information concerning the intellectual property related to the License Agreement.

The term of the License Agreement expires on licensed product-by-licensed product and country-by-country basis until the expiration of all royalty terms, unless earlier terminated as described below.

The License Agreement may be terminated (i) by either party if the other party remains in breach of the license agreement following a cure period to remedy the breach, (ii) by us at will, (iii) by the University, in its entirety, upon our bankruptcy or insolvency, or (iv) by the University, in its entirety, if we challenge a patent licensed by the University to us under the license agreement.

License Agreement with AskAt

In connection of our acquisition of Arrys Therapeutics, Inc. ("Arrys"), in December 2018, we acquired in-process research and development assets related to AskAt Inc.'s, ("AskAt") selective EP4 antagonists based on the intellectual property associated with a License Agreement (the "AskAt Agreement") between Arrys and AskAt, dated December 14, 2017. Pursuant to the AskAt Agreement, AskAt granted Arrys an exclusive license worldwide, other than China and Taiwan, to the research and development of the licensed compounds in human diseases. AskAt controls the prosecution and maintenance of all intellectual property rights pertaining the licensed technology.

Pursuant to the AskAt Agreement, we are obligated to make milestone payments to AskAt, including up to $4.0 million upon the achievement of certain clinical development milestones, as well as milestone payments of up to an aggregate of $600 million upon the achievement of certain worldwide annual net sales milestones. We are also obligated to pay low single-digit royalties on annual worldwide net sales on a licensed-product-by-licensed product and country-by-country basis, for the period beginning upon the first commercial sale in such country and ending upon the later of (i) 10 years from the first commercial sale in such country, or (ii) the expiration of valid claims in such country.

To date, we have paid total consideration in the amount of $28.5 million pursuant to the AskAt Agreement, which was recognized as research and development expenses upon our acquisition of Arrys. We intended to use the license granted pursuant to the AskAt Agreement in our future development of therapeutic drug candidates for eventual clinical development and commercialization. The AskAt Agreement will be terminated as of March 20, 2024 and all assets will be returned to AskAt, at which point no further costs will be incurred by us.

Intellectual Property

We seek to protect the intellectual property and proprietary technology that we consider important to our business, including by pursuing patent applications that cover our product candidates and future products, and methods of using the same, as well as any other relevant inventions and improvements that we believe to be commercially important to the development of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. Our commercial success depends, in part, on our ability to obtain, maintain, enforce and protect our intellectual property and other proprietary rights for the technology, inventions and improvements we consider important to our business, and to defend any patents we may own or in-license in the future, prevent others from infringing any patents we may own or in-license in the future, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and proprietary rights of third parties.

Patent Protection

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates, future products, and proprietary technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our pending patent applications, and any patent applications that we may in the future file or license from third parties, may not result in the issuance of patents and any issued patents we may obtain do not guarantee us the right to practice our technology or commercialize our product candidates. We also cannot predict the breadth of claims that may be allowed or enforced in any patents we may own or in-license in the future. Any issued patents that we may own or in-license in the future may be challenged, invalidated, circumvented, or have the scope of their claims narrowed. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting the protection such patent would afford the respective product and any competitive advantage such patent may provide.

The term of individual patents depends upon the date of filing of the patent application, the date of patent issuance, and the legal term of patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office ("USPTO") in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier expiring patent. The term of a patent claiming a new drug product may also be eligible for a limited patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The term extension period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. The term extension period cannot be longer than five years, and the term extension period may not extend the patent term beyond 14 years from the date of FDA approval. Only one patent applicable to an approved product is eligible for the extension, and only those claims covering the approved product, a method for using it, or a method for manufacturing it may be extended. Additionally, the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension in consultation with the FDA. In the future, if our product candidates receive approval by the FDA, we expect to apply for patent term extensions on any issued patents covering those products, depending upon the length of the clinical studies for each product and other factors. There can be no assurance that our pending patent applications, and any patent applications that we may in the future file or license from third parties, will issue or that we will benefit from any patent term extension or favorable adjustments to the terms of any patents we may own or in-license in the future. In addition, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Patent term may be inadequate to protect our competitive position on our products for an adequate amount of time.

As of February 15, 2024, our overall patent portfolio includes over thirty-five (35) patent families comprising issued patents, pending U.S. and PCT International patent applications, and pending patent applications in foreign jurisdictions. The patents and patent applications have claims relating to our current product candidates, methods of use and manufacturing processes, as well as claims directed to potential future products and developments.

TEAD Inhibitor Patent Families

As of February 15, 2024, we solely own nine patent families related to TEAD inhibitors, compositions thereof, and methods of their use. Any U.S. or foreign patents that issue from these patent families, if granted and all appropriate maintenance fees paid, are expected to expire from 2040 to 2044, not including any patent term adjustment, patent term extension, or supplementary protection certificate ("SPC"). These patent families are described in more detail below.

- We have one TEAD patent family directed to a first collection of TEAD inhibitors, compositions thereof, and methods of their use. As of February 15, 2024, this TEAD patent family contains two issued U.S. patents and one pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, China, Australia, Canada, India, South Korea, Mexico, Argentina, and Taiwan. The issued U.S. patents include composition of matter claims encompassing IK-930 and method of treatment claims. Our issued U.S. patents and any U.S. or foreign patents that issue in the future from this TEAD patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2040, not including any patent term adjustment, patent term extension, or SPC.
- We have one TEAD patent family directed to a second collection of TEAD inhibitors, compositions thereof, and methods of their use. As of February 15, 2024, this TEAD patent family contains one issued U.S. patent and a pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, China, Australia, Canada, India, South Korea, Mexico, Argentina, and Taiwan. Our issued U.S. patent and any U.S. or foreign patents that issue in the future from this TEAD patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2040, not including any patent term adjustment, patent term extension, or SPC.
- We have one TEAD patent family directed to a third collection of TEAD inhibitors, compositions thereof, and methods of their use. As of February 15, 2024, this patent family contains one pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, China, Australia, Canada, India, and South Korea. Any U.S. or foreign patents that issue from this TEAD patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2041, not including any patent term adjustment, patent term extension, or SPC.
- We have one TEAD patent family directed to combinatorial methods of using TEAD inhibitors. As of February 15, 2024, this patent family contains one pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, China, Australia, Canada, and South Korea. Any U.S. or foreign patents that issue from this TEAD patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2042, not including any patent term adjustment, patent term extension, or SPC.
- We have one TEAD patent family directed to translational methods of selecting patients for treatment with TEAD inhibitors. As of February 15, 2024, this patent family contains one pending PCT application. Any U.S. or foreign patents that issue from this TEAD patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2042, not including any patent term adjustment, patent term extension, or SPC.
- We have one TEAD patent family directed to certain TEAD inhibitor formulations, and methods of their use. As of February 15, 2024, this patent family contains one pending PCT application. Any U.S. or foreign patents that issue from this TEAD patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2042, not including any patent term adjustment, patent term extension, or SPC.
- We have one TEAD patent family directed to crystal and salt forms of certain TEAD inhibitors, compositions thereof, and methods of their use. As of February 15, 2024, this patent family contains one pending PCT application. Any U.S. or foreign patents that issue from this TEAD patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2043, not including any patent term adjustment, patent term extension, or SPC.
- We have one TEAD patent family directed to certain TEAD inhibitor combination therapy technologies. As of February 15, 2024, this patent family contains one pending PCT application. Any U.S. or foreign patents that issue from this TEAD patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2043, not including any patent term adjustment, patent term extension, or SPC.
- We have one TEAD patent family directed to the use of certain TEAD inhibitors for treating certain selected patients. As of February 15, 2024, this patent family contains one U.S. provisional patent application. Any U.S. or foreign patents that issue from this TEAD patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2044, not including any patent term adjustment, patent term extension, or SPC.

Our current lead TEAD inhibitor, IK-930, is covered by our solely owned U.S. patents with composition of matter claims and method of treatment claims, which are expected to expire in 2040, not including any patent term adjustment, patent term extension, or SPC. Our current lead TEAD inhibitor, IK-930, compositions thereof, and methods of the use, are also covered by our solely owned pending U.S. and foreign patent applications, whereby any U.S. or foreign patents that, if granted and all appropriate maintenance fees paid, are expected to expire from 2040 to 2044, not including any patent term adjustment, patent term extension, or SPC.

MEK Inhibitor Patent Families

As of February 15, 2024, we solely own seven patent families related to MEK inhibitors, compositions thereof, and methods of their use. Any U.S. or foreign patents that issue from these patent families, if granted and all appropriate maintenance fees paid, are expected to expire from 2042 to 2044, not including any patent term adjustment, patent term extension or SPC. These patent families are described in more detail below.

- We have one MEK patent family directed to a first collection of MEK inhibitors, compositions thereof, and methods of their use. As of February 15, 2024, this MEK patent family contains one pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, China, Australia, Canada, India, and South Korea. Any U.S. or foreign patents that issue from this MEK patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2042, not including any patent term adjustment, patent term extension, or SPC.
- We have one MEK patent family directed to a second collection of MEK inhibitors, compositions thereof, and methods of their use. As of February 15, 2024, this MEK patent family contains one pending PCT application. Any U.S. or foreign patents that issue from this MEK patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2043, not including any patent term adjustment, patent term extension, or SPC.
- We have one MEK patent family directed to a third collection of MEK inhibitors, compositions thereof, and methods of their use. As of February 15, 2024, this MEK patent family contains one pending PCT application. Any U.S. or foreign patents that issue from this MEK patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2043, not including any patent term adjustment, patent term extension, or SPC.
- We have one MEK patent family directed to a fourth collection of MEK inhibitors, compositions thereof, and methods of their use. As of February 15, 2024, this MEK patent family contains one issued U.S. patent, one pending U.S. non-provisional application, one pending PCT application, and pending applications in foreign jurisdictions, such as Argentina and Taiwan. The issued U.S. patent includes composition of matter claims encompassing IK-595. Our issued U.S. patent and any U.S. or foreign patents that issue in the future from this MEK patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2043, not including any patent term adjustment, patent term extension, or SPC.
- We have one MEK patent family directed to combinatorial methods of using MEK inhibitors. As of February 15, 2024, this MEK patent family contains three pending U.S. provisional applications. Any U.S. or foreign patents that issue from this MEK patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2044, not including any patent term adjustment, patent term extension, or SPC.
- We have one MEK patent family directed to crystal and salt forms of certain MEK inhibitors, compositions thereof, and methods of their use. As of February 15, 2024, this MEK patent family contains one pending U.S. provisional application. Any U.S. or foreign patents that issue from this MEK patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2044, not including any patent term adjustment, patent term extension, or SPC.
- We have one MEK patent family directed to crystal and salt forms of certain MEK inhibitors, compositions thereof, and methods of their use. As of February 15, 2024, this MEK patent family contains one pending U.S. provisional application. Any U.S. or foreign patents that issue from this MEK patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2044, not including any patent term adjustment, patent term extension, or SPC.

Our current lead MEK inhibitor, IK-595, is covered by our solely owned U.S. patent with composition of matter claims, which is expected to expire in 2043, not including any patent term adjustment, patent term extension, or SPC. Our current lead MEK inhibitor, IK-595, compositions thereof, and methods of the use, are also covered by our solely owned pending U.S. and foreign patent applications, whereby any U.S. or foreign patents that, if granted and all appropriate maintenance fees paid, are expected to expire from 2043 to 2044, not including any patent term adjustment, patent term extension, or SPC.

Other Ikena Patent Families

As of February 15, 2024, we exclusively own three patent families related to inhibitors and other molecules targeting the RAS signaling pathway, compositions thereof, and methods of their use, including one pending PCT application and at least four pending U.S. provisional patent applications. Any U.S. or foreign patents that issue from these patent families, if granted and all appropriate maintenance fees paid, are expected to expire from 2043 to 2044, not including any patent term adjustment, patent term extension, or SPC.

As of February 15, 2024, we solely own seven patent families related to AHR antagonists, compositions thereof, and methods of their use. U.S. patents that have issued in these patent families and any further U.S. or foreign patents that issue from these patent families, if granted and all appropriate maintenance fees paid, are expected to expire from 2038 to 2043, not including any patent term adjustment, patent term extension, or SPC. The published patent families are described in more detail below.

- AHR antagonists patent family one is directed to AHR antagonists, compositions thereof, and methods of their use. As of February 15, 2024, this AHR antagonists patent family contains three U.S. patents, patents in foreign jurisdictions such as Japan, China, India, Mexico, Singapore, Taiwan, Eurasia, and Chile, and pending applications in the U.S. and foreign jurisdictions, such as Europe, Australia, Canada, and South Korea. These U.S. and foreign patents and any further U.S. or foreign patents that may issue from AHR antagonists patent family one, if granted and all appropriate maintenance fees paid, are expected to expire in 2038, not including any patent term adjustment, patent term extension, or SPC.
- AHR antagonists patent family two is directed to AHR antagonists, compositions thereof, and methods of their use. As of February 15, 2024, this AHR antagonists patent family contains two U.S. patents, patents in foreign jurisdictions such as Japan, India, Mexico, and Israel, and pending applications in foreign jurisdictions, such as Europe, China, Australia, Canada, and South Korea. These U.S. and foreign patents and any further foreign patents that may issue from AHR antagonists patent family two, if granted and all appropriate maintenance fees paid, are expected to expire in 2038, not including any patent term adjustment, patent term extension, or SPC.
- AHR antagonists patent family three is directed to AHR antagonists, compositions thereof, and methods of their use. As of February 15, 2024, this AHR antagonists patent family contains a pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, China, and Canada. Any U.S. or foreign patents that issue from AHR antagonists patent family three, if granted and all appropriate maintenance fees paid, are expected to expire in 2039, not including any patent term adjustment, patent term extension, or SPC.
- AHR antagonists patent family four is directed to crystal forms of certain AHR antagonists, compositions thereof, and methods of their use. As of February 15, 2024, this AHR antagonists patent family contains one issued U.S. patent, and pending applications in the U.S. and foreign jurisdictions, such as Europe, Japan, China, and Canada. Any U.S. or foreign patents that issue from AHR antagonists patent family four, if granted and all appropriate maintenance fees paid, are expected to expire in 2040, not including any patent term adjustment, patent term extension, or SPC.
- AHR antagonists patent family five is directed to certain AHR antagonist formulations, and methods of their use. As of February 15, 2024, this AHR antagonists patent family contains a pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, China, and Canada. Any U.S. or foreign patents that issue from AHR antagonists patent family five, if granted and all appropriate maintenance fees paid, are expected to expire in 2040, not including any patent term adjustment, patent term extension, or SPC.
- AHR antagonists patent family six is directed to methods of selecting patients for AHR antagonist treatment. As of February 15, 2024, this AHR antagonists patent family contains a pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, China, and Canada. Any U.S. or foreign patents that issue from AHR antagonists patent family six, if granted and all appropriate maintenance fees paid, are expected to expire in 2041, not including any patent term adjustment, patent term extension, or SPC.
- AHR antagonists patent family seven is directed to methods of using AHR antagonists. As of February 15, 2024, this AHR antagonists patent family contains a pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, China, and Canada. Any U.S. or foreign patents that issue from AHR antagonists patent family seven, if granted and all appropriate maintenance fees paid, are expected to expire in 2041, not including any patent term adjustment, patent term extension, or SPC.

As of February 15, 2024, we have an exclusive license through the AskAt Agreement to six patent families directed to EP4 antagonists, crystal forms thereof, compositions thereof, and methods of their use. The U.S. and foreign patents that have issued in these patent families and any further U.S. or foreign patents that may issue from these patent families, if granted and all appropriate maintenance fees paid, are expected to expire from 2024 to 2037, not including any patent term adjustment, patent term extension, or SPC.

As of February 15, 2024, we and AskAt Inc. jointly own three patent families directed to EP4 antagonist compositions, methods of making certain EP4 antagonists and their formulations, and methods of their use. Any U.S. or foreign patents that issue from these patent families, if granted and all appropriate maintenance fees paid, are expected to expire in 2039, not including any patent term adjustment, patent term extension, or SPC.

As of February 15, 2024, we solely own one patent family directed to EP4 antagonist salts and crystal forms, and methods of using the same. Any U.S. or foreign patents that issue from this patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2039, not including any patent term adjustment, patent term extension or SPC. The AskAt Agreement will be terminated as of March 20, 2024, and all assets, including the jointly owned patent families, will be returned to AskAt, at which point no further costs will be incurred by us.

As of February 15, 2024, we have an exclusive license through the License Agreement with the University to three patent families related to the IK-412 kynurenine program. The U.S. and foreign patents that have issued in these three patent families and any further U.S. or foreign patents that may issue from these patent families, if granted and all appropriate maintenance fees paid, are expected to expire from 2034 to 2039, not including any patent term adjustment, patent term extension, or SPC.

As of February 15, 2024, we also solely own one patent family related to the IK-412 kynurenine program. Any U.S. or foreign patents that issue from this patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2040, not including any patent term adjustment, patent term extension, or SPC.

Trade Secret Protection

In addition to patents, we rely on unpatented trade secrets, know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and confidential know-how are difficult to protect. In particular, we anticipate that with respect to the building of our compound library, our trade secrets and know-how will over time be disseminated within the industry through independent development and public presentations describing the methodology. We seek to protect our proprietary information, in part, by executing confidentiality agreements with our collaborators and scientific advisors and non-competition, non-solicitation, confidentiality and invention assignment agreements with our employees and consultants. We have also executed agreements requiring assignment of inventions with selected consultants, scientific advisors and collaborators. The confidentiality agreements we enter into are designed to protect our proprietary information and the agreements or clauses requiring assignment of inventions to us are designed to grant us ownership of technologies that are developed through our relationship with the respective counterparty. We cannot guarantee that we will have executed such agreements with all applicable employees and contractors, or that these agreements will afford us adequate protection of our intellectual property and proprietary information rights. In addition, our trade secrets and/or confidential know-how may become known or be independently developed by a third party or misused by any collaborator to whom we disclose such information. These agreements may also be breached, and we may not have an adequate remedy for any such breach. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to copy aspects of our products or to obtain or use information that we regard as proprietary. Although we take steps to protect our proprietary information, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information. For more information regarding the risks related to our intellectual property, please see “Risk Factors—Risks Related to Our Intellectual Property.”

Trademark Protection

We have obtained registered trademarks with the USPTO for the IKENA and IKENA ONCOLOGY word marks for services. We have pending applications for trademark protection with the USPTO for the IKENA and IKENA ONCOLOGY word marks for goods.

Commercialization

Subject to receiving marketing approvals, we expect to commence commercialization activities by building a focused sales and marketing organization in the United States to sell our products. We believe that such an organization will be able to address the community of oncologists who are the key specialists in treating the patient populations for which our product candidates are being developed. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with researchers and practitioners in relevant fields of medicine. Outside the United States, we expect to enter into distribution and other marketing arrangements with third parties for any of our product candidates that obtain marketing approval.

Manufacturing

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates as well as for clinical testing and commercial manufacture if our product candidates receive marketing approval.

All of our drug candidates are small molecules and are manufactured in synthetic processes from available starting materials. The chemistry appears amenable to scale-up and does not currently require unusual equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

If necessary, we expect to rely on third parties for the manufacture of companion diagnostics for our products, which are assays or tests to identify an appropriate patient population. Depending on the technology solutions we choose, we may rely on multiple third parties to manufacture and sell a single test.

Governmental Regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, recordkeeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drugs. We, along with our vendors, contract research organizations ("CROs"), clinical investigators, and contract manufacturing organizations ("CMOs") will be required to navigate the various preclinical, clinical, manufacturing and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our product candidates. The process of obtaining regulatory approvals of drugs and ensuring subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

In the United States, where we are initially focusing our drug development, the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act, as amended ("FD&C Act"), and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. If we fail to comply with applicable FDA or other requirements at any time with respect to product development, clinical testing, approval or any other regulatory requirements relating to product manufacture, processing, handling, storage, quality control, safety, marketing, advertising, promotion, packaging, labeling, export, import, distribution, or sale, we may become subject to administrative or judicial sanctions or other legal consequences. These sanctions or consequences could include, among other things, the FDA's refusal to approve pending applications, issuance of clinical holds for ongoing studies, suspension or withdrawal of approved applications, warning or untitled letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

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

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice ("GLP") requirements;
- completion of the manufacture, under current Good Manufacturing Practices ("cGMP") conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;
- submission to the FDA of an IND which must become effective before clinical trials may begin and must be updated annually and when certain changes are made;
- approval by an institutional review board ("IRB") or independent ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with applicable IND regulations, good clinical practice ("GCP") requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- preparation and submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review;

- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the drug will be produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug product's identity, strength, quality and purity;
- satisfactory completion of FDA audit of the clinical trial sites that generated the data in support of the NDA;
- payment of user fees for FDA review of the NDA; and
- FDA review and approval of the NDA, including, where applicable, consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States.

Preclinical Studies and Clinical Trials for Drugs

Before testing any drug in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of product chemistry, formulation and stability, as well as *in vitro* and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulation and requirements, including GLP requirements for safety/toxicology studies. The results of the preclinical studies, together with manufacturing information and analytical data, must be submitted to the FDA as part of an IND.

An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before clinical trials may begin. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes the results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. Some long-term preclinical testing may continue after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks, and imposes a full or partial clinical hold. FDA must notify the sponsor of the grounds for the hold and any identified deficiencies must be resolved before the clinical trial can begin. Submission of an IND may result in the FDA not allowing clinical trials to commence or not allowing clinical trials to commence on the terms originally specified in the IND. A clinical hold can also be imposed once a trial has already begun, thereby halting the trial until the deficiencies articulated by FDA are corrected.

The clinical stage of development involves the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, who generally are physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable compared to the anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trials to public registries. Information about clinical trials, including results for clinical trials other than Phase 1 investigations, must be submitted within specific timeframes for publication on www.ClinicalTrials.gov, a clinical trials database maintained by the National Institutes of Health.

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

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

- *Phase 1*—Phase 1 clinical trials involve initial introduction of the investigational product in a limited population of healthy human volunteers or patients with the target disease or condition. These studies are typically designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, excretion the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.

- *Phase 2*—Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the drug's potential efficacy, to determine the optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks.
- *Phase 3*—Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and physician labeling. Generally, two adequate and well-controlled Phase 3 trials are required by the FDA for approval of an NDA.

In March 2022, the FDA released final guidance titled "Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics," which outlines how drug developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology drug development (*i.e.*, the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by FDA. Expansion cohort trials can potentially bring efficiency to drug development and reduce development costs and time.

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

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators fifteen (15) days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk for human volunteers and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor's initial receipt of the information.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing the drug product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and manufacturers must develop, among other things, methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Marketing Approval for Drugs

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA package requesting approval to market the product for one or more indications. An NDA is a request for approval to market a new drug for one or more specified indications and must contain proof of the drug's safety and efficacy for the requested indications. The marketing application is required to include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational drug to the satisfaction of the FDA. FDA must approve an NDA before a drug may be marketed in the United States.

The FDA reviews all submitted NDAs to ensure they are sufficiently complete to permit substantive review before it accepts them for filing and may request additional information rather than accepting the NDA or BLA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt, and such decision could include a refusal to file by the FDA. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA. The FDA reviews an NDA to determine, among other things, whether the product is safe and effective for the indications sought and whether the facility in which it is manufactured, processed, packaged or held meets standards designed, including cGMP requirements, designed to assure and

preserve the product's continued identity, strength, quality and purity. Under the goals and polices agreed to by the FDA under the Prescription Drug User Fee Act ("PDUFA"), the FDA targets ten months, from the filing date, in which to complete its initial review of a new molecular entity NDA and respond to the applicant, and six months from the filing date of a new molecular entity NDA for priority review. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs and the review process is often extended by FDA requests for additional information or clarification.

Further, under PDUFA, as amended, each NDA must be accompanied by a substantial user fee. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy ("REMS") if it believes that a risk evaluation and mitigation strategy is necessary to ensure that the benefits of the drug outweigh its risks. A REMS can include use of risk evaluation and mitigation strategies like medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, special monitoring or other risk-minimization tools.

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

Before approving an NDA the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP and other requirements and the integrity of the clinical data submitted to the FDA.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a Complete Response Letter. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response Letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response Letter, the FDA may require additional clinical or preclinical testing or recommend other actions, such as requests for additional information or clarification, that the applicant might take in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications.

Even if the FDA approves a product, depending on the specific risk(s) to be addressed it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Drug Designation and Exclusivity

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

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to a seven-year period of marketing exclusivity during which the FDA may not approve any other applications to market the same therapeutic agent for the same indication, except in limited circumstances, such as a subsequent product's showing of clinical superiority over the product with orphan exclusivity or where the original applicant cannot produce sufficient quantities of product. Competitors, however, may receive approval of different therapeutic agents for the indication for which the orphan product has exclusivity or obtain approval for the same therapeutic agent for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for the same therapeutic agent for the same indication before we do, unless we are able to demonstrate that our product is clinically superior. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. Further, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Expedited Development and Review Programs for Drugs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include fast track designation, breakthrough therapy designation, priority review and accelerated approval, and the purpose of these programs is to either expedite the development or review of important new drugs to get them to patients more quickly than standard FDA review timelines typically permit.

A new drug is eligible for fast track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast track designation applies to the combination of the product candidate and the specific indication for which it is being studied. Fast track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed. Rolling review means that the FDA may review portions of the marketing application before the sponsor submits the complete application.

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

Any product submitted to the FDA for approval, including a product with fast track or breakthrough therapy designation, may also be eligible for additional FDA programs intended to expedite the review and approval process, including priority review designation and accelerated approval. A product is eligible for priority review, once an NDA is submitted, if the product that is the subject of the marketing application has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. Under priority review, the FDA's goal date to take action on the marketing application is six months compared to ten months for a standard review.

Products are eligible for accelerated approval if they are designed to treat a serious or life-threatening disease or condition and can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, which is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

Accelerated approval is usually contingent on a sponsor's agreement to conduct, in a diligent manner, adequate and well-controlled additional post-approval confirmatory trials to verify and describe the product's clinical benefit. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after accelerated approval is granted. Additionally, under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or an indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the Agency, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the pre-approval review period. After the 120-day period has passed, all advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, fast track designation, breakthrough therapy designation, priority review and accelerated approval do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval, though they may expedite the development or review process.

Pediatric Information and Pediatric Exclusivity

Under the Pediatric Research Equity Act ("PREA"), certain NDAs and certain NDA supplements must contain data that can be used to assess the safety and efficacy of the product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The FD&C Act requires that a sponsor who is planning to submit a marketing application for a product candidate that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan ("PSP") within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs. Unless otherwise required by regulation, PREA does not apply to a drug for an indication for which orphan designation has been granted, except that PREA will apply to an original NDA for a new active ingredient that is orphan-designated if the drug is a molecularly targeted cancer product intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer.

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

U.S. Post-approval Requirements for Drugs

Drugs manufactured or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, reporting of adverse experiences with the product, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe approved products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, including not only by company employees but also by agents of the company or those speaking on the company's behalf, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties, including liabilities under the False Claims Act ("FCA") where products obtain reimbursement under federal health care programs. Promotional materials for approved drugs must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-market testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. In addition, manufacturers and their subcontractors involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements on sponsors and their CMOs. 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 a sponsor may use. Manufacturers and manufacturers' facilities are also required to comply with applicable product tracking and tracing requirements. 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. Failure to comply with statutory and regulatory requirements may subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution. There is also a continuing, annual program user fee for any marketed product.

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

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

Regulation of Companion Diagnostics

Companion diagnostics identify patients who are most likely to benefit from a particular therapeutic product; identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness. Companion diagnostics are regulated as medical devices by the FDA. In the United States, the FD&C Act, and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption or FDA exercise of enforcement discretion applies, diagnostic tests generally require marketing clearance or approval from the FDA prior to commercialization. The two primary types of FDA marketing authorization applicable to a medical device are clearance of a premarket notification ("510(k)") and approval of a premarket approval application ("PMA").

To obtain 510(k) clearance for a medical device, or for certain modifications to devices that have received 510(k) clearance, a manufacturer must submit a premarket notification demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or to a pre-amendment device that was in commercial distribution before May 28, 1976 (a "predicate device") for which the FDA has not yet called for the submission of a PMA. In making a determination that the device is substantially equivalent to a predicate device, the FDA compares the proposed device to the predicate device and assesses whether the subject device is comparable to the predicate device with respect to intended use, technology, design and other features which could affect safety and effectiveness. If the FDA determines that the subject device is substantially equivalent to the predicate device, the subject device may be cleared for marketing. The 510(k) premarket notification pathway generally takes from three to twelve months from the date the application is completed, but can take significantly longer.

A PMA must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the quality system regulation ("QSR"), which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. The FDA's review of an initial PMA is required by statute to take between six to ten months, although the process typically takes longer, and may require several years to complete. If the FDA evaluations of both the PMA and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny the approval of the PMA or issue a not approvable letter. A not approvable letter will

outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. Once granted, PMA approval may be withdrawn by the FDA if compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

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

In January 2024, the FDA announced its intention to initiate the reclassification process for most in vitro diagnostics, including companion diagnostics. Further, the FDA indicated that in addition to the reclassification process, the FDA will continue taking a risk-based approach in the initial classification of individual in vitro diagnostics to determine whether a new test may be classified into Class II through the de novo classification process. In so doing, the FDA indicated that it may regulate most future companion diagnostics as Class II devices, which would likely entail less onerous development, approval, and post-market regulatory requirements than what is required for Class III medical devices and diagnostics that are subject to the PMA pathway.

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

Other Regulatory Matters

Following product approval, where applicable, the manufacturing, sales, promotion and other activities around product candidates and/or commercialization are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA. Regulatory agencies with authority over product candidates may include, and are not limited to, the Centers for Medicare & Medicaid Services ("CMS") other divisions of the U.S. Department of Health and Human Services ("HHS"), the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments and governmental agencies.

Other Healthcare Laws

Healthcare providers, physicians, and third-party payors, both governmental and commercial, will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we develop, market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including, but not limited to, those described below.

- The federal Anti-Kickback Statute ("AKS") prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity need not have actual knowledge of the federal AKS or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus treble damages, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal AKS constitutes a false or fraudulent claim for purposes of the civil FCA.
- The federal civil and criminal false claims laws, including the FCA, prohibit individuals or entities from, among other things, knowingly presenting or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using, or causing to be made or used, a false statement or record

material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity, and potentially individuals associated with the entity, from participation in Medicare, Medicaid and other federal healthcare programs.

- The federal civil monetary penalties laws impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary, if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies.
- The Health Insurance Portability and Accountability Act of 1996 ("HIPAA") imposes criminal and civil liability for knowingly and willfully executing a scheme or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, or falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the AKS, a person or entity may be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH") and their respective implementing regulations, impose, among other things, specified requirements on covered entities and their respective business associates relating to the privacy and security of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates in some cases, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.
- The Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "ACA") imposed new annual reporting requirements for certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, for certain payments and "transfers of value" provided to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors); other non-physician providers such as physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives; and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.
- Federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products.
- Federal consumer protection and unfair competition laws broadly regulate marketplace activities and activities that potentially harm consumers.
- Analogous state and foreign laws and regulations, including, but not limited to, state anti-kickback and false claims laws, may be broader in scope than the provisions described above and may apply regardless of payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and relevant federal government compliance guidance; require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers; restrict marketing practices or require disclosure of marketing expenditures and pricing information. State and foreign laws may govern the privacy and security of health information in some circumstances. These myriad data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies continue to scrutinize interactions between healthcare companies and healthcare providers and increase investigations, prosecutions, convictions and significant settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other

healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to similar actions, penalties and sanctions. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

Insurance Coverage and Reimbursement

In the U.S. and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the U.S. such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. In the U.S., the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within the HHS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Factors payors consider in determining reimbursement are based on whether the product is, among other considerations:

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

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, which will require additional expenditure above and beyond the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Current and Future Healthcare Reform Legislation

In the United States and certain foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the United States

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

- created an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs;
- expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price" ("AMP") for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide point-of-sale-discounts off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and
- created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been judicial, Congressional and executive challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, will remain in effect through 2031. The American Rescue Plan Act of 2021 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. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025, absent further legislation. These laws and regulations may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

The Inflation Reduction Act of 2022 (the "IRA") includes several provisions that may impact our business to varying degrees, including provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries to $2,000 starting in 2025, thereby effectively eliminating the coverage gap; impose new manufacturer financial liability on certain drugs under Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition; require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation; and delay until January 1, 2032 the implementation of the HHS rebate rule that would have limited the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that rare disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation that challenges the constitutionality of the IRA's Medicare drug price negotiation program. The effects of the IRA on our business and the healthcare industry in general is not yet known.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, including bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. For example, in 2020, FDA released its regulations regarding the importation of drugs under section 804 of the Medicare Prescription Drug, Improvement, and Modernization Act of

2003, providing guidance for states to build and submit importation plans for drugs from Canada. CMS has stated drugs imported by states under this rule will not be eligible for federal Medicaid rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes under the Medicaid Drug Rebate Program. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates.

Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. The IRA further delayed implementation of this rule to January 1, 2032. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

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

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed upon. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union Member States may approve a specific price for a product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

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

If any products that we may develop are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, labeling, packaging, distribution, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws, among other requirements to which we may be subject.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive recordkeeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements may subject firms to legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, exclusion from federal healthcare programs, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, relabeling or repackaging, or refusal to allow a firm to enter into supply contracts, including government contracts. Any claim or action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on marketing, sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling or packaging; (iii) the recall or discontinuation of our products; or (iv) additional recordkeeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Other U.S. Environmental, Health and Safety Laws and Regulations

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

We maintain workers' compensation insurance to cover us for costs and expenses that we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

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

Government Regulation of Drugs Outside of the United States

To market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, manufacturing, commercial sales and distribution of our products. For instance, in the United Kingdom and the EU, medicinal products must be authorized for marketing by using either the centralized authorization procedure or national authorization procedures.

- *Centralized procedure*—The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid throughout the EU, and in the additional Member States of the European Economic Area (Iceland, Lichtenstein and Norway) ("EEA"). Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene therapy, somatic cell therapy and tissue engineered products) and products with a new active substance indicated for the treatment of certain diseases, which includes products for the treatment of cancer. For medicines that do not fall within one of the mandatory categories, an applicant still has the option of submitting an application for a centralized marketing authorization to the European Medicines Agency ("EMA") as long as the medicine concerned contains a new active substance not yet authorized in the EU, is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health in the EU. If pursuing a marketing authorization of a product candidate for a therapeutic indication under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use ("CHMP") is responsible for conducting an initial assessment of whether a product meets the required quality, safety and efficacy requirements, and whether a product has a positive benefit/risk ratio. Under the centralized procedure the maximum timeframe for the evaluation of a marketing authorization application ("MAA") by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding clock stops, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

- *National authorization procedures*—There are also two other possible routes to authorize products for therapeutic indications in several countries, which are available for products that fall outside the scope of the centralized procedure:
    - *Decentralized procedure*—Using the decentralized procedure, an applicant may apply for simultaneous authorizations in more than one EU Member State for a medicinal product that has not yet been authorized in any EU Member State and that does not fall within the mandatory scope of the centralized procedure.
    - *Mutual recognition procedure*—In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, additional marketing authorizations can be sought from other EU Member States in a procedure whereby the countries concerned recognize the validity of the original, national marketing authorization.

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

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain is no longer covered by centralized marketing authorizations currently (under the Northern Ireland Protocol, centralized marketing authorizations continue to be recognized in Northern Ireland). On January 1, 2024, a new international recognition framework was put in place by the Medicines and Healthcare Products Regulatory Agency ("MHRA"), under which the MHRA will have regard to decisions on the approval of a marketing authorization made by the EMA and certain other regulators when considering whether to grant a UK marketing authorization. The MHRA also has the power to have marketing authorizations approved in EU Member States through decentralized or mutual recognition procedures with a view to more quickly grant a marketing authorization in the UK or Great Britain.

In the EU, new products for therapeutic indications that are authorized for marketing (i.e., innovator products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic applicants from referencing the preclinical and clinical trial data contained in the dossier of the innovator product when applying for a generic marketing authorization in the EU during a period of eight years from the date on which the innovator product was first authorized in the EU. The additional two-year period of market exclusivity period prevents a successful generic applicant from commercializing its product in the EU until ten years have elapsed from the initial authorization of the reference product in the EU. The overall ten-year period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with currently approved therapies. There is no guarantee that a product will be considered by the EMA to be a new chemical entity, and products may not qualify for data exclusivity. Even if a product is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company could nevertheless also market another version of the product if such company obtained a marketing authorization based on an MAA with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, in the EU a medicinal product may be designated as an orphan medicinal product if it meets the following criteria: (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EU to justify the investment needed for its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition, or if such a method exists, the product will be of a significant benefit to those affected by that condition. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. During this ten-year orphan market exclusivity period, no MAA shall be accepted, and no marketing authorization shall be granted for a similar medicinal product. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Market exclusivity may also be revoked in very select cases, such as if (i) it is established that a similar medicinal product is safer, more effective or otherwise clinically superior than the authorized product; (ii) the marketing authorization holder of the authorized product consents to such revocation; or (iii) the marketing authorization holder of the authorized product cannot supply enough orphan medicinal product. An orphan medicinal product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. The application for orphan designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the MAA if the orphan designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Prior to obtaining a marketing authorization in the EU, applicants must demonstrate compliance with all measures included in an EMA-approved pediatric investigation plan ("PIP") covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, the so-called Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA ("PDCO") may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP. If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the SPC, provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to 2 years before the SPC expires, even where the trial results are negative. In the case of orphan medicinal products, a two year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

In May 2017, the EU adopted the Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices ("IVDR") which became applicable on 26 May 2022 and repealed Directive 98/79/EC on *in vitro* diagnostic medical devices. Devices that comply with the requirements of the IVDR are entitled to bear the CE conformity marking, indicating that the device conforms to the general safety and performance requirements of the IVDR, and, accordingly, can be commercially distributed throughout the EU (in-vitro diagnostic medical devices cannot be marketed in the EU without a CE Mark). The method of assessing conformity varies depending on the class of the product, but normally involves a third-party assessment by a "Notified Body". This third-party assessment may consist of an audit of the manufacturer's quality system and specific testing of the manufacturer's product.

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

In April 2014, the Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted which replaced the Clinical Trials Directive 2001/20/EC. The Clinical Trials Regulation was entered into application on January 31, 2022 and is directly applicable in all the EU Member States (meaning no national implementing legislation in each Member State is required). The transitory provisions of the Clinical Trials Regulation provide that, by January 31, 2025, all ongoing clinical trials must have transitioned to the EU Clinical Trials Regulation. The Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single-entry point, through the Clinical Trials Information System, ("CTIS"); a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The aforementioned EU rules are generally applicable in the EEA.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the EU for all medicines (including those for rare diseases and for children). The European Commission has provided the legislative proposals to the European Parliament and the European Council for their review and approval. In October 2023, the European Parliament published draft reports proposing amendments to the legislative proposals, which will be debated by the European Parliament. Once the European Commission's legislative proposals are approved (with or without amendment), they will be adopted into EU law.

Government Regulation of Data Collection Outside of the United States

Internationally, numerous jurisdictions have their own data security and privacy legal frameworks with which we will be required to comply if we conduct clinical trials in those jurisdictions or otherwise conduct business in those jurisdictions. We conduct clinical trials, and plan to conduct future clinical trials, in the EEA and the UK and therefore will collect personal data from data subjects in the EEA and the UK, and we will be subject to additional privacy restrictions. The collection, use, storage, disclosure, transfer or other processing of personal data in the EEA and UK is governed by the EU General Data Protection Regulation (the "EU GDPR"), with regards to the EEA, and the UK General Data Protection Regulation ("UK GDPR"), with regards to the UK, as well as applicable national data protection legislation and requirements in force within the EEA Member States and the UK (including the UK Data Protection Act 2018). In this Annual Report on Form 10-K, "GDPR" refers to both the EU GDPR and the UK GDPR, unless specified otherwise. The GDPR applies to the processing of personal data by any company established in the EEA/UK and to companies established outside the EEA/UK to the extent they process personal data in connection with the offering of goods or services to data subjects in the EEA/UK or the monitoring of the behavior of data subjects in the EEA/UK. The GDPR enhances data protection obligations for controllers of personal data, including stringent requirements relating to ensuring an appropriate legal basis or conditions applies to the processing of personal data, the consent (if required) of data subjects, expanded disclosures about how personal data is used, enhanced requirements for securing personal data, requirements to conduct data protection assessments for "high risk" processing, limitations on retention of personal data, mandatory data breach notification and "privacy by design" requirements, and creates direct obligations on service providers acting as processors. The GDPR also imposes strict rules on the transfer of personal data outside of the EEA to countries that do not ensure an adequate level of protection, like the United States in certain circumstances. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EA Member States, (which may deviate slightly from the GDPR) and the UK, may result in fines of up to 4% of a company's global revenue for the preceding financial year, or €20,000,000 (£17.5 million for the UK), whichever is greater. Moreover, the GDPR grants data subjects and non-profit associations the right to lodge complaints with supervisory authorities, seek judicial remedies, and claim material and non-material damages resulting from infringement of the GDPR. Given the strict nature of its data protection obligations, maintaining compliance with the GDPR will require significant time, resources and expense, and we may be required to put in place additional controls and processes ensuring compliance the GDPR.

In addition, many jurisdictions outside of Europe are also considering and/or have enacted comprehensive data protection legislation. Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. In addition, should we utilize third party distributors outside of the United States, compliance with such foreign governmental regulations would generally be the responsibility of such distributors, who may be independent contractors over whom we have limited control. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition and results of operations.

Brexit and the Regulatory Framework in the United Kingdom

The UK formally left the EU on January 31, 2020, and, the EU and the UK have concluded a trade and cooperation agreement ("TCA") which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not provide for wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework currently continues to apply in Northern Ireland). The regulatory regime in Great Britain therefore aligns in many ways with current EU regulations, however it is likely that these regimes will diverge significantly in the future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation. However, notwithstanding that there is no wholesale recognition of EU pharmaceutical legislation under the TCA, under a new international recognition procedure which was put in place by the MHRA on January 1, 2024, the MHRA may take into account decisions on the approval of a marketing authorization from the EMA (and certain other regulators) when considering an application for a Great Britain marketing authorization.

On February 27, 2023, the UK government and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA will be responsible for approving all medicinal products destined for the UK market (*i.e.*, Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. A single UK-wide marketing authorization will be granted by the MHRA for all medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. The Windsor Framework was approved by the EU-UK Joint Committee on March 24, 2023, so the UK government and the EU will enact legislative measures to bring it into law. On June 9, 2023, the MHRA announced that the medicines aspects of the Windsor Framework will apply from January 1, 2025.

Human Capital

As of March 6, 2024, we had forty-three (43) full-time employees, of which seventeen (17) have M.D. or Ph.D. degrees. Within our workforce, twenty-seven (27) employees are engaged in research and development and sixteen (16) are engaged in business development, finance, legal, human resources, and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good. Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

Available Information

Our website address is https://www.ikenaoncology.com/. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Exchange Act, are available through the "Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Our code of conduct, corporate governance guidelines and the charters of our audit committee, compensation committee and nominating and corporate governance committee are available through the "Corporate Governance" portion of our website.

ITEM 1A. RISK FACTORS.

Investing in our common stock involves a high degree of risk. In evaluating the Company and our business, careful consideration should be given the risks described below, as well as the other information in this Annual Report on Form 10-K and in other documents that we file with the SEC. 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. 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 Limited Operating History, Financial Position, and Capital Requirements

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

We commenced operations in 2016 and are a targeted oncology company with a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Since our inception, we have devoted substantially all of our efforts to organizing and staffing our company, acquiring intellectual property, business planning, raising capital, conducting discovery, research and development activities, and providing general and administrative support for these operations. We have no products approved for commercial sale and therefore, have never generated any revenue from product sales, and we do not expect to in the foreseeable future. We have not obtained regulatory approvals for any of our product candidates, and there is no assurance that we will obtain approvals in the future. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

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

Our net losses were 68.2 million and $68.8 million for the twelve months ended December 31, 2023 and 2022, respectively. We had an accumulated deficit of $282.4 million as of December 31, 2023. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect our research and development expenses to increase significantly in connection with the commencement and continuation of clinical trials of our product candidates. In addition, if we obtain regulatory approval for our product candidates, we will incur significant sales, marketing, and manufacturing expenses. As a public company, we will continue to incur additional costs that we did not incur as a private company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

The amount of our future losses is uncertain and our quarterly and annual operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline. Our quarterly and annual operating results may fluctuate significantly in the future due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following:

- our ability to attract, hire, and retain qualified personnel;
- the timing and success or failure of clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- our ability to successfully open clinical trial sites and recruit and retain subjects for clinical trials, and any delays caused by difficulties in such efforts;
- our ability to obtain regulatory approval for our product candidates, and the timing and scope of any such approvals we may receive;
- the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time;
- the cost of manufacturing our product candidates and products, should they receive regulatory approval, which may vary depending on the quantity of production and the terms of our agreements with manufacturers; expenditures that we will or may incur to develop additional product candidates;
- the level of demand for our products should they receive regulatory approval, which may vary significantly;

- the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future therapeutics that compete with our product candidates;
- the changing and volatile U.S. and global economic environments; and
- future accounting pronouncements or changes in our accounting policies.

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

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

Our ability to become profitable depends upon our ability to generate revenue. To date, we have generated minimal collaborative revenue from our product candidates and have not generated revenue from product sales, and we do not expect to generate any revenue from the sale of products in the near future. We do not expect to generate significant revenue unless and until we obtain regulatory approval of, and begin to sell, one or more of our product candidates. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- successfully complete our ongoing and planned nonclinical and clinical studies for our programs;
- timely file and obtain clearance of INDs by the FDA or comparable clinical trial applications by foreign regulatory authorities, for our programs in order to commence future clinical trials;
- successfully enroll subjects in, and complete, our ongoing and planned clinical trials;
- initiate and successfully complete all safety and efficacy studies required to obtain U.S. and foreign regulatory approval for our product candidates;
- establish commercial manufacturing capabilities or make arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- obtain and maintain patent and trade secret protection or regulatory exclusivity for our product candidates;
- launch commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- obtain and maintain acceptance of the products, if and when approved, by patients, the medical community, and third-party payors;
- position our products to effectively compete with other therapies;
- obtain and maintain healthcare coverage and adequate reimbursement;
- enforce and defend intellectual property rights and claims; and
- maintain a continued acceptable safety profile of our products following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

We will require additional capital to finance our operations, which may not be available on acceptable terms, or at all. If we are unable to raise capital when needed or on terms acceptable to us, we would be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts.

The development of pharmaceutical products is capital-intensive. We are conducting clinical trials for multiple product candidates. We expect our expenses to significantly increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate and complete clinical trials of, and seek regulatory approval for, our product candidates. In addition, depending on the status of regulatory approval or, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We may also need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our current or future

product candidates or otherwise expand more rapidly than we presently anticipate. We also continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, or eliminate certain of our research and development programs or future commercialization efforts.

On May 17, 2023, we completed an underwritten registered offering ("URO"), of common stock pursuant to which we issued and sold 6,110,000 shares of our common stock at a purchase price of $6.55 per share. On August 4, 2023, we acquired Pionyr Immunotherapeutics, Inc. ("Pionyr"), in accordance with the terms of the Agreement and Plan of Merger, dated August 4, 2023 (the "Merger Agreement"). Under the terms of the Merger Agreement, at the closing of the acquisition, we acquired all of Pionyr's assets, including approximately $48.0 million in net cash at the time of closing, and we issued the holders of Pionyr common stock a total of 1,800,652 shares of the our common stock (including 153,121 shares of our non-voting common stock) at the purchase price of $7.15 per share and 4,153,439 shares of Series A Preferred Stock, also at the purchase price of $7.15 per share, each share of which was subsequently converted into one (1) share of the our common stock at a special shareholders meeting October 11, 2023. As a result of the workforce reduction that we began implementing in the first quarter of 2024 and the associated anticipated reduction in our operating expenses, we expect that our cash, cash equivalents and marketable securities are sufficient to fund our operations into the second half of 2026. However, our future capital requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, results and costs of development and clinical trials for our product candidates;
- the costs, timing, and outcomes of regulatory reviews of our product candidates;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements we may establish;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of securing manufacturing arrangements for clinical and commercial production;
- costs related to the development of any companion diagnostics we may use in the future; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our product candidates.

Identifying potential product candidates and conducting preclinical development testing and clinical trials is a time-consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenue, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Disruptions in the financial markets in general and the recent volatility in the capital markets may make equity and debt financing more difficult to obtain and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product that has received regulatory approval or be unable to expand our operations or otherwise capitalize on our business opportunities as desired, which could materially affect our business, financial condition and results of operations.

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

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

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

Furthermore, based on our public float as of the date of the filing of this Annual Report on Form 10-K, and for so long as our public float is less than $75.0 million, the amount we can raise through primary public offerings of securities in any twelve-month period using shelf registration statements is limited to an aggregate of one-third of our public float pursuant to Instruction I.B.6. to Form S-3, which is referred to as the “baby shelf” rule.

We have recently undertaken internal restructuring activities, and may do so again in the future. The assumptions underlying these activities may prove to be inaccurate, or we may fail to achieve the expected benefits therefrom.

In light of recent macroeconomic conditions, we have made, and will continue to make, judgments as to whether we should further reduce or otherwise change our workforce. For example, in the first quarter of 2024, we began implementing a plan to reduce our workforce by approximately 35%, to align our workforce with our strategy to focus on our clinical stage, targeted oncology programs, IK-930 and IK-595. We expect that this workforce reduction will result in a reduction of our operating expenses and, based on our current operating plans, extend our cash runway into the second half of 2026. This workforce reduction, and any other future reductions, and the attrition that may occur following them, may result in the loss of institutional knowledge and expertise and the reallocation and combination of certain roles and responsibilities across the organization, all of which could adversely affect our operations. These restructurings, and other additional measures we might take to reduce costs, could strain our workforce, divert management attention, yield attrition beyond our intended reduction in force, reduce employee morale, cause us to delay, limit, reduce or eliminate certain development plans, or otherwise interfere with our ability to operate and grow our business effectively, each of which could have an adverse impact on our business, operating results, and financial condition. We may not complete current or any future restructuring activities on the anticipated timetable, and even if successfully completed, we may not achieve the anticipated cost savings, operating efficiencies, or other benefits of such activities.

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

We have never successfully completed any clinical trials for our target oncology programs, and we may be unable to do so for any of our current product candidates.

We have not yet demonstrated our ability to successfully complete clinical trials, including large-scale, pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Before commencing certain clinical trials, we may finalize the trial design based on discussions with the FDA and other regulatory authorities. Any guidance we receive from the FDA or other regulatory authorities is subject to change. These regulatory authorities could change their positions, including, but not limited to, regarding the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional clinical trials or result in the composition of stricter approval conditions than we currently expect. Successful completion of our clinical trials is a prerequisite to submitting an NDA to the FDA, MAA, to the EMA, or other marketing applications to regulatory authorities in other jurisdictions, for each product candidate and, consequently, the regulatory approval of each product candidate.

If we are required to conduct additional preclinical studies or clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive, or are only modestly positive, or, if there are safety concerns, we may:

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

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

The discovery and development of oncology therapeutics for patients with genetically defined or biomarker-driven cancers is 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, that the genetic alterations targeted by our programs drive the formation and spread of cancer, clinical results may not confirm this hypothesis or may only confirm it for certain alterations or certain tumor types. The patient populations for our product candidates are limited to those with specific target alterations and may not be completely defined but are substantially smaller than the general treated cancer population, and we will need to screen and identify these patients with targeted alterations. Successful identification of patients is dependent on several factors, including achieving certainty as to how specific alterations respond to our product candidates and the ability to identify such alterations. Furthermore, even if we are successful in identifying patients with specific target alterations, 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, commercialize our product candidates and achieve profitability.

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

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

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

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

We intend to rely on third parties for the design, development, and manufacture of companion diagnostic tests for our therapeutic product candidates that may require such tests. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining approval for these companion diagnostics. It

may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our future collaborators may encounter difficulties in developing, obtaining regulatory approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our therapeutic product candidates themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we are unable to successfully develop companion diagnostics for these therapeutic product candidates, or experience delays in doing so, the development of these therapeutic product candidates may be adversely affected, these therapeutic product candidates may not obtain regulatory approval, and we may not realize the full commercial potential of any of these therapeutic products that obtain regulatory approval. As a result, our business, results of operations and financial condition could be materially harmed. In addition, a diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of our product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our therapeutic product candidates.

Interim, top-line, 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 confirmation, audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose interim, top-line, or preliminary data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received all of the necessary data or had the opportunity to fully and carefully evaluate all data. As a result, the interim, top-line or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Interim data from clinical trials 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. Preliminary, interim, or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary top-line data we previously published. As a result, preliminary, interim, and top-line data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the price of our common stock to fluctuate or decline.

Further, regulatory agencies and others may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses, or may interpret or weigh the importance of data differently, which could adversely impact the potential of the particular program, the likelihood of obtaining regulatory approval of the particular product candidate, commercialization of any approved product and the business prospects of our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is derived from information that is typically extensive, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

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

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

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

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

- regulators, IRBs or ethics committees may delay or may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- nonclinical studies or clinical trials of our product candidates may fail to show safety or efficacy or otherwise produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials, or we may decide to abandon product development programs;
- nonclinical studies or clinical trials of our product candidates may not produce differentiated or clinically significant results across tumor types or indications;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls, be unable to provide us with sufficient product supply to conduct or complete nonclinical studies or clinical trials, fail to meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators or IRBs or ethics committees may require us or our investigators to, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our clinical trials are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from nonclinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our product candidates; and
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we currently anticipate.

We could encounter delays if a clinical trial is suspended or terminated by us, including upon the recommendation of the Safety Monitoring Committee ("SMC") if applicable for such trial, by the IRBs of the institutions at which such trials are being conducted, or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination or clinical hold due to a number of factors, including, but not limited to, failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, adverse findings upon an inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA may disagree with, among other considerations, our clinical trial design or our interpretation of data from clinical trials or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

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

Our product development costs will also increase if we experience delays in testing or regulatory approvals. We do not know whether any of our future clinical trials will begin as planned, or whether any of our current or future clinical trials will need to be

restructured or will be completed on schedule, if at all. Significant preclinical study or clinical trial delays could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates and may significantly harm our business, operating results, financial condition and prospects.

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities, or as needed to provide appropriate statistical power for a given trial. For example, because we are focused on patients with specific genetic mutations or biomarkers for the development of our targeted oncology programs, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.

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

In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications as do our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

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

We may also engage third parties to develop companion diagnostics for use in our clinical trials, but such third parties may not be successful in developing such companion diagnostics, limiting our ability to identify patients with the targeted genetic mutations for our clinical trials. Further, if we are required to develop companion diagnostics and are unable to include patients with the targeted genetic mutations, this could compromise our ability to seek participation in the FDA's expedited review and development programs, including breakthrough therapy designation and fast track designation, or otherwise seek to accelerate clinical development and regulatory timelines. Patient enrollment may be affected by other factors, including:

- the severity of the disease under investigation;
- the efforts to obtain and maintain patient consents and facilitate timely enrollment in clinical trials;
- the ability to monitor patients adequately during and after treatment;
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- reporting of the preliminary results of any of our clinical trials; and
- factors we may not be able to control that may limit patients, principal investigators or staff or clinical site availability.

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

Certain of our current product candidates and any future product candidates have the potential to be administered in combination with other targeted therapies or checkpoint inhibitor immunotherapies, and other standards of care, like chemotherapies, or radiotherapy. For example, through our clinical supply collaboration with AstraZeneca, we plan to explore IK-930 in combination with AstraZeneca's EGFR inhibitor, osimertinib. Our ability to develop and ultimately commercialize our current programs and

product candidates and any future programs or product candidates used in combination with osimertinib, or checkpoint inhibitor immunotherapies or other targeted therapies, will depend on our ability to access such drugs or biologics on commercially reasonable terms for the clinical trials and their availability for use with our commercialized product, if approved. We cannot be certain that current or potential future commercial relationships will provide us with a steady supply of such drugs or biologics on commercially reasonable terms or at all.

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

Moreover, the development of product candidates for use in combination with another product or product candidate may present challenges that are not faced for single agent product candidates. The FDA, other U.S. regulatory agencies and/or comparable foreign regulatory authorities may require us to use more complex clinical trial designs in order to evaluate the contribution of each product and product candidate to any observed effects. It is possible that the results of such trials could show that any positive previous trial results are attributable to the combination therapy and not our current product candidates and any future product candidates. Moreover, following product approval, the FDA, other U.S. regulatory agencies and/or comparable foreign regulatory authorities may require that products used in conjunction with each other be cross labeled for combined use. To the extent that we do not have rights to the other product, this may require us to work with a third party to satisfy such a requirement. Moreover, developments related to the other product may impact our clinical trials for the combination as well as our commercial prospects should we receive regulatory approval. Such developments may include changes to the other product's safety or efficacy profile, changes to the availability of the other product, quality, manufacturing and supply issues with respect to the other product, and changes to the standard of care.

In the event that AstraZeneca, or any future collaborator or supplier cannot continue to supply their products on commercially reasonable terms, we would need to identify alternatives for accessing targeted therapies, checkpoint inhibitor immunotherapies or other combination agents. Additionally, should the supply of products from any current or future collaborator or supplier be interrupted, delayed or otherwise be unavailable to us, our clinical trials may be delayed. In the event we are unable to source an alternative supply, or are unable to do so on commercially reasonable terms, our business, financial condition, operating results, stock price, and prospects may be materially harmed.

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

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

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

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

We plan to progress candidates to IND or similar applications, however, we may not be able to file such INDs or similar applications on the timelines we expect. Additionally, even if the FDA agrees with the design and implementation of the clinical trials set forth in an IND, we cannot guarantee that it will not change its requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or similar applications to a new IND or similar application. Any failure to file INDs or similar applications on the timelines we expect or to obtain regulatory approvals for our planned clinical trials may prevent us from initiating or completing our clinical trials or commercializing our product candidates on a timely basis, if at all.

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

Before obtaining regulatory approvals for the commercial sale of any products, we must demonstrate through lengthy, complex, and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. Clinical testing is expensive and can take many years to complete, and outcomes are inherently uncertain. Failure can occur at any time during the clinical trial process. Because our targeted oncology programs and our product candidates are in an early stage of development, there is a high risk of failure, and we may never succeed in developing marketable products. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials also may fail to show the desired safety and efficacy profile despite having progressed through nonclinical studies and initial clinical trials. If the results of our ongoing or future preclinical studies and clinical trials are inconclusive with respect to the safety and efficacy of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be prevented from, or delayed in, obtaining regulatory approval for such product candidates. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Although we are currently conducting clinical trials of multiple of our product candidates, it is likely, as is the case with many oncology therapies, that there may be side effects associated with their use. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims.

Further, our product candidates could cause undesirable side effects in clinical trials related to on-target toxicity. If on-target toxicity is observed, or if our product candidates have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk-benefit perspective. In addition, our product candidates could cause undesirable side effects that we have not yet observed. Many compounds that initially showed promise in early-stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound. Most product candidates that commence clinical trials are never approved as products, and there can be no assurance that any of our current or future clinical trials will ultimately be successful or support further clinical development or regulatory approval of any of our product candidates.

We plan to develop certain of our product candidates, in combination with one or more cancer therapies. The uncertainty resulting from the use of our product candidates, in combination with other cancer therapies, may make it difficult to accurately predict side effects in future clinical trials. As is the case with many treatments for cancer and rare diseases, it is likely that there may be side effects associated with the use of our product candidates. If significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to our clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of one or more product candidates altogether. We, the FDA or other applicable regulatory authorities, or an IRB may suspend or terminate clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product from obtaining or maintaining regulatory approval, undesirable side effects may inhibit market acceptance of the approved product due to its tolerability versus other therapies. Any of these developments could materially harm our business, operating results, financial condition, and prospects.

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

Some of our product candidates modulate pathways for which there are currently no approved or effective therapies, which may result in uncertainty. We select programs for cancer driver targets based on compelling biological rationale. We explore new programs based on extensive preclinical data analysis which sometimes cannot predict efficacy or safety in humans.

Some of our product candidates utilize novel binding locations, which may result in greater research and development expenses, regulatory issues that could delay or prevent approval, or discovery of unknown or unanticipated adverse effects. We utilize structural biology in tight integration with our medicinal chemistry and biology capabilities to predict and design the compounds that will achieve the most desirable characteristics, including potency, selectivity, bioavailability, and drug-like properties. A disruption in any

of these capabilities may have significant adverse effects in our ability to expand our pipeline of product candidates, and we cannot predict whether we will continue to have access to these capabilities in the future to support our pipeline development. In addition, there can be no assurance that we will be able to rapidly identify, design and synthesize the necessary compounds or that these or other problems related to the development of product candidates will not arise in the future, which may cause significant delays or we raise problems we may not be able to resolve.

Regulatory approval of novel product candidates such as ours can be more expensive, riskier, and take longer than for other, more well-known or extensively studied pharmaceutical or biopharmaceutical product candidates due to our and regulatory agencies' lack of experience with them. The novelty of the mechanism of action of any of our product candidates may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. The novel mechanism of action also means that fewer people are trained in or experienced with product candidates of this type, which may make it more difficult to find, hire and retain personnel for research, development, and manufacturing positions. If our inhibitors utilize a novel mechanism of action that has not been the subject of extensive study compared to more well-known product candidates, there is also an increased risk that we may discover previously unknown or unanticipated adverse effects during our preclinical studies and clinical trials. Any such events could adversely impact our business prospects, operating results and financial condition.

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

We currently conduct additional clinical trials outside the United States, including in the United Kingdom, Australia, and other foreign jurisdictions. The acceptance of trial data from clinical trials conducted outside the United States by the FDA may be subject to certain conditions. In cases where data from clinical trials conducted outside the United States are intended to serve as the sole basis for regulatory approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practices, (ii) the trials were performed by clinical investigators of recognized competence, and (iii) the data may be 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. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. The EMA, the MHRA and many other comparable foreign regulatory bodies have similar approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, the EMA, the MHRA, or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States, the European Union, the United Kingdom, or the applicable jurisdiction. If the FDA, the EMA, or the MHRA, or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving regulatory approval or clearance for commercialization in the applicable jurisdiction.

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

Research programs to pursue the development of our existing and planned product candidates for additional indications and disease targets require substantial technical, financial and human resources whether or not they are ultimately successful. Our research programs may initially show promise in identifying potential indications, yet fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications;
- potential product candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective products; or
- it may take greater human and financial resources than we will possess to identify additional therapeutic opportunities for our product candidates, thereby limiting our ability to develop, diversify and expand our product portfolio.

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

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

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

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

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

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

Even if we were to obtain regulatory approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, thereby narrowing the commercial potential of the product candidate. In addition, regulatory

authorities may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

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

Pandemics, epidemics, or any outbreak of an infectious disease, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. Such global outbreaks of infectious diseases could materially and adversely impact our operations, including, without limitation, our nonclinical studies or clinical trial operations and our ability to recruit and retain patients and principal investigators and site staff. For example, similar to other biopharmaceutical companies, we may experience delays in initiating IND-enabling studies, protocol deviations, enrolling our clinical trials, or dosing of patients in our clinical trials, as well as in activating new trial sites. Any negative impact a public health crisis has on patient enrollment or treatment or the execution of our product candidates could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, and have a material adverse effect on our financial results.

These, and other factors related to any such disruptions that are unforeseen, could have a material adverse effect on our business and our results of operation and financial condition. Further, uncertainty around these and related issues could lead to adverse effects on global economies and financial markets, which could impact our ability to raise the necessary capital needed to develop and commercialize our programs and product candidates.

We may need to reformulate our product candidates which could require additional nonclinical studies or clinical trials and delay the development or regulatory approval of such product candidates.

New risks, pharmacokinetic variability, and side effects associated with our product candidates may be discovered during clinical testing. Our product candidates also may experience stability issues. For these or other reasons, we may need to reformulate our product candidates. For example, in the Phase 1 clinical program of IK-930, a second formulation that was designed to resolve exposure variability was introduced. Such reformulation may require us to conduct additional nonclinical studies or clinical trials to bridge or demonstrate the comparability of our modified product candidate to earlier versions, which could delay our clinical development plan or marketing approval for our product candidate. Reformulating a product candidate may also result in a delay in continuing a clinical trial. There can be no assurance that we will not experience delays in the completion of a clinical trial or in the commencement and completion of our future trials due to the need to reformulate our product candidates and subsequently discuss with or receive authorization from regulatory authorities to implement these changes in clinical trials. Additionally, reformulating a product candidate may cause us to experience a shortage in supply or cause the cost to manufacture our product candidate to increase. Any reformulation of our product candidates could substantially increase the costs and expenses of developing our product candidates and delay such development and marketing approval.

Risks Related to Commercialization

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

The development and commercialization of new products in the biopharmaceutical and related industries is highly competitive. We compete in the segments of the pharmaceutical, biotechnology, and other related markets that address structural biology-guided chemistry-based drug design to develop therapies in the fields of cancer and genetic diseases. There are other companies focusing on targeted oncology to develop therapies in the fields of cancer and other diseases. We also compete more broadly across the market for cost-effective and reimbursable cancer treatments. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes. 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. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

Any product candidates that we successfully develop and commercialize will compete with currently approved therapies and new therapies that may become available in the future from segments of the pharmaceutical, biotechnology and other related markets. Key product features that would affect our ability to effectively compete with other therapeutics include the efficacy, safety, and convenience of our products. We believe principal competitive factors to our business include, among other things, our ability to identify biomarkers, ability to successfully transition research programs into clinical development, ability to raise capital, and the scalability of the platform, pipeline, and business.

Many of the companies that we compete against or which we may compete against in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. If these or other barriers to entry do not remain in place, other companies may be able to more directly or effectively compete with us.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we or our collaborators may develop. Our competitors also may obtain FDA or other regulatory approval for their products sooner than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, level of generic competition and availability of reimbursement from government and other third-party payors.

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

The incidence and prevalence for target patient populations of our programs and product candidates have not been established with precision. Our most advanced targeted oncology product candidate, IK-930, is an oral, TEAD1-selective, small molecule inhibitor of the Hippo signaling pathway. The Hippo pathway is genetically altered in approximately 10% of all cancers and these genetic alterations are generally associated with poor clinical outcomes. The Hippo pathway is also associated with mechanisms of resistance to targeted therapeutics and could represent a larger population of patients. In addition, our IK-595 program candidate is an oral, small molecule MEK-RAF molecular glue. KRAS mutations in the RAS signaling pathway occur in approximately 26% of all cancers. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our programs and product candidates, are based on our estimates.

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

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

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

may not be accepted by the general public or the medical community. Future adverse events in targeted oncology, immune-oncology or the biopharmaceutical industry could also result in greater governmental regulation, stricter labeling requirements, and potential regulatory delays in the testing or approvals of our product candidates.

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels.

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

- the efficacy of our current product candidates and any future product candidates as single agents and in combination with marketed checkpoint inhibitor immunotherapies, targeted agents, and other combination agents;
- the commercial success of the checkpoint inhibitor immunotherapy drugs, targeted agents, and other combination agents with which our products may be co-administered;
- the prevalence and severity of adverse events associated with our current product candidates and any future product candidates or those products with which they may be co-administered;
- the clinical indications for which our product candidates are approved and the approved claims that we may make for the products;
- limitations or warnings contained in the product's FDA-approved labeling or those of comparable foreign regulatory authorities, including potential limitations or warnings for our current product candidates and any future product candidates that may be more restrictive than other competitive products;
- changes in the standard of care for the targeted indications for our current product candidates and any future product candidates, which could reduce the marketing impact of any claims that we could make following FDA approval or approval by comparable foreign regulatory authorities, if obtained;
- the relative convenience and ease of administration of our current product candidates and any future product candidates and any products with which they are co-administered;
- the cost of treatment compared with the economic and clinical benefit of alternative treatments or therapies;
- the availability of adequate coverage or reimbursement by third party payors, including government healthcare programs such as Medicare and Medicaid and other healthcare payors;
- the price concessions required by third-party payors to obtain coverage;
- the willingness of patients to pay out-of-pocket in the absence of adequate coverage and reimbursement;
- the extent and strength of our marketing and distribution of our current product candidates and any future product candidates;
- the safety, efficacy, and other potential advantages over, and availability of, alternative treatments already used or that may later be approved;
- distribution and use restrictions imposed by the FDA or comparable foreign regulatory authorities with respect to our current product candidates and any future product candidates or to which we agree as part of a REMS or voluntary risk management plan;
- the timing of market introduction of our current product candidates and any future product candidates, as well as competitive products;
- our ability to offer our current product candidates and any future product candidates for sale at competitive prices;

- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the extent and strength of our third-party manufacturer and supplier support;
- the actions of companies that market any products with which our current product candidates and any future product candidates may be co-administered;
- the approval of other new products;
- adverse publicity about our current product candidates and any future product candidates or any products with which they are co-administered, or favorable publicity about competitive products; and
- potential product liability claims.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement by government authorities for new products are typically made by CMS, since CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare. Private payers tend to follow CMS to a substantial degree. However, one payer's determination to provide coverage for a product does not assure that other payers will also provide coverage for the drug product. Further, a payer's decision to provide coverage for a drug product does not imply that the payor will provide adequate reimbursement. Reimbursement agencies in the European Union may be more conservative than CMS. Factors payors consider in determining reimbursement are based on whether the product is:

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

Additionally, net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. 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. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. 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. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. 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. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

Risks Related to Our Reliance on Third Parties

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

We do not have the ability to independently conduct clinical trials. We rely and expect to continue to rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct or otherwise support clinical trials for our product candidates.

We rely and expect to continue to rely heavily on these parties for execution of clinical trials for our product candidates and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements, and scientific standards, and our reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

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

Although we designed our current ongoing clinical trials, and intend to design the future clinical trials for our product candidates, these trials are conducted by CROs and we expect CROs will conduct all of our future clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, are outside of our direct control. Our reliance on third parties to conduct future clinical trials also results in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

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

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

We may also rely on academic and private non-academic institutions to conduct and sponsor clinical trials relating to our product candidates. We will not control the design or conduct of the investigator-sponsored trials, and it is possible that the FDA or non-U.S. regulatory authorities will not view these investigator-sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results.

Such arrangements will likely provide us certain information rights with respect to the investigator-sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator-sponsored trials. However, we would not have control over the timing and reporting of the data from investigator-sponsored trials, nor would we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator-sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our product candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the first-hand knowledge we might have gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected.

We have entered into collaborations and may enter into additional collaborations in the future, and we might not realize the anticipated benefits of such collaborations.

Research, development, commercialization and/or strategic collaborations are subject to numerous risks, which include the following:

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

In addition, funding provided by a collaborator might not be sufficient to advance product candidates under the collaboration.

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

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

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

We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical development and clinical testing, as well as for the commercial manufacture of our products if any of our product candidates receive regulatory approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

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

If any CMO with whom we contract fails to perform its obligations, we may be forced to enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In such a scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

Further, our failure, or the failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, if approved, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business and supplies of our product candidates.

We may be unable to establish any additional agreements with third-party manufacturers or do so on acceptable terms. Reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

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

Any performance failure on the part of our existing or future manufacturers could delay clinical development or regulatory approval. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. We may incur added costs and delays in identifying and qualifying any such replacement.

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

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

The active pharmaceutical ingredients ("API") used in all of our product candidates are supplied to us from single-source suppliers. Our ability to successfully develop our product candidates, and to ultimately supply our commercial products in quantities sufficient to meet the market demand, depends in part on our ability to obtain the API for these products in accordance with regulatory requirements and in sufficient quantities for clinical testing and commercialization.

We are also unable to predict how changing global economic conditions or potential global health concerns will further affect our third-party suppliers and manufacturers. Any negative impact of such matters on our third-party suppliers and manufacturers may also have an adverse impact on our results of operations or financial condition.

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

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

We may seek to establish additional collaborations, and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.

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

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's own evaluation of a potential collaboration. Such factors a potential collaborator will use to evaluate a collaboration may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

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

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

In addition, any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent and other intellectual property protection for our technology and product candidates or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired.

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection in the U.S. and other countries for our current or future product candidates, as well as for their respective compositions, formulations, methods used to manufacture them, and methods of treatment, in addition to successfully defending these patents against third-party challenges. We seek to protect our proprietary and intellectual property position by, among other methods, filing patent applications in the U.S. and abroad related to our proprietary technology, inventions, and improvements that are important to the development and implementation of our business. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. The degree of patent protection we require to successfully commercialize our current or future product candidates may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect our current or future product candidates. In addition, if the breadth or strength of protection provided by our patent applications or any patents we may own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. For example, in jurisdictions outside the U.S., a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license. Accordingly, any actual or purported co-owner of our patent rights could seek monetary or equitable relief requiring us to pay it compensation for, or refrain from, exploiting these patents due to such co-ownership. Furthermore, patents have a limited lifespan. In the U.S., and most other jurisdictions in which we have undertaken patent filings, the natural expiration of a patent is generally twenty years after it is filed, assuming all maintenance fees are paid. Various extensions may be available, on a jurisdiction-by-jurisdiction basis; however, the life of a patent, and thus the protection it affords, is limited. Given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, patents we may own or in-license may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our current or future product candidates, including generic versions of such drugs.

Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents, with respect to either the same compounds, methods, formulations or other subject matter, in either case that we may rely upon to dominate our patent position in the market. Publications of discoveries in the

scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until at least 18 months after the earliest priority date of patent filing, or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in patents we may own or in-license patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights cannot be predicted with any certainty.

In addition, the patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Further, with respect to certain pending patent applications covering our current or future product candidates, prosecution has yet to commence. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the relevant patent office(s) may be significantly narrowed by the time they issue, if they ever do. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing, and prosecution of patent applications, or to maintain the patents, covering technology that we license from or to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Even if we acquire patent protection that we expect should enable us to establish and/or maintain a competitive advantage, third parties may challenge the validity, enforceability, or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the U.S. and abroad. We may become involved in post-grant proceedings such as opposition, derivation, reexamination, *inter partes* review, post-grant review, or interference proceedings challenging our patent rights or the patent rights of others from whom we may in the future obtain licenses to such rights, in the USPTO, the European Patent Office ("EPO"), or in other countries. In addition, we may be subject to a third-party submission to the USPTO, the EPO, or elsewhere, that may reduce the scope or preclude the granting of claims from our pending patent applications. Competitors may allege that they invented the inventions claimed in our issued patents or patent applications prior to us, or may file patent applications before we do. Competitors may also claim that we are infringing their patents and that we therefore cannot practice our technology as claimed under our patents or patent applications. Competitors may also contest our patents by claiming to an administrative patent authority or judge that the invention was not patent-eligible, was not original, was not novel, was obvious, and/or lacked inventive step, and/or that the patent application filing failed to meet relevant requirements relating to description, basis, enablement, and/or support; in litigation, a competitor could claim that our patents, if issued, are not valid or are unenforceable for a number of reasons. If a court or administrative patent authority agrees, we would lose our protection of those challenged patents.

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

An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, without payment to us, or could limit the duration of the patent protection covering our technology and current or future product candidates. Such challenges may also result in our inability to manufacture or commercialize our current or future product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if they are unchallenged, our issued patents and our pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent patents we may own or in-license by developing similar or alternative technologies or drugs in a non-infringing manner. For example, a third-party may develop a competitive drug that provides benefits similar to one or more of our current or future product candidates, but that has a different composition that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our current or future product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our current or future product candidates could be negatively affected, which would harm our business.

Furthermore, even if we are able to issue patents with claims of valuable scope in one or more jurisdictions, we may not be able to secure such claims in all relevant jurisdictions, or in a sufficient number to meaningfully reduce competition. Our competitors may be able to develop and commercialize their products, including products identical to ours, in any jurisdiction in which we are unable to obtain, maintain, or enforce such patent claims.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, deadlines, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated if we fail to comply with these requirements. We may miss a filing deadline for patent protection on these inventions.

The USPTO and foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process and after issuance of any patent. In addition, periodic maintenance fees, renewal fees, annuity fees and/or various other government fees are required to be paid periodically. While an inadvertent lapse can, in some cases, be cured by payment of a late fee, or by other means in accordance with the applicable rules, there are situations in which 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. Noncompliance events that could result in abandonment or lapse of a patent include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market with similar or identical products or platforms, which could have a material adverse effect on our business prospects and financial condition.

If our trademarks and trade names for our products or company name are not adequately protected in one or more countries where we intend to market our products, we may delay the launch of product brand names, use different trademarks or tradenames in different countries, or face other potentially adverse consequences to building our product brand recognition.

Our trademarks or trade names may be challenged, infringed, diluted, circumvented, or declared generic or determined to be infringing on other marks. We intend to rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During the trademark registration process, we may receive Office Actions from the USPTO or from comparable agencies in foreign jurisdictions objecting to the registration of our trademark. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and/or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademark applications or registrations, and our trademark applications or registrations may not survive such proceedings. If we are unable to obtain a registered trademark or establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

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

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

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

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our

trade secrets or disclose our technology. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third-party, we would have no right to prevent them from using that technology or information to compete with us.

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

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

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

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

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

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

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

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

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

The intellectual property landscape relevant to our product candidates and programs is crowded, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability to develop, manufacture, market and sell our current and future product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including derivation, interference, reexamination, *inter partes* review and post grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We or any of our current or future licensors or strategic partners may be party to, exposed to, or threatened with, future adversarial proceedings or litigation by third parties having patent or other intellectual property rights alleging that our current or future product candidates and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. We cannot assure you that our current or future product candidates and other technologies that we have developed, are developing or may develop in the future do not or will not infringe, misappropriate or otherwise violate existing or future patents or other intellectual property rights owned by third parties. For example, many of our employees were previously employed at other biotechnology or pharmaceutical companies. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's former employer. We may also be subject to claims that patents and applications we have filed to protect inventions of our employees, consultants and advisors, even those related to one or more of our current or future product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims.

While certain activities related to development and clinical testing of our current or future product candidates may be subject to safe harbor of patent infringement under 35 U.S.C. §271(e)(1), upon receiving FDA approval for such candidates we or any of our future licensors or strategic partners may immediately become party to, exposed to, or threatened with, future adversarial proceedings or litigation by third parties having patent or other intellectual property rights alleging that such product candidates infringe, misappropriate or otherwise violate their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our current or future product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our current or future product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because

of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our current or future product candidates, technologies or methods.

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

- infringement, misappropriation and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business and may impact our reputation;
- substantial damages for infringement, misappropriation or other violations, which we may have to pay if a court decides that the product candidate or technology at issue infringes, misappropriates or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our current product candidates, including IK-930 and IK-595, or future product candidates, or from using our proprietary technologies, unless the third-party licenses its product rights to us, which it is not required to do, on commercially reasonable terms or at all;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products, or the license to us may be non-exclusive, which would permit third parties to use the same intellectual property to compete with us;
- redesigning our current or future product candidates or processes so they do not infringe, misappropriate or violate third-party intellectual property rights, which may not be possible or may require substantial monetary expenditures and time; and
- there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects.

We may choose to challenge the patentability of claims in a third-party's U.S. patent by requesting that the USPTO review the patent claims in an ex-parte re-exam, *inter partes* review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third-party's patent in patent opposition proceedings in the EPO, or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third-party alleging that the patent may be infringed by our current or future product candidates or proprietary technologies.

Third parties may assert that we are employing their proprietary technology without authorization. Patents issued in the U.S. by law enjoy a presumption of validity that can be rebutted in U.S. courts only with evidence that is "clear and convincing," a heightened standard of proof. There may be issued third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our current or future product candidates. Patent applications can take many years to issue. In addition, because some patent applications in the U.S. may be maintained in secrecy until the patents are issued and patent applications in the U.S. and many foreign jurisdictions are typically not published until 18 months after their earliest priority filing date, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications covering our current or future product candidates or technology. If any such patent applications issue as patents, and if such patents have priority over our patent applications or patents we may own or in-license, we may be required to obtain rights to such patents owned by third parties which may not be available on commercially reasonable terms or at all, or may only be available on a non-exclusive basis. There may be currently pending third-party patent applications which may later result in issued patents that our current or future product candidates may infringe. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our current or future product candidates or other technologies, could be found to be infringed by our current or future product candidates or other technologies. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our current or future product candidates, molecules used in or formed during the manufacturing process, or any final

product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our current or future product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be nonexclusive, thereby giving our competitors access to the same technologies licensed to us.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our current or future product candidates. Defense of these claims, regardless of their merit, could involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement, misappropriation or other violation against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our current or future product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our current or future product candidates, which could harm our business significantly.

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

We may not be able to pursue patent coverage of our current or future product candidates in all countries. Filing, prosecuting and defending patents on current or future product candidates in all countries throughout the world would be prohibitively expensive, and intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. 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 U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the U.S. These products may compete with our current or future product candidates and in jurisdictions where we do not have any issued patents our patent applications or other intellectual property rights may not be effective or sufficient to prevent them from competing. Much of our patent portfolio is at the very early stage. We will need to decide whether and in which jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines.

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

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

We may not obtain or grant licenses or sublicenses to intellectual property rights in all markets on equally or sufficiently favorable terms with third parties.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. The licensing of third-party intellectual property rights is a competitive area, and more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. More established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected current or future 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 or other forms of compensation. 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. Any of the foregoing could harm our competitive position, business, financial condition, results of operations and prospects.

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

We may from time to time be party to license and collaboration agreements with third parties to advance our research or allow commercialization of current or future product candidates. Such agreements may impose numerous obligations, such as development, diligence, payment, commercialization, funding, milestone, royalty, sublicensing, insurance, patent prosecution, enforcement and other obligations on us and may require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technologies covered by these license agreements.

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

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

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

In addition, the agreements under which we may license intellectual property or technology from third parties are likely to be complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we may license prevent or impair our ability to maintain future licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected current or future product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

Any granted patents we may own or in-license covering our current or future product candidates or other valuable technology could be narrowed or found invalid or unenforceable if challenged in court or before administrative bodies in the U.S. or abroad, including the USPTO and the EPO. A patent asserted in a judicial court could be found invalid or unenforceable during the enforcement proceeding. Administrative or judicial proceedings challenging the validity of our patents or individual patent claims could take months or years to resolve.

If we or our licensors or strategic partners initiate legal proceedings against a third-party to enforce a patent covering one of our current or future product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third-party can assert invalidity or unenforceability of a patent. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of patentable subject matter, lack of written description, lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, in the process of obtaining the patent during patent prosecution. Third parties may also raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post grant review and equivalent proceedings in foreign jurisdictions (such as opposition proceedings). Such proceedings could result in revocation or amendment to our patent applications or any patents we may own or in-license in such a way that they no longer cover our current or future product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, any rights we may have from our patent applications or any patents we may own or in-license, allow third parties to commercialize our current or future product candidates or other technologies and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our or our future licensors' priority of invention or other features of patentability with respect to our patent applications and any patents we may own or in-license. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our current or future product candidates and other technologies. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our future licensing partners and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our current or future product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and current or future 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. If we are unsuccessful in any such proceeding or other priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the current or future product candidates we may develop. The loss of exclusivity or the narrowing of our patent application claims could limit our ability to stop others from using or commercializing similar or identical technology and products. Any of the foregoing could have a material adverse effect on our business, results of operations, financial condition and prospects.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our current or future 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 both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Patent reform legislation in the U.S. and other countries could increase those uncertainties and costs. For example, the Leahy-Smith Act, signed into law in 2011, introduced provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a "first inventor to file" system. The Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent

proposals for additional changes to the patent laws of the U.S. and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

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

If we fail to identify and correctly interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay damages, which may be significant, we may be temporarily or permanently prohibited from commercializing any of our current or future product candidates that are held to be infringing. We might, if possible, also be forced to redesign current or future product candidates so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business and could adversely affect our business, financial condition, results of operations and prospects.

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

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

- patent applications that we own or may in-license may not lead to issued patents;
- patents, should they issue, that we may own or in-license, may not provide us with any competitive advantages, may be narrowed in scope, or may be challenged and held invalid or unenforceable;
- others may be able to develop and/or practice technology, including compounds that are similar to the chemical compositions of our current or future product candidates, that is similar to our technology or aspects of our technology but that is not covered by the claims of any patents we may own or in-license, should any patents issue;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we, or our future licensors or collaborators, might not have been the first to make the inventions covered by a patent application that we own or may in-license;

- we, or our future licensors or collaborators, might not have been the first to file patent applications covering a particular invention;
- others may independently develop similar or alternative technologies without infringing, misappropriating or otherwise violating our intellectual property rights;
- our competitors might conduct research and development activities in the U.S. and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and may then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not be able to obtain and/or maintain necessary licenses on reasonable terms or at all;
- third parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights, or any rights at all, over that intellectual property;
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third-party may subsequently file a patent covering such trade secrets or know-how;
- we may not be able to maintain the confidentiality of our trade secrets or other proprietary information;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

Risks Related to Government Regulation

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.

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

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

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

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

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

As part of our business strategy, we may seek orphan drug designation for certain of our product candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug or biologic as an orphan drug if it is a product intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population of more than 200,000 in the United States where there is no reasonable expectation that the cost of developing the product will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

Similarly, in the EU, the European Commission, upon the recommendation of the EMA's Committee for Orphan Medicinal Products, grants an orphan designation in respect of a product if its sponsor can show that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (i) such condition affects no more than 5 in 10,000 persons in the EU when the application is made, or (ii) it is unlikely that, without the benefits derived from orphan status, sales of the product in the EU would generate sufficient return in the EU to justify the necessary investment in its development; and (3) there must be no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or, if such a method exists, the product would be of a significant benefit to those affected by that condition. In the EU, orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers.

We have received orphan drug designation from the FDA for IK-930 for the treatment of mesothelioma and for the treatment of EHE. Generally, if a product with an orphan designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States and ten years in EU. The EU market exclusivity period can be reduced to six years if, at the end of the fifth year, a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. The European Commission introduced a legislative proposal in April 2023 that, if implemented, could reduce the current ten-year marketing exclusivity period in the EU for certain orphan medicines. Even if we obtain orphan drug exclusivity for any product candidates in addition to IK-930, that exclusivity may not effectively protect IK-930 or our other product candidate from competition because different products can be approved for the same condition.

Even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a product nor gives the product any advantage in the regulatory review or approval process. While we may seek orphan drug designation for our product candidates, we may never receive such designations. Even if we do receive such designations, there is no guarantee that we will enjoy the benefits of those designations.

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

We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Products designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if

one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

We have received fast track designation from the FDA for IK-930 for the treatment of unresectable NF2-deficient mesothelioma. If a drug or biologic is intended for the treatment of a serious or life-threatening condition and the drug or biologic demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for fast track designation. We may seek fast track designation for some of our other product candidates. The FDA has broad discretion whether or not to grant this designation, so even if we believe another particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive fast track designation, as we have for IK-930, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

Accelerated approval by the FDA, even if granted for our current or any other future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive regulatory approval.

We may seek accelerated approval of our current or future product candidates using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality ("IMM") that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA generally requires that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post approval confirmatory clinical trials, which must be completed with due diligence. FDORA gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such trials in a timely manner or if such post-approval trials fail to verify the drug's predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory trial or submit timely reports to the agency on their progress. In addition, the FDA currently requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. 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.

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

The FDA, the EMA, the MHRA and regulatory authorities in other countries have each expressed interest in further regulating biotechnology products. Agencies at both the federal and state level in the United States, as well as the U.S. Congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our product candidates. Adverse developments in clinical trials of products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any of our product candidates. These regulatory review agencies and committees and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory agencies and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

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

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

may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. 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.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. For more information, please see "Business – Governmental Regulation – Current & Future Healthcare Reform Legislation."

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our current or future product candidates or additional pricing pressures. In particular any policy changes through CMS as well as through local state Medicaid programs could have a significant impact on our business.

We expect that healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies, beyond those reductions which have already gone into effect. Such additional reductions could potentially lower the price that we receive for our products. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize our products. It is not clear how other future potential changes to existing legislation, or other similar measures, will change the reimbursement model and market outlook for our current and future product candidates.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

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

Although we do not currently have any products on the market, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business once we begin commercializing our product candidates. Healthcare entities, physicians and other providers, and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain regulatory approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable federal and state fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our product candidates for which we obtain regulatory approval. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. For more information, please see "Business – Governmental Regulation - Other Healthcare Laws."

The scope and enforcement of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement has led to an increasing number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring that our internal operations and future business arrangements with third parties comply with all applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may

apply to us, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, reputational harm, and the curtailment or restructuring of our operations, as well as 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. Further, defending against any such actions would likely be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against, settling and/or otherwise resolving any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and individual imprisonment. If any of the above occur, our ability to operate our business and our results of operations could be adversely affected.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. 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 biological, hazardous or radioactive materials.

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

If the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, import, export, adverse event reporting, storage, advertising, promotion, monitoring, and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and listing, as well as continued compliance with cGMP and GCP for any clinical trials that we conduct post-approval. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing studies, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. The FDA may also require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations and applicable product tracking and tracing requirements. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or product recalls;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;

- clinical trial holds;
- fines, warning letters or other regulatory enforcement action;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

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

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

We conduct clinical trials and continue to enroll subjects in our ongoing or future clinical trials, and therefore will be subject to additional privacy restrictions. Most notably, in the EEA and the UK, the collection, use, storage, disclosure, transfer, or other processing of personal data, including personal health data, is subject to the EU GDPR (with regards to the EEA) and the UK GDPR (with regards to the UK), as well as applicable national data protection legislation and requirements in force within the EEA Member States and the UK (including the UK Data Protection Act 2018). In this Annual Report on Form 10-K, "GDPR" refers to both the EU GDPR and the UK GDPR, unless specified otherwise. The GDPR are wide-ranging in scope and impose numerous requirements on companies that process personal data, including requirements relating to ensuring an appropriate legal basis or condition applies to the processing of personal data, the processing of sensitive data (such as health data), obtaining consent (if required) of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, requirements to conduct data protection impact assessments and taking certain measures when engaging third-party processors. Failure to comply with the requirements of the GDPR may result in warning letters, mandatory audits, orders to cease/change the use of data, and financial penalties, including fines of up to 4% of global revenues, or 20,000,000 Euro (£17.5 million for the UK), whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR.

The GDPR provides that EEA Member States may make their own further laws and regulations in relation to the processing of genetic, biometric or health data. In the UK, the UK Data Protection Act 2018 complements the UK GDPR in this regard. This could result in differences in the law that applies to the processing of such personal data across EEA Member States and the UK, which may, limit our ability to use and share personal data or could cause our costs to increase, and harm our business and financial condition.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA and UK not deemed adequate for the transfer of such personal data by competent data protection authorities ("third countries"), including the United States in certain circumstances, unless a derogation exists or we incorporate a GDPR transfer mechanism (such as the European Commission approved standard contractual clauses or the UK International Data Transfer Addendum ("IDTA") into our agreements with third parties to govern such transfers of personal data and carry out transfer impact assessments. Further, the EU and United States have adopted its adequacy decision for the EU-U.S. Data Privacy Framework ("Framework"), which entered into force on July 11, 2023. The international transfer obligations under the EEA and UK data protection regimes will require effort and cost and may result in us needing to make strategic considerations around where EEA/UK personal data is located and which service providers we can utilize for the processing of EEA/UK personal data. Any inability to transfer personal data from the EEA and UK to the United States in compliance with data protection laws may impede our ability to conduct trials and may adversely affect our business and financial position.

Although the UK is regarded as a third country under the EU GDPR, the European Commission has issued an "Adequacy Decision" recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data subject to the EU GDPR to the UK remain unrestricted. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The UK's data protection regime is independent from but aligned to the EU's data protection regime. However, following the UK's exit from the EU ("Brexit"), there will be increasing scope for divergence in application, interpretation and enforcement of the data protection laws between these territories. For example, the UK Government has now introduced a Data Protection and Digital Information Bill (the "UK Bill") into the UK legislative process with the intention for this bill to reform the

UK's data protection regime following Brexit. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EU data protection regime and threaten the UK Adequacy Decision from the EU Commission, which. may lead to additional compliance costs and could increase our overall risk. The lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, uncertainty, complexity and cost to our handling of European personal data and our privacy and data security compliance programs and could require us to implement different compliance measures for the UK and the EEA. Further, data protection authority activity differs across the EEA and the UK, with certain authorities applying their own agenda which shows there is uncertainty in the manner in which data protection authorities will seek to enforce compliance with GDPR. Enforcement uncertainty and the costs associated with ensuring GDPR compliance are onerous and may adversely affect our business, financial condition, results of operations and prospects.

Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European and UK-based activities. Similar comprehensive data protection requirements exist in many other jurisdictions around the world and will have any impact on any plans for expansion outside of the United States.

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

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

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

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

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

Risks Relating to Employee Matters and Managing Growth

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

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

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

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

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

We rely on information technology systems that we or our third-party providers operate to process, transmit and store electronic information in our day-to-day operations. In connection with our business, we may collect and use a variety of personal data, such as names, mailing addresses, email addresses, phone numbers and clinical trial information. A successful cybersecurity incident could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cybersecurity incidents are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. Cybersecurity incidents could include industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, including ransomware, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. A successful cybersecurity incident could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we develop and maintain systems and controls designed to prevent these events from occurring, there can be no assurance our internal information technology systems or those of our third-party vendors will be sufficient to protect against breakdowns, service disruption, data deterioration or loss in the event of a system malfunction, or prevent data from being stolen or corrupted in the event of a cyberattack, security incident, industrial espionage attacks, ransomware, or insider threat attacks. If we were to experience an attempted or successful cybersecurity attack of our information systems or data, the costs associated with the investigation, remediation and potential notification of the attack to counterparties, data subjects, regulators or others, including costs to deploy additional personnel and protection technologies, train employees, and engage third-party experts and consultants, could be material. In addition, following any such attack, our remediation efforts may not be successful. Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under state (e.g., state breach notification laws), federal (e.g., HIPAA, as amended by HITECH), and international law (e.g., the GDPR) and may cause a material adverse impact to our reputation, affect our ability to conduct new studies, and potentially disrupt our business.

If we or our third-party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third-party providers could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in the losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenue or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by us or such third parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy incidents, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business. By way of example, the California Consumer Privacy Act ("CCPA"), as amended by the California Privacy Rights Act creates individual comprehensive privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal data. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation.

Additionally, the CCPA marks the beginning of a trend toward more stringent privacy legislation in the United States, which could increase our potential liability and adversely affect our business. Similar comprehensive privacy laws have been passed in numerous other states. While these new state laws incorporate many similar concepts, there are also several key differences in the scope, application, and enforcement of the law that will change the operational practices of regulated businesses. The new laws will, among other things, impact how regulated businesses collect and process personal sensitive data, conduct data protection assessments, transfer personal data to affiliates, and respond to consumer rights requests. In addition to these comprehensive consumer privacy laws, a small number of states have also enacted laws focused on particular aspects of privacy. For example, the state of Washington has enacted a law that regulates the privacy of medical and health related information not subject to HIPAA, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data. A small number of states have also passed laws that regulate biometric information.

In addition, a number of other states have proposed new comprehensive privacy laws, some of which are similar to the above discussed recently passed laws. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance. At the federal level, there is discussion of a new comprehensive data privacy law which, if passed, would help to streamline certain of our privacy obligations but would also introduce new stringent privacy and data security obligations that would apply to personal data collected from throughout the United States. All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, utilize management's time and/or divert resources from other initiatives and projects.

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

Artificial intelligence presents risks and challenges that can impact our business including by posing security risks to our confidential information, proprietary information, and personal data.

Issues in the development and use of artificial intelligence, combined with an uncertain regulatory environment, may result in reputational harm, liability, or other adverse consequences to our business operations. As with many technological innovations, artificial intelligence presents risks and challenges that could impact our business. We may adopt and integrate generative artificial intelligence tools into our systems for specific use cases reviewed by legal and information security. Our vendors may incorporate generative artificial intelligence tools into their offerings without disclosing this use to us, and the providers of these generative artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards with respect to privacy and data protection and may inhibit our or our vendors' ability to maintain an adequate level of service and experience. If we, our vendors, or our third-party partners experience an actual or perceived breach or privacy or security incident because of the use of generative artificial intelligence, we may lose valuable intellectual property and confidential information and our reputation and the public perception of the effectiveness of our security measures could be harmed. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information, and intellectual property. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business.

We may be unable to successfully integrate acquisitions, which may adversely impact our operations.

We have in the past and in the future may continue to acquire complementary businesses or technologies. Acquired technologies, products or businesses may not perform as we expect, and we may fail to realize anticipated synergies or results. In addition, our acquisition strategy may divert management's attention away from our existing business, and expose us to unanticipated problems or legal liabilities, including responsibility as a successor for undisclosed or contingent liabilities of acquired businesses or assets.

We have successfully integrated our past acquisitions of Arrys, Amplify Medicines, Inc., and Pionyr, however, if we are unsuccessful in integrating any future acquisitions, it could impede us from realizing all of the benefits of those acquisitions and could weaken our business operations or future prospectus. The integration process may disrupt our business and, if new technologies, products or businesses are not implemented effectively, may preclude the realization of the full benefits expected by us and could harm our results of operations. In addition, the overall integration of new technologies, products or businesses may result in unanticipated problems, expenses, liabilities and competitive responses. The difficulties of integrating an acquisition include, among other things:

- issues in integrating the target company's technologies, product candidates or capabilities with ours;
- maintaining employee morale and retaining key employees;
- integrating the culture of the target company with ours;
- preserving important strategic relationships and collaborations; and
- consolidating corporate and administrative infrastructures and eliminating duplicative operations.

In addition, even if the operations of an acquisition are integrated successfully, we may not realize the full benefits of the acquisition, including the synergies, pipeline expansion or growth opportunities that we expect. These benefits may not be achieved within the anticipated time frame, or at all.

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

As of March 6, 2024, we had forty-three (43) full-time employees. As we advance our development programs in the future, we will be required to increase the number of our employees and the scope of our operations, particularly as we function as a public company and grow in the areas of product development, regulatory affairs and, if any of our product candidates receives regulatory approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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

Risks Related to Our Common Stock

The dual class structure of our common stock may limit your ability to influence corporate matters and may limit your visibility with respect to certain transactions.

The dual class structure of our common stock may also limit your ability to influence corporate matters. Holders of our common stock are entitled to one vote per share, while holders of our non-voting common stock are not entitled to any votes. Nonetheless, each share of our non-voting common stock may be converted at any time into one share of our common stock at the option of its holder by providing written notice to us, subject to the limitations provided for in our amended and restated certificate of incorporation that entities affiliated with or managed by certain of our stockholders will hold an aggregate of 5,586,311 shares of our non-voting common stock, out of a total of 6,215,466 shares of our non-voting common stock issued and outstanding. Upon written notice, these entities could convert a portion of these shares of non-voting common stock into up to an aggregate of 9.99% of our shares of common stock. Upon 61 days' prior written notice, these entities could convert all of their respective shares of non-voting common stock into shares of common stock. Consequently, the holders of our non-voting common stock who have exercised their option to make this conversion, will have the effect of increasing the relative voting power of those prior holders of our non-voting common stock, and correspondingly decreasing the voting power of the holders of our common stock, which may limit your ability to influence corporate matters. Additionally, stockholders who hold, in the aggregate, more than 10% of our common stock and non-voting common stock, but 10% or less of our common stock, and are not otherwise a company insider, may not be required to report changes in their

ownership due to transactions in our non-voting common stock pursuant to Section 16(a) of the Exchange Act, and may not be subject to the short-swing profit provisions of Section 16(b) of the Exchange Act.

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

Under Section 382 and Section 383 of the Internal Revenue Code of 1986, as amended ("the Code") if a corporation undergoes an "ownership change" (generally defined as one or more shareholders or groups of shareholders who own at least 5 percent of the corporation's equity increasing their equity ownership in the aggregate by a greater than 50 percentage point change (by value) over a three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income may be limited. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future or subsequent shifts in our stock ownership, some of which are outside our control. As of December 31, 2023, we had federal and state net operating loss carryforwards of approximately $140.6 million and $135.8 million respectively, and our ability to utilize those net operating loss carryforwards could be limited by an "ownership change" as described above, which could result in increased tax liability to us. Furthermore, our ability to utilize our net operating losses or credits is conditioned upon our attaining profitability and generating U.S. federal and state taxable income. As a result, the amount of the net operating loss and tax credit carryforwards presented in our consolidated financial statements could be limited and may expire unutilized. Under the current law, federal net operating loss carryforwards generated in taxable years beginning after December 31, 2017 will not be subject to expiration. However, any such net operating loss carryforwards may only offset 80% of our annual taxable income in taxable years beginning after December 31, 2020. State net operating loss carryforwards and other tax attributes may be similarly limited. Any such limitations may result in increased tax liabilities that could adversely affect our business, results of operations, financial position and cash flows.

We have commenced an at-the-market ("ATM") offering program to raise capital. Increased volatility and decreases in market prices of equity securities generally and of our common shares in particular may have an adverse impact on our willingness and/or ability to continue to sell our common shares through our ATM offering. Decreases in these sales would/could affect the cost or availability of equity capital, which could in turn have an adverse effect on our business, including current operations, future growth, revenues, net income and the market prices of our common shares.

In April 2022, we commenced an ATM program to raise capital. Under our ATM program, we have entered into a sales agreement to sell common shares, up to a maximum aggregate market value of $100.0 million, through one or more ATM offerings. Given the decrease in the market price of our common shares and volatility in the capital markets, we may not be willing or able to continue to raise equity capital through our ATM program. We may, therefore, need to turn to other sources of funding that may have terms that are not favorable to us, or reduce our business operations given capital constraints.

Alternative financing arrangements, if we pursue any, could involve issuances of one or more types of securities, including common stock, preferred stock, convertible debt, warrants to acquire common stock, or other securities. These securities could be issued at or below the then prevailing market price for our common shares. In addition, if we issue debt securities, the holders of the debt would have a claim to our assets that would be superior to the rights of stockholders until the principal, accrued and unpaid interest, and any premium or make-whole has been paid. In addition, if we borrow funds and/or issue debt securities through a subsidiary, the lenders and/or holders of those debt securities would have a right to payment that would be effectively senior to the Company's equity ownership in the subsidiary, which would adversely affect the rights of holders of both the Company's equity securities and its debt and debt securities.

Interest in any newly-issued debt securities and/or newly-incurred borrowings would increase our operating costs and increase our net loss, and these impacts may be material. If the issuance of new securities results in diminished rights to holders of our common stock, the market price of our common shares could be materially and adversely affected. Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences could result in a material adverse effect on our business, operating results, financial condition and prospects.

Changes in tax legislation could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service ("IRS") and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, under Section 174 of the Code, in taxable years beginning after December 31, 2021, expenses that are incurred for research and development in the U.S. will be capitalized and amortized, which may have an adverse effect on our cash flow. It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be promulgated or issued under existing or

new tax laws, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

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

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

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of the stockholders may be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office, and special meetings of stockholders may not be called by any other person or persons;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds (2/3) of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than a majority of all outstanding shares of our voting stock to amend any bylaws by stockholder action and not less than two-thirds (2/3) of all outstanding shares of our voting stock to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval, which preferred stock may include rights superior to the rights of the holders of common stock.

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

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

Pursuant to our bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, or other employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, or our amended and restated certificate of incorporation or our amended and restated bylaws (including the interpretation, validity or enforceability thereof) or (iv) any action asserting a claim that is governed by the internal affairs doctrine (the Delaware Forum Provision). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act of 1933, as amended (the "Securities Act") or the Exchange Act. Our amended and restated bylaws will further provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the Federal Forum Provision). In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the U.S. federal securities laws and the rules and regulations thereunder.

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

General Risk Factors

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

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

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, in 2008, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets and the COVID-19 pandemic caused significant volatility and uncertainty in U.S. and international markets. Please see "Risks Related to the Development of our Targeted Oncology and Other Programs and Product Candidates. Pandemics, epidemics or any outbreak of an infectious disease, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates." Inflation rates, particularly in the United States, have increased recently to levels not seen in years. Increased inflation may result in increased operating costs (including our labor costs), reduced liquidity, and limitations on our ability to access credit or otherwise raise debt and equity capital. In addition, the United States Federal Reserve has raised, and may again raise, interest rates in response to concerns about inflation. Increases in interest rates, especially if coupled with reduced government spending and volatility in financial markets, may have the effect of further increasing economic uncertainty and heightening these risks, which may impact our ability to raise additional capital in the future. Potential instability throughout the banking industry and their potential near- and long-term effects on the biotechnology industry and its participants such as our vendors, suppliers, and investors, may also adversely affect our operations and stock price. In addition, U.S. and global markets are experiencing volatility and disruption following the escalation of geopolitical tensions, the start of the military conflict between Russia and Ukraine, and evolving events in Israel and Gaza. On February 24, 2022, a full-scale military invasion of Ukraine by Russian troops began. Although the length and impact of the ongoing military conflict is highly unpredictable, the conflict in Ukraine has led to market disruptions, including significant volatility in commodity prices, credit and capital markets, as well as supply chain disruptions. Various of Russia's actions have led to sanctions and other penalties being levied by the United States, Australia, the European Union, and other countries, as well as other public and private actors and companies, against Russia and certain other geographic areas, including agreement to remove certain Russian financial institutions from the Society for Worldwide Interbank Financial Telecommunication payment system and restrictions on imports of Russian oil, liquified natural gas and coal. Additional potential sanctions and penalties have also been proposed and/or threatened. Russian military actions and the resulting sanctions could disrupt or otherwise adversely impact our operations and the operations of third parties upon which we rely, as well as the global economy and financial markets, and lead to instability and lack of liquidity in capital markets, potentially making it more difficult for us to obtain additional funds. Related sanctions, export controls or other actions that may be initiated by nations including the United States, the European Union or Russia (e.g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our

business and/or our supply chain, our CROs, CMOs and other third parties with which we conduct business. A severe or prolonged economic downturn, inflationary environment, rising interest rates, or political unrest could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. The extent and duration of the military action, sanctions, and resulting market disruptions are impossible to predict, but could be substantial. Any such disruptions may also magnify the impact of other risks described in this Annual Report on Form 10-K and the documents incorporated by reference herein.

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

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

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act") and a "smaller reporting company" as defined in the Exchange Act and will be able to avail ourselves of reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies, which could make our common stock less attractive to investors and adversely affect the market price of our common stock.

We are an "emerging growth company," as defined in the JOBS Act. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.235 billion or more; (ii) December 31, 2026; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- providing only two years of audited financial statements in addition to any required unaudited interim financial statements and a correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- the requirement to provide detailed compensation discussion and analysis in proxy statements and reports filed under the Exchange Act and instead provide a reduced level of disclosure regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved and some of the disclosure requirements of the Dodd-Frank Act relating to compensation of executive officers.

We have taken advantage of reduced reporting burdens in this Annual Report on Form 10-K. In particular, we have provided only two years of audited financial statements and have not included all of the executive compensation information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for new or revised accounting standards during the period in which we remain an emerging growth company; however, we may adopt certain new or revised accounting standards early.

We have elected to avail ourselves of this exemption and, therefore, we are not subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, changes in rules of U.S. generally accepted accounting principles ("GAAP") or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations. In addition, our independent registered public accounting firm will not be required to provide an attestation report on the effectiveness of our internal control over financial reporting so long as we qualify as an "emerging growth company," which may increase the risk that material weaknesses or significant deficiencies in our internal control over financial reporting go undetected. Likewise, so long as we qualify as an "emerging growth company," we may elect not to provide you with certain information, including certain financial information and certain information regarding compensation of our executive officers, that we would otherwise have been required to provide in filings we make with the SEC, which may make it more difficult for investors and securities analysts to evaluate our company. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile and may decline.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

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

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

As a public company, and particularly after we are no longer an "emerging growth company" or a "smaller reporting company," we will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company or a smaller reporting company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate

internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

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

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

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

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

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

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

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 1C. CYBERSECURITY

Cyber Risk Management and Strategy

We have adopted cybersecurity risk management activities and processes that are informed by and incorporate elements of recognized industry standards, such as the National Institute of Standards and Technology Cybersecurity Framework, and that are designed to identify, assess, and mitigate critical risks from cybersecurity threats. We have, for example, implemented a process to monitor for potential critical risks from cybersecurity threats using automated tools. To support our cybersecurity risk management efforts, we leverage a managed service provider that provides ongoing support for the protection of our information technology infrastructure.

We have an employee security awareness training program, required upon onboarding and on an annual basis thereafter, that is designed to raise awareness of cybersecurity threats across functions, as well as to encourage consideration of cybersecurity risks across our company. As part of this employee training program, we periodically conduct phishing simulations designed to raise employee awareness of such risks.

We have also implemented a process to assess and review the cybersecurity practices of certain third-party vendors and service providers that may be critical to the operations of our business and who have access to our information systems or store our confidential clinical trial data, including, as appropriate, through review of System and Organization Controls reports and security questionnaires and the inclusion of cybersecurity requirements in relevant contracts.

As part of our cybersecurity risk management, we have adopted an incident response plan that has been designed to identify and manage significant events that may impact our information technology infrastructure, including those arising from or related to cybersecurity threats.

We have not identified any cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations or financial condition; however, like other companies in our industry, we and our third-party vendors may, from time to time, experience threats and security incidents relating to our and our third-party vendors' information systems and infrastructure. For more information, please see "Risk Factors."

Cybersecurity Governance

Our Head of Information Technology ("Head of IT") is responsible for the establishment and maintenance of our cybersecurity risk management processes, including the day-to-day oversight of the assessment and management of cybersecurity risks. The individual who is currently in this role has more than eight (8) years of experience in information security and over eighteen (18) years of IT experience in the biotechnology and pharmacology industr. Our Head of IT directly reports to, and meets periodically with, our Senior Vice President of Finance and Administration to discuss and review our cybersecurity risk management processes.

Our board of directors has delegated oversight of our company's cybersecurity risk management to our audit committee. The audit committee, pursuant to the audit committee charter, is responsible for reviewing our company's information security and technology risks (including cybersecurity), including high-level review of the threat landscape facing our company and our company's strategy to mitigate cybersecurity risks and potential breaches. We have recently implemented a process for our Senior Vice President of Finance and Administration and/or our Chief Financial Officer, as appropriate, to provide periodic updates to the audit committee on the status of our cybersecurity program and on an as needed basis.

ITEM 2. PROPERTIES

Our corporate headquarters is located in Boston, Massachusetts where we lease and occupy 20,752 square feet of office, laboratory and animal care space. The lease (the "Boston lease"), commenced on February 19, 2021, and the term is expected to expire on May 31, 2026.

We also lease 28,029 square feet of office and laboratory space in San Francisco, California. The lease (the "San Francisco lease"), was acquired in the acquisition of Pionyr on August 4, 2023. The lease is expected to expire on April 30, 2027. We do not currently occupy the San Francisco facility and intend to sublease the space.

We believe our existing facilities are sufficient for our needs for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space, and we believe suitable additional or alternative space will be available in the future on commercially reasonable terms.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we may become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

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

Our common stock trades under the symbol "IKNA" on The Nasdaq Global Market and has been publicly traded since March 26, 2021. Prior to this time, there was no public market for our common stock.

Holders of Our Common Stock

As of March 1, 2024, there were approximately 61 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Dividends

We have never declared or paid any cash dividends on our common stock. We currently intend to retain earnings, if any, to support our business strategy and do not anticipate paying cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the sole discretion of our board of directors after taking into account various factors, including our financial condition, operating results, capital requirements and any plans for expansion.

Securities Authorized for Issuance under Equity Compensation Plans

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

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

None.

ITEM 6. RESERVED

Not applicable.

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

The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by these forward-looking statements. For convenience of presentation some of the numbers have been rounded in the text below. Please also see the section titled "Special Note Regarding Forward-Looking Statements." We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Overview

We are a clinical stage, targeted oncology company, focused on developing differentiated therapies for patients in need that target nodes of cancer growth, spread, and therapeutic resistance in the Hippo and RAS onco-signaling network. Our approach in each of our programs is to target both cancer-driving targets and mechanisms of resistance to other therapies. Our most advanced program, IK-930, is a selective inhibitor of TEAD1. The TEAD transcription factors (TEAD 1-4) execute the ultimate step in the Hippo signaling pathway, a known oncogenic pathway that also drives resistance to multiple targeted and chemo therapies. Our program in the RAS pathway, IK-595, is a molecular glue designed to trap MEK and RAF in an inactive complex, more completely inhibiting RAS signals than existing inhibitors. Since we commenced operations in 2016, we have advanced multiple product candidates into clinical development.

Our most advanced targeted oncology product candidate, IK-930, is an oral, TEAD1-selective, small molecule inhibitor of the Hippo signaling pathway. The Hippo pathway is genetically altered in approximately 10% of human cancers and is widely accepted as a prevalent driver of cancer pathogenesis and a mediator of poor outcomes for patients. In our ongoing first-in-human Phase 1 clinical trial, we are focusing on indications that provide the potential to achieve rapid proof-of-concept, such as NF2 deficient mesothelioma and solid tumors with YAP1 or TAZ gene fusions, including EHE. Approximately 40% of mesothelioma patients are genetically deficient for the tumor suppressor NF2 and 100% of EHE patients have oncogenic YAP1 or TAZ gene fusions. In October 2021, our IND for IK-930 was cleared by the FDA and we subsequently initiated a first-in-human Phase 1 clinical trial to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity of IK-930 as a monotherapy in patients with advanced solid tumors with or without gene alterations in the Hippo pathway. IK-930 received orphan drug designation from the FDA for the treatment of mesothelioma and EHE in March 2022 and December 2023, respectively. IK-930 was granted fast track designation from the FDA for the treatment of unresectable NF2-deficient mesothelioma in June 2022. In November 2023, we shared initial dose escalation safety data and initial anti-tumor activity data from EHE patients enrolled in the dose escalation monotherapy portion of the trial. In addition to the monotherapy approach, we plan to assess IK-930 in combination with other targeted therapies across several indications with multiple targeted therapies. Based on the role that the Hippo pathway plays in resistance to other targeted therapies, we believe that IK-930 may expand the patient populations that could benefit from therapies like EGFR inhibitors, KRAS inhibitors, and MEK inhibitors, among others. We have an established clinical collaboration with AstraZeneca for the evaluation of osimertinib in combination with IK-930 for patients with EGFR-mutant lung cancers as a cohort in the clinical program. Additional data from the monotherapy IK-930 clinical program is expected in the second half of 2024.

In addition to our work in the Hippo pathway, we are developing targeted therapies within the RAS pathway, one of the most highly dysregulated pathways in cancer. The RAS pathway is implicated in at least half a million new cancer diagnoses each year in the United States alone. Our goal is to achieve deep and sustained responses through targeting the pathway on multiple levels and leveraging the biology of known resistance mechanisms in our therapeutic design. We nominated IK-595 as our development candidate in our RAS pathway program in November 2022. IK-595 is designed to robustly inhibit MEK-RAF by gluing MEK and the RAFs (A, B, and C) in an inactive complex, thus more completely inhibiting RAS signals than existing inhibitors. IK-595's potential ability to complex CRAF, in particular, has been shown in preclinical models to prevent a well-recognized signaling bypass mechanism that cancer cells employ to drive therapeutic resistance to other MEK and RAF drugs in this class. In addition, trapping CRAF in an inactive complex has been shown in preclinical models to prevent the kinase independent anti-apoptotic function in RAS and RAF mutant cancers, a mechanism that cannot be addressed with first generation MEK inhibitors or pan-RAF inhibitors. We are developing IK-595 as an oral therapy, with a half-life designed to enable a pharmacokinetic profile that we believe can be potentially superior to other pathway inhibitors, with the goal of optimizing the therapeutic window for patients. We treated the first patient in the dose escalation Phase 1 study of IK-595 in December 2023.

On August 4, 2023, we acquired Pionyr, in accordance with the terms of the Merger Agreement. Under the terms of the Merger Agreement, at the closing of the acquisition, we acquired all of Pionyr's assets, including approximately $48.0 million in net cash at the time of closing, and we issued the holders of Pionyr common stock a total of 1,800,652 shares of the our common stock (including

153,121 shares of our non-voting common stock) at the purchase price of $7.15 per share and 4,153,439 shares of Series A Preferred Stock, also at the purchase price of $7.15 per share, each share of which was subsequently converted into one (1) share of the our common stock at a special meeting of stockholders held on October 11, 2023. As a result of the workforce reduction that we began implementing in the first quarter of 2024 and the associated anticipated reduction in our operating expenses, we expect that our cash, cash equivalents and marketable securities are sufficient to fund our operations into the second half of 2026.

To date, we have not had any products approved for sale and have not generated any revenue from product sales.

Financial Operations

To date, we have primarily financed our operations through proceeds from private placements of preferred stock, payments from a collaboration agreement, related party revenue, the completion of our IPO, URO, and the acquisition of Pionyr.

Since inception, we have incurred significant operating losses. Our net losses were $68.2 million and $68.8 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $282.4 million. We expect to continue to incur significant expenses and operating losses for at least the next several years as we:

- advance the development of our product candidate pipeline;
- initiate and continue research and preclinical and clinical development of potential new product candidates;
- maintain, expand and protect our intellectual property portfolio;
- acquire or in-license additional product candidates and technologies;
- expand our infrastructure and facilities to accommodate our growing employee base and ongoing development activities;
- continue to establish agreements with CROs and CMOs in connection with our preclinical studies and clinical trials;
- require the manufacture of larger quantities of our product candidates for clinical development and potential commercialization;
- seek marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval; and
- add operational, financial and management information systems and personnel to support our research and development programs, any future commercialization efforts and our continued operations as a public company.

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

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain marketing approval for our product candidates. The lengthy process of securing marketing approvals for new drugs requires the expenditure of substantial resources. Any delay or failure to obtain regulatory approvals would materially adversely affect the development efforts of our product candidates and our business overall. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2023, we had cash, cash equivalents and marketable securities of $175.5 million. As a result of the workforce reduction that we began implementing in the first quarter of 2024 and the associated anticipated reduction in our operating expenses, we believe that our cash and cash equivalents on hand as of December 31, 2023 will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2026. To date, we have primarily financed our operations through proceeds from private placements of preferred stock, payments from a collaboration agreement, related party revenue, completion of the IPO and URO, and the acquisition of Pionyr. We expect to incur substantial operating losses and negative cash flows from operations for the foreseeable future as we continue to invest significantly in research and development of our programs.

Our belief with respect to our ability to fund operations is based on estimates that are subject to risks and uncertainties. If actual results are different from our estimates, we may need to seek additional funding sooner than would otherwise be expected. There can be no assurance that we will be able to obtain additional funding on acceptable terms, if at all.

Components of our Results of Operations

Revenue

We have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval and successful commercialization efforts, we may generate revenue in the future from product sales. We cannot predict if, when, or to what extent we will generate revenue from the commercialization and sale of our product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

All of our revenue has been derived from research and development revenue under our Bristol-Myers Squibb Collaboration Agreement.

Collaboration Agreement and Stock Purchase Agreement with Bristol-Myers Squibb

In January 2019, we entered into the Bristol-Myers Squibb Collaboration Agreement with Celgene Corporation (which was acquired by Bristol-Myers Squibb in November 2019), pursuant to which Bristol-Myers Squibb could elect in its sole discretion to exclusively license rights to develop and commercialize compounds (and products and diagnostic products containing such compounds) that modulate the activity of two collaboration targets, kynurenine and AHR, excluding AHR agonists for inverse agonists, known as IK-412 and IK-175, respectively. On a program-by-program basis, through the earlier of January 2024 or the completion of a Phase 1b clinical trial for each of IK-175 and IK-412, Bristol-Myers Squibb had the exclusive option to exclusively license to develop, commercialize and manufacture the relevant product candidate worldwide. Concurrent with execution of the Bristol-Myers Squibb Collaboration Agreement, we entered into a stock purchase agreement with Celgene Corporation (now Bristol-Myers Squibb) in November 2019 (the "Stock Purchase Agreement"), pursuant to which we issued Celgene Corporation 14,545,450 shares of Series A-1 preferred stock.

Bristol-Myers Squibb paid a total of $95.0 million in aggregate upfront consideration related to the Bristol-Myers Squibb Collaboration Agreement and Stock Purchase Agreement. The IK-412 and IK-175 programs were eligible for opt-in through early 2024. On January 17, 2024, Bristol-Myers Squibb notified us of its decision not to opt-in on the IK-175 program. In addition, Bristol-Myers Squibb did not provide an opt-in exercise for the IK-412 program. As a result, we have regained full global rights to the IK-175 and IK-412 programs. We will not invest further in the clinical development of IK-175 or IK-412, but will pursue strategic business development opportunities, including out-licensing. Our operating expenses since inception consist solely of research and development costs and general and administrative costs.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research and development activities. These efforts and costs include external research costs, personnel costs, consultants, supplies, license fees and facility-related expenses. We expense research and development costs as incurred. These expenses include:

- employee-related expenses, including salaries, related benefits and stock-based compensation expense, for employees engaged in research and development functions;
- expenses incurred under agreements with CROs, which are primarily engaged to support our clinical trials;
- expenses incurred under agreements with CMOs, which are primarily engaged to provide drug substance and product for our preclinical research and development programs, nonclinical studies and other scientific development services;
- the cost of acquiring and manufacturing preclinical study materials, including manufacturing registration and validation batches;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance;
- acquisition of in-process research and development assets that have no alternative future use;
- costs related to compliance with quality and regulatory requirements; and
- payments made under third-party licensing agreements.

Advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will increase substantially in connection with our planned clinical development activities in the near term and in the future. At this time, we cannot accurately estimate or know the nature, timing and costs of the efforts that will be necessary to complete the clinical development of, or obtain regulatory approval for, any of our current or future product candidates. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the following:

- our ability to add and retain key research and development personnel;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates;
- our successful enrollment in and completion of clinical trials, including our ability to generate positive data from any such trials;
- the size and cost of any future clinical trials for existing or future product candidates in our pipeline;
- the costs associated with the development of any additional programs we identify in-house or acquire through collaborations and other arrangements and the success of such collaborations;
- the terms and timing of any additional collaborations, license or other arrangement, including the timing of any payments thereunder;
- our ability to establish and maintain agreements and operate with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if any of our product candidates are approved;
- costs related to manufacturing of our product candidates or to account for any future changes in our manufacturing plans;
- our ability to obtain and maintain patents, trade secret, and other intellectual property protection and regulatory exclusivity for our product candidates, both in the United States and internationally;
- our ability to obtain and maintain third-party insurance coverage and adequate reimbursement for our product candidates, if and when approved;
- the acceptance of our product candidates, if approved, by patients, the medical community and third-party payors;
- effectively competing with other products if our product candidates are approved;
- the impact of any business interruptions to our operations, including the timing and enrollment of patients in our planned clinical trials, or to those of our manufacturers, suppliers, or other vendors resulting from pandemics or similar public health crisis; and
- our ability to maintain a continued acceptable safety profile for our therapies following approval.

A change in the outcome of any of these variables with respect to the development of our product candidates could significantly change the costs and timing associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, and administrative functions. General and administrative expenses also include direct and allocated facility-related costs as well as professional fees for legal, patent, consulting, investor and public relations, accounting, auditing, tax services, and insurance costs.

We expect that our general and administrative expenses will increase as our organization grows in the future to support continued research and development activities and potential commercialization of our product candidates. These increases will likely include increased costs related to the hiring of additional personnel and fees for outside consultants, attorneys, and accountants, among other expenses. Additionally, we expect to incur increased expenses associated with being a public company, including costs of additional personnel, 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.

Results of Operations

Comparison of the Years Ended December 31, 2023 and 2022

The following table summarizes our results of operations:

	Year Ended December 31,			
(In thousands, except percentages)	**2023**	**2022**	**Dollar Change**	**Percent Change**
Revenue:				
Research and development revenue under collaboration agreement	$ 9,160	$ 15,618	$ (6,458)	(41)%
Operating expenses:				
Research and development	59,652	64,321	(4,669)	-7%
General and administrative	24,925	22,201	2,724	12%
Total operating expenses	84,577	86,522	(1,945)	-2%
Loss from operations	(75,417)	(70,904)	(4,513)	6%
Other income, net	7,089	2,139	4,950	231%
Loss before income taxes	(68,328)	(68,765)	437	-1%
Income tax benefit (expense)	162	—	162	—
Net loss	$ (68,166)	$ (68,765)	$ 599	-1%

Revenue

The research and development revenue under collaboration agreement is related to the Bristol-Myers Squibb Collaboration Agreement for the IK-175 and IK-412 programs which was executed in January 2019. The decrease in revenue during the twelve months ended December 31, 2023, as compared to the same period in the prior year, was primarily due to an increase in manufacturing activities as a result of the substantial completion of manufacturing efforts related to the IK-412 program in 2022.

Research and Development Expenses

The following table summarizes our research and development expenses:

	Year Ended December 31,			
(In thousands, except percentages)	**2023**	**2022**	**Dollar Change**	**Percent Change**
Direct research and development expenses by program:				
IK-930	$ 11,608	$ 10,377	$ 1,231	12%
IK-175	2,677	6,829	(4,152)	(61)%
IK-595	8,068	7,499	569	8%
Other assets, discovery, and early stage programs	11,173	14,884	(3,711)	(25)%
Research and development personnel and overhead expenses and unallocated	26,126	24,732	1,394	6%
Total research and development expenses	$ 59,652	$ 64,321	$ (4,669)	(7)%

The decrease in research and development expense of $4.7 million during the twelve month ended December 31, 2023 compared to the same period in the prior year was primarily attributable to due to decreases in clinical trial costs related to IK-175, and decreases in other discovery and early stage programs as a result of the Company prioritizing its focus on advancing its clinical stage programs. These decreases were partially offset by costs associated with the wind down of Pionyr programs, increased clinical trial costs for IK-930 and IK-595 due to increased patient enrollment over the prior year, and increased research and development personnel and overhead expenses, primarily due to increased consulting fees.

General and Administrative Expenses

The following table summarizes our general and administrative expenses:

	Year Ended December 31,			
(In thousands, except percentages)	**2023**	**2022**	**Dollar Change**	**Percent Change**
General and administrative	$ 24,925	$ 22,201	$ 2,724	12%

The increase in general and administrative expense of $2.7 million was primarily attributable to the impairment of a portion of the San Francisco lease assumed in the acquisition of Pionyr and an increases in facility, legal and audit expenses, partially offset by a decrease in insurance costs.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have not generated any revenue from product sales and have incurred significant operating losses. 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. To date, we have financed our operations primarily through private placements of preferred stock, from upfront payments from the Bristol-Myers Squibb Collaboration Agreement, from cash obtained from acquisitions, from common stock in our IPO and URO, and most recently, through the acquisition of Pionyr. As of December 31, 2023, we had cash, cash equivalents and marketable securities of $175.5 million.

Cash Flows

The following table summarizes our sources and uses of cash for the years ended December 31, 2023 and 2022:

	Year Ended December 31,	
(In thousands)	**2023**	**2022**
Net cash used in operating activities	$ (79,743)	$ (74,109)
Net cash provided by (used in) investing activities	64,144	(99,284)
Net cash provided by financing activities	75,980	1,095
Net increase (decrease) in cash and cash equivalents	$ 60,381	$ (172,298)

Operating Activities

Cash flows from operating activities are greatly influenced by our use of cash for operating expenses and working capital requirements to support the business. We have historically experienced negative cash flows from operating activities as we invested in developing our platform, drug discovery efforts, and related infrastructure. Net cash used in operating activities for the twelve months ended December 31, 2023 increased by $5.6 million compared to the same period in 2022. Cash used in operating activities was primarily related to our net loss of $68.2 million, the payout of operating liabilities assumed in connection with the acquisition of Pionyr, partially offset by a decrease in deferred revenue.

Investing Activities

The increase in cash provided by investing activities of $163.4 million was primarily attributable to proceeds from the sales and maturities of marketable securities of $154.6 million, offset by the purchase of marketable securities of $90.1 million during the year ended December 31, 2023, compared to the sales and maturities of marketable securities of $118.5 million and the purchase of marketable securities of $216.3 million during the year ended December 31, 2022.

Financing Activities

The increase in cash provided by financing activities of $74.9 million primarily reflects the net cash received in connection with the acquisition of Pionyr of $39.1 million and the net cash proceeds received from our May 17, 2023 offering of common stock of $37.4 million in our URO.

Funding Requirements

We expect to continue to incur significant expenses for the foreseeable future in connection with our ongoing activities, particularly as we continue the research and development for, initiate clinical trials for, 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. Furthermore, we expect to continue to incur additional costs associated with operating as a public company, including increased costs of accounting, audit, legal, regulatory, and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs, and investor and public relations costs. Accordingly, we will need to obtain substantial additional funding in

connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, or eliminate our research and development programs or future commercialization efforts.

We expect that our existing cash, cash equivalents, and marketable securities as of December 31, 2023, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2026. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Our future operating and capital requirements will depend on many factors, including:

- the scope, progress, results and costs of discovery, preclinical development, laboratory testing, and clinical trials for other potential product candidates we may develop, if any;
- the costs, timing, and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements we might have at such time;
- the costs and timing of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the amount of 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, and enforcing our intellectual property rights, and defending intellectual property-related claims;
- the in-licensing or acquisition of assets in line with our strategy;
- our headcount growth and associated costs, as we expand our business operations and our research and development activities; and
- the costs of operating as a public company.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interests may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect your rights as a common stockholder. Any debt financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

On April 27, 2022, we filed a shelf registration statement on Form S-3 (“Shelf”), with the SEC, which covers the offering, issuance, and sale by us of up to an aggregate of $300.0 million of our common stock, preferred stock, debt securities, warrants and/or units of any combination thereof. We simultaneously entered into a sales agreement with Jefferies LLC, as sales agent, to provide for the issuance and sale by us of up to $100.0 million of our common stock from time to time in “at-the-market” offerings under the Shelf, which we refer to as the “ATM Program.” The Shelf was declared effective by the SEC on May 5, 2022. As of the date hereof, no sales have been made pursuant to the ATM Program.

Contractual Obligations

We have a non-cancelable operating lease agreement for our office, lab, and animal care facility space in our Boston, Massachusetts corporate headquarters. We expect the total future minimum lease payments from December 31, 2023 to lease expiration in May 2026 to be $4.5 million. Additionally, in connection with the acquisition of Pionyr, we acquired an operating lease agreement for office and lab space in San Francisco, California. The space is currently vacant and we are actively seeking a tenant to sublease the space. We expect the total future minimum lease payments from December 31, 2023 to lease expiration in April 2027 to be $7.5 million. Our total future minimum lease payments for each of the next five years and in total are included in Note 15.

We enter into contracts in the normal course of business with CROs and CMOs for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts typically do not contain any minimum purchase commitments and are generally cancelable by us, typically upon prior notice of 30 days. Payments due upon cancelation typically consist only of payments for services provided and expenses incurred up to the date of cancelation.

We may incur potential contingent payments upon our achievement of clinical, regulatory, and commercial milestones, as applicable, or that we may be required to make royalty payments under license agreements we have entered into with various entities pursuant to which we have in-licensed certain intellectual property, such as our patent license agreement with the University of Texas at Austin. Due to the uncertainty of the achievement and timing of the events requiring payment under these agreements, the amounts to be paid by us are not fixed or determinable at this time and have not been included in the table above.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in the Notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be the most critical in understanding the judgments and estimates we use in preparing our consolidated financial statements:

Revenue Recognition

To determine revenue recognition we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. At contract inception, once the contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract and determine those that are performance obligations, then assess whether each promised good or service is distinct. When we offer options for additional goods or services, such as to receive a license for intellectual property or for additional goods or services, we evaluate whether such options contain material rights that should be treated as additional performance obligations. Once performance obligations are identified, we then recognize as revenue the amount of the transaction price that the Company allocated to the respective performance obligation when (or as) each performance obligation is satisfied, either at a point in time or over time. If the performance obligation is satisfied over time, we recognize revenue based on the use of an input method.

At each reporting date, we calculate the measure of progress for the performance obligations transferred over time. The calculation generally uses an input measure based on costs incurred to-date relative to estimated total costs to complete the transfer of the performance obligation. The measurement of progress is then used to calculate the total revenue earned, including any cumulative catch-up adjustment.

Accrued Research and Development Expenses

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

- vendors, including research laboratories, in connection with preclinical development activities;
- CROs and investigative sites in connection with preclinical studies; and

- CMOs in connection with drug substance and drug product formulation of preclinical studies.

We base the expense recorded related to external research and development on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CMOs and CROs that supply, conduct and manage nonclinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We account for stock-based compensation awards in accordance with ASC 718, *Compensation—Stock Compensation* (ASC 718). ASC 718 requires all stock-based payments, including grants of stock options, to be recognized in the consolidated statement of operations and comprehensive loss based on their grant date fair values. We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model. Calculating the fair value of stock-based awards requires that we make subjective assumptions.

Pursuant to ASC 718, we measure stock-based awards at fair value on the date of grant and recognize the corresponding stock-based compensation expense of those awards on a straight-line basis over the requisite service period, which is generally the vesting period of the respective award. We have historically granted stock options with exercise prices equivalent to the fair value of our common stock as of the date of grant.

The Black-Scholes option-pricing model uses the following inputs: the fair value of our common stock, the expected volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. Due to the lack of a public market for our common stock and a lack of company-specific historical and implied volatility data, we have based our computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to us, including stage of product development, life science industry focus, length of trading history and similar vesting provisions. The historical volatility data is calculated based on a period of time commensurate with the expected term assumption. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation. We use the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. Under this approach, the weighted-average expected option term is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of our stock options. We utilize this method due to lack of historical exercise data and the "plain-vanilla" nature of our stock-based awards. The expected term is applied to the stock option grant group as a whole, as we do not expect substantially different exercise or post-vesting termination behavior among our employee population. For options granted to non-employees, we utilize the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as we have never paid cash dividends and have no current plans to pay any cash dividends on our common stock. The fair value of each restricted common stock award is estimated on the date of grant based on the fair value of our common stock on that same date.

Emerging Growth Company

In April 2012, the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for new or revised accounting standards during the period in which we remain an emerging growth company; however, we may adopt certain new or revised accounting standards early.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than $1.235 billion in annual revenue; (2) the date we qualify as a "large accelerated filer," with at least $700.0 million of equity

securities held by non-affiliates; (3) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (4) the last day of the fiscal year ending after the fifth anniversary of our IPO.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than $700.0 million measured on the last business day of our second fiscal quarter.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide this information required under this item.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Our consolidated financial statements, together with the reports of our independent registered public accounting firms, appear beginning on page F-1 of this Annual Report for the year ended December 31, 2023.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Our Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (i) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (ii) accumulated and communicated to our management, including our Principal Executive Officer and Principal Financial Officer, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our management, under the supervision and with the participation of our Principal Executive Officer and Principal Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2023, the end of the period covered by this Annual Report on Form 10-K. Based upon such evaluation, our Principal Executive Officer and Principal Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;

- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and

- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. 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.

Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2023. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013 framework) (COSO). Based on its assessment, management believes that, as of December 31, 2023, our internal control over financial reporting is effective based on those criteria.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm on internal control over financial reporting due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the quarter ended December 31, 2023 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

(a) None.

(b) 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 under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

ITEM 11. EXECUTIVE COMPENSATION

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Our independent public accounting firm is Ernst & Young LLP, Boston, Massachusetts, PCAOB Auditor ID: 42.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(1) Financial Statements

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

(2) Financial Statement Schedules

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

(3) Exhibits

Exhibit Index

Exhibit Number	Description
2.1	Agreement and Plan of Merger by and among the Registrant, Arrys Merger Sub, Inc., Arrys Therapeutics, Inc. and OrbiMed Private Investments VI, LP, as stockholder representative, dated December 18, 2018 (Incorporated by reference to Exhibit 2.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-253919) filed with the Securities and Exchange Commission on March 5, 2021).
2.2	Agreement and Plan of Merger by and among the Registrant, AMI Merger Sub, Inc., Amplify Medicines, Inc. and Atlas Venture Fund XI, L.P. as stockholder representative, dated October 1, 2020 (Incorporated by reference to Exhibit 2.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-253919) filed with the Securities and Exchange Commission on March 5, 2021).
2.3#	Agreement and Plan of Merger by and among the Registrant, Portsmouth Merger Sub I, Inc., Portsmouth Merger Sub II, LLC, Pionyr Immunotherapeutics, Inc. and Fortis Advisors LLC, as securityholder agent, dated August 4, 2023 (Incorporated by reference to Exhibit 2.1 to the Registrant's Current Report on Form 8-K (File No. 001-40287 filed with the Securities and Exchange Commission on August 7, 2023).
3.1	Fifth Amended and Restated Certificate of Incorporation of the Registrant (Incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-40287) filed with the Securities and Exchange Commission on March 30, 2021).
3.2	Amended and Restated Bylaws of the Registrant (Incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-40287) filed with the Securities and Exchange Commission on March 30, 2021).
3.3	Certificate of Designations of Series A Non-Voting Convertible Preferred Stock (Incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-40287) filed with the Securities and Exchange Commission on August 7, 2023).
4.1	Specimen Common Stock Certificate (Incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-253919) filed with the Securities and Exchange Commission on March 22, 2021).
4.2	Fourth Amended and Restated Investors' Rights Agreement (Incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-253919) filed with the Securities and Exchange Commission on March 5, 2021).
4.3	Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934, as amended (Incorporated by reference to Exhibit 4.3 to the Registrant's Annual Report on Form 10-K (File No. 001-40287) filed with the Securities and Exchange Commission on March 17, 2022).
4.4	Form of Senior Indenture between Registrant and one or more trustees to be named (Incorporated by reference to Exhibit 4.5 to the Registrant's Registration Statement on Form S-3 (File No. 333-264517) filed with the Securities and Exchange Commission on April 27, 2022).
4.5	Form of Subordinated Indenture between Registrant and one or more trustees to be named, (Incorporated by reference to Exhibit 4.6 to the Registrant's Registration Statement on Form S-3 (File No. 333-264517) filed with the Securities and Exchange Commission on April 27, 2022).
10.1†	2016 Stock Incentive Plan, and form of award agreements thereunder (Incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-253919) filed with the Securities and Exchange Commission on March 5, 2021).

10.2†	2021 Stock Option and Incentive Plan, and form of award agreements thereunder (Incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1/A (File No. 333-253919) filed with the Securities and Exchange Commission on March 22, 2021).
10.3†	2021 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1/A (File No. 333-253919) filed with the Securities and Exchange Commission on March 22, 2021).
10.4†	Amended & Restated Non-Employee Director Compensation Policy (Incorporated by reference to Exhibit 10.4 to the Registrant's Annual Report on Form 10-K (File No. 001-40287) filed with the Securities and Exchange Commission on March 14, 2023).
10.5	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers (Incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1/A (File No. 333-253919) filed with the Securities and Exchange Commission on March 22, 2021).
10.6†	Form of Amended and Restated Employment Agreement (Incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1/A (File No. 333-253919) filed with the Securities and Exchange Commission on March 22, 2021).
10.7	License Agreement by and between the Registrant and AskAt, Inc., dated December 14, 2017, as amended on December 18, 2018 (Incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1 (File No. 333-253919) filed with the Securities and Exchange Commission on March 5, 2021).
10.8	Master Collaboration Agreement by and between the Registrant and Celgene Corporation (now Bristol-Myers Squibb), dated January 14, 2019 (Incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 (File No. 333-253919) filed with the Securities and Exchange Commission on March 5, 2021).
10.9	Patent License Agreement by and between the Registrant and The University of Texas at Austin, on behalf of the Board of Regents of the University of Texas System, dated March 29, 2015, as amended on May 18, 2016, December 15, 2016, October 24, 2017, April 25, 2018 and January 9, 2019 (Incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 (File No. 333-253919) filed with the Securities and Exchange Commission on March 5, 2021).
10.10	Lease Agreement between the Registrant and OPG MP Parcel Owner (DE) LLC, dated July 31, 2020 (Incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (File No. 333-253919) filed with the Securities and Exchange Commission on March 5, 2021).
10.11	Contingent Value Rights Agreement, by and between the Registrant and Computershare Trust Company N.A, as rights agent, dated August 4, 2023 (Incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-40287) filed with the Securities and Exchange Commission on August 7, 2023).
19.1*	Insider Trading Policy.
21.1	Subsidiaries of the Registrant (Incorporated by reference to Exhibit 21.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-253919) filed with the Securities and Exchange Commission on March 5, 2021).
23.1*	Consent of Independent Registered Public Accounting Firm.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1+	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1*†	Compensation Recovery Policy.
101.INS*	Inline XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.
104*	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.*

* Filed herewith.

+ The certifications furnished in Exhibit 32.1 hereto are deemed to be furnished with this Annual Report on Form 10-K and will not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

Certain information in this document has been excluded pursuant to Regulation S-K, Item 601(b)(2). Such excluded information is not material and the Registrant customarily and actually treats as private or confidential.

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

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

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

IKENA ONCOLOGY, INC.

Date: March 12, 2024

By: /s/ Mark Manfredi
Mark Manfredi, Ph.D.
President and Chief Executive Officer

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 on the dates indicated.

Name	Title	Date
/s/ Mark Manfredi **Mark Manfredi, Ph.D.**	President, Chief Executive Officer and Director *Principal Executive Officer*	March 12, 2024
/s/ Jotin Marango **Jotin Marango, M.D., Ph.D.**	Chief Financial Officer and Head of Corporate Development *Principal Financial Officer and Principal Accounting Officer*	March 12, 2024
/s/ Owen Hughes **Owen Hughes**	Director	March 12, 2024
/s/ David Bonita **David Bonita, M.D.**	Director	March 12, 2024
/s/ Iain D. Dukes **Iain D. Dukes, D.Phil.**	Director	March 12, 2024
/s/ Jean-François Formela **Jean-François Formela, M.D.**	Director	March 12, 2024
/s/ Maria Koehler **Maria Koehler, M.D., Ph.D.**	Director	March 12, 2024
/s/ Otello Stampacchia **Otello Stampacchia, Ph.D.**	Director	March 12, 2024
/s/ Richard Wooster **Richard Wooster, Ph.D.**	Director	March 12, 2024

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Ikena Oncology, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Ikena Oncology, Inc. (the Company) as of December 31, 2023 and 2022, the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity and cash flows for each of the two years in the period ended December 31, 2023, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2019.

Boston, Massachusetts
March 12, 2024

IKENA ONCOLOGY, INC.

CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 119,894	$ 59,919
Marketable securities	55,571	97,028
Prepaid expenses and other current assets	3,197	3,063
Total current assets	178,662	160,010
Property and equipment, net	2,335	3,205
Right-of-use asset	5,686	5,255
Deposits and other assets	5,409	3,789
Total assets	$ 192,092	$ 172,259
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,066	$ 2,093
Accrued expenses and other current liabilities	8,581	8,343
Operating lease liability	3,558	1,907
Deferred revenue	—	9,160
Total current liabilities	14,205	21,503
Long-term portion of operating lease liability	7,180	3,787
Other long-term liabilities	950	—
Total liabilities	22,335	25,290
Commitments and contingencies (Note 15)		
Stockholders' equity:		
Preferred Stock, $0.001 par value, 10,000,000 shares authorized as of December 31, 2023 and 2022; No shares issued and outstanding as of December 31, 2023 or December 31, 2022	—	—
Common stock, $0.001 par value, 150,000,000 shares authorized, 48,258,111 shares issued and outstanding as of December 31, 2023; 150,000,000 shares authorized, 36,257,493 shares issued and outstanding as of December 31, 2022	48	36
Additional paid-in capital	452,142	361,915
Accumulated other comprehensive loss	(48)	(763)
Accumulated deficit	(282,385)	(214,219)
Total stockholders' equity	169,757	146,969
Total liabilities and stockholders' equity	$ 192,092	$ 172,259

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

IKENA ONCOLOGY, INC.

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

	Year Ended December 31,	
	2023	2022
Research and development revenue under collaboration agreement	$ 9,160	$ 15,618
Operating expenses:		
Research and development	59,652	64,321
General and administrative	24,925	22,201
Total operating expenses	84,577	86,522
Loss from operations	(75,417)	(70,904)
Other income (expense):		
Investment income	7,111	2,149
Other expense	(22)	(10)
Total other income, net	7,089	2,139
Loss before income taxes	(68,328)	(68,765)
Income tax benefit (expense)	162	—
Net loss	$ (68,166)	$ (68,765)
Other comprehensive loss:		
Unrealized gain (loss) on marketable securities	715	(763)
Total comprehensive loss	$ (67,451)	$ (69,528)
Net loss per share:		
Net loss per share attributable to common stockholders basic and diluted	$ (1.63)	$ (1.90)
Weighted-average common shares outstanding, basic and diluted	41,735,081	36,188,420

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

IKENA ONCOLOGY, INC.

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

	Redeemable Convertible Preferred Stock		Common Stock					
	Shares	Amount	Shares	Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
Balance as of December 31, 2021	—	$ —	35,975,034	$ 36	$ 353,295	$ —	$ (145,454)	$ 207,877
Exercise of stock options	—	—	282,459	—	1,095	—	—	1,095
Stock-based compensation	—	—	—	—	7,525	—	—	7,525
Other comprehensive loss	—	—	—	—	—	(763)	—	(763)
Net loss	—	—	—	—	—	—	(68,765)	(68,765)
Balance as of December 31, 2022	—	$ —	36,257,493	$ 36	$ 361,915	$ (763)	$ (214,219)	$ 146,969
Issuance of common stock for underwritten registered offering, net of offering costs of $2.6 million	—	—	6,110,000	6	37,415	—	—	37,421
Repurchase of common stock	—	—	(97,500)	—	(663)	—	—	(663)
Issuance of preferred stock in connection with the Acquisition, net of issuance costs of $0.9 million	4,153,439	32,545	—	—	—	—	—	—
Conversion of preferred stock to common stock	(4,153,439)	(31,886)	4,153,439	4	31,883	—	—	31,887
Issuance of common stock in connection with the Acquisition, net of issuance costs of $0.4 million	—	—	1,800,652	2	14,109	—	—	14,111
Cash consideration paid to settle Pionyr restricted stock units, stock options, and unaccredited stockholders	—	(659)	—	—	(285)	—	—	(285)
Exercise of stock options	—	—	34,027	—	136	—	—	136
Stock-based compensation	—	—	—	—	7,632	—	—	7,632
Other comprehensive income	—	—	—	—	—	715	—	715
Net loss	—	—	—	—	—	—	(68,166)	(68,166)
Balance as of December 31, 2023	$ —	$ —	48,258,111	$ 48	$ 452,142	$ (48)	$ (282,385)	$ 169,757

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

IKENA ONCOLOGY, INC.

CONSOLIDATED STATEMENT OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2023	2022
Cash flows from operating activities		
Net loss	$ (68,166)	$ (68,765)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation	1,020	751
Amortization of marketable securities	(2,023)	50
Stock-based compensation expense	7,632	7,525
Non-cash operating lease expense	1,714	1,283
Loss on disposal of property and equipment	5	173
Impairment of right of use asset	1,744	—
Net realized loss on marketable securities	—	12
Changes in operating assets and liabilities		
Prepaid expenses and other current assets	1,835	1,236
Accounts payable	(2,870)	(291)
Accrued expenses and other current liabilities	(7,660)	2,230
Lease liability	(2,087)	(1,292)
Deferred revenue	(9,160)	(15,618)
Deposits and other assets	(1,824)	(1,403)
Other long-term liabilities	97	—
Net cash flows used in operating activities	(79,743)	(74,109)
Cash flows from investing activities		
Purchases of property and equipment	(414)	(1,431)
Purchases of marketable securities	(90,052)	(216,338)
Sales and maturities of marketable securities	154,610	118,485
Net cash flows provided by (used in) investing activities	64,144	(99,284)
Cash flows from financing activities		
Cash and cash equivalents acquired in connection with the acquisition of Pionyr, net of issuance costs paid	40,030	—
Cash consideration paid in connection with the acquisition of Pionyr	(944)	—
Proceeds from issuance of common stock for underwritten registered offering, net of offering costs	37,421	—
Repurchase of common stock	(663)	—
Proceeds from exercise of stock options	136	1,095
Net cash flows provided by financing activities	75,980	1,095
Net increase (decrease) in cash and cash equivalents	60,381	(172,298)
Cash, cash equivalents and restricted cash, beginning of year	60,791	233,089
Cash, cash equivalents and restricted cash, end of year	$ 121,172	$ 60,791
Reconciliation of cash, cash equivalents, and restricted cash to the consolidated balance sheets		
Cash and cash equivalents	$ 119,894	$ 59,919
Restricted cash included in other assets	1,278	872
Cash, cash equivalents and restricted cash, end of year	$ 121,172	$ 60,791
Supplemental disclosure of non-cash activities		
Right-of-use asset recognized upon assumption of San Francisco, CA lease from Pionyr	$ 3,889	$ —
Purchases of property and equipment in accounts payable and accrued expenses	$ —	$ 259

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

1. NATURE OF BUSINESS AND ORGANIZATION

Ikena Oncology, Inc. (the "Company") is a clinical stage targeted oncology company, focused on developing differentiated therapies for patients in need that target nodes of cancer growth, spread, and therapeutic resistance in the Hippo and RAS onco-signaling network. The Company's approach in each of its programs is to target both cancer-driving targets and mechanisms of resistance to other therapies. The Company's most advanced program, IK-930, is a selective inhibitor of the transcriptional enhanced associate domain 1 ("TEAD 1"). The TEAD transcription factors (TEAD 1-4) execute the ultimate step in the Hippo signaling pathway, a known oncogenic pathway that also drives resistance to multiple targeted and chemo therapies. The Company's program in the RAS pathway, IK-595, is a molecular glue designed to trap MEK and RAF in an inactive complex, more completely inhibiting RAS signals than existing inhibitors. Since the Company commenced operations in 2016, it has advanced multiple product candidates into clinical development.

On March 30, 2021 the Company completed an initial public offering ("IPO") in which the Company issued and sold 8,984,375 shares of common stock, including full exercise of the underwriters' over-allotment option to purchase an additional 1,171,875 shares, at a public offering price of $16.00 per share and received $131.3 million in net proceeds after deducting underwriting discounts and commissions and offering expenses.

The Company acquired Pionyr Immunotherapeutics, Inc., a Delaware corporation ("Pionyr"), pursuant to an Agreement and Plan of Merger, dated August 4, 2023 by and among the Company, Portsmouth Merger Sub I, Inc., a Delaware corporation and a wholly owned subsidiary of the Company ("Merger Sub I"), Portsmouth Merger Sub II, LLC, a Delaware limited liability company and wholly owned subsidiary of the Company ("Merger Sub II"), Pionyr, and Fortis Advisors LLC, as securityholder agent (the "Pionyr Acquisition Agreement"). Pursuant to the Pionyr Acquisition Agreement, Merger Sub I merged with and into Pionyr, after which Pionyr was the surviving corporation and became a wholly owned subsidiary of the Company (the "First Merger"). Immediately after the First Merger, Pionyr merged with and into Merger Sub II, after which Merger Sub II was the surviving entity (collectively with the First Merger, the "Acquisition").

Under the terms of the Pionyr Acquisition Agreement, at the closing, the Company issued to the stockholders of Pionyr 1,800,652 shares of its common stock (including 153,121 shares of its non-voting common stock), and 4,153,439 shares of Series A Non-Voting Convertible Preferred Stock ("Series A Preferred Stock"), which was a newly designated series of preferred stock that is intended to have economic rights equivalent to the Company's common stock, but with only limited voting rights. The Series A Preferred Stock was converted to shares of the Company's common stock pursuant to stockholder approval at a special meeting of stockholders held on October 11, 2023. Each stockholder of Pionyr at the time of closing also received one contractual contingent value right ("CVR") for each share of Pionyr stock held at closing. The CVR entitles the holder to receive 50% of net proceeds, outside of royalties, for any potential monetization of Pionyr legacy programs within two years.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Principles of Consolidation: The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, Arrys Therapeutics, Inc. ("Arrys"), Ikena Oncology Securities Corporation and Amplify Medicines, Inc, ("Amplify"), and Portsmouth Merger Sub II, LLC. All intercompany balances and transactions have been eliminated in consolidation. These consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the ASC and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

Use of Estimates: The preparation of the Company's financial statements requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. Estimates and judgments are based on historical information and other market-specific or various relevant assumptions, including in certain circumstances, future projections, that management believes to be reasonable under the circumstances. Actual results could differ materially from estimates. Estimates and assumptions are used for, but not limited to the accruals for research and development expenses research and development revenue under a collaboration agreement.

Liquidity: The Company is subject to a number of risks similar to other early-stage life science companies, including, but not limited to, successful development of its product candidates, raising additional capital with favorable terms, protection of proprietary

technology and market acceptance of any approved future products. The successful development of product candidates requires substantial working capital, which may not be available to the Company on favorable terms or at all.

To date, the Company has financed its operations primarily from common stock in its IPO and Underwritten Registered Offering ("URO"), private placements of preferred stock, payments from a collaboration arrangement, related party revenue, and most recently, through the acquisition of Pionyr. The Company currently has no source of product revenue, and it does not expect to generate product revenue for the foreseeable future. To date, the Company's revenue has primarily been from a collaboration agreement. The Company has devoted substantially all of its financial resources and efforts to identifying potential product candidates and conducting preclinical studies and clinical trials.

As of December 31, 2023, the Company's cash, cash equivalents, marketable securities were $175.5 million. The Company believes the cash, cash equivalents, marketable securities as of December 31, 2023 will enable it to fund its current planned operations for at least the next twelve months from the date of issuance of these financial statements, though it may pursue additional cash resources through public or private equity or by establishing collaborations with other companies.

Management's expectations with respect to its ability to fund current and long term planned operations are based on estimates that are subject to risks and uncertainties. If actual results are different from management's estimates, the Company may need to seek additional strategic or financing opportunities sooner than would otherwise be expected. However, there is no guarantee that any collaboration exercise options will be achieved or that any of these strategic or financing opportunities will be executed on favorable terms, and some could be dilutive to existing stockholders.

If the Company is unable to obtain additional funding on a timely basis, it may be forced to significantly curtail, delay, or discontinue one or more of its planned research or development programs or be unable to expand its operations. As of December 31, 2023, the Company had an accumulated deficit of $282.4 million. The Company anticipates operating losses to continue for the foreseeable future due to, among other things, costs related to research and development of its product candidates and its administrative organization.

Segments: Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the Chief Operating Decision Maker ("CODM") in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its Chief Executive Officer. The Company has determined it operates in a single operating segment and has one reportable segment. All long-lived assets of the Company reside in the United States.

Concentration of Credit Risk and of Significant Suppliers: Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash, cash equivalents, and marketable securities. Cash and cash equivalents are deposited with federally insured financial institutions in the United States and may, at times, exceed federally insured limits. The Company places marketable securities with a highly rated financial institution. Additionally, as of December 31, 2023, the Company has not experienced any credit related losses on accounts that hold the Company's cash, cash equivalents and marketable securities.

The Company is dependent on third-party manufacturers and Clinical Research Organizations ("CROs") to supply products and provide services for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. The Company also relies on at least two CROs to conduct its clinical trials. The Company's programs could be adversely affected if a third-party manufacturer or a CRO is unable to successfully carry out their contractual obligations or meet expected deadlines. If a third-party manufacturer or a CRO needs to be replaced, the Company may not be able to complete its program development on its anticipated timelines and may incur additional expenses as a result, which could be significant.

Fair Value of Financial Instruments: The Company's financial instruments consist mainly of cash equivalents, restricted cash, accounts payable, and marketable securities. The carrying amounts of cash equivalents, restricted cash, and accounts payable approximate their estimated fair value due to their short-term maturities. Fair value is estimated based on a three-tier fair value hierarchy to prioritize the inputs used in the Company's fair value measurements. These tiers include: Level 1, defined as observable inputs such as quoted prices in active markets for identical assets; Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable; and Level 3, defined as unobservable inputs in which little or no market data exists.

The Company recognizes transfers between levels of the fair value hierarchy on the date of the event or change in circumstances that caused the transfer.

Cash and Cash Equivalents: The Company considers all short-term, highly liquid investments with original maturities of 90 days or less at acquisition date to be cash equivalents. The Company's cash equivalents are generally composed of commercial paper, U.S. government-sponsored enterprise securities, U.S. treasury securities and money market funds.

Marketable securities: The Company invests its excess cash balances in marketable securities and classifies its investments as available-for-sale based on facts and circumstances present at the time it purchased the securities. At each balance sheet date presented, the Company classified all of its investments in marketable securities as available-for-sale and as current assets as they represent the investment of funds available for current operations. The Company reports available-for-sale securities at fair value at each balance sheet date and includes any unrealized holding gains and losses (the adjustment to fair value) in accumulated other comprehensive loss, a component of stockholders' equity. Realized gains and losses are determined using the specific identification method and are included in other income (expense). If any adjustment to fair value reflects a decline in the value of the marketable securities, the Company considers all available evidence to evaluate if an impairment loss exists, and if so, adjusts the investment to market value through a charge to its consolidated statements of operations and comprehensive loss.

Restricted Cash: As of December 31, 2023 and 2022, the Company maintained restricted cash totaling approximately $1.3 million and $0.9 million, respectively, held in the form of a money market account as collateral for the Company's facility lease obligations. The balance is included within other non-current assets in the accompanying consolidated balance sheets.

Property and Equipment: Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful life of each asset. Lab equipment is depreciated over five years. Electronic equipment and software are depreciated over three years. Leasehold improvements are amortized over the shorter of their useful life or lease term. When an item is sold or retired, the costs and related accumulated depreciation are eliminated, and the resulting gain or loss, if any, is credited or charged to income in the statement of operations. Repairs and maintenance costs are expensed as incurred.

Long-lived Assets: Long-lived assets consist of property and equipment. The Company reviews the recoverability of its long-lived assets, including the related useful lives, whenever events or changes in circumstances indicate that the carrying amount of a long-lived asset might not be recoverable, based on undiscounted cash flows. If such assets are considered to be impaired, an impairment loss is recognized and is measured as the amount by which the carrying amount of the assets exceed their estimated fair value, which is measured based on the projected discounted future net cash flows arising from the assets.

Income Taxes: The Company utilizes the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities using the enacted statutory tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. Recognition of deferred tax assets is limited to amounts for which, in the opinion of management, realization is considered more likely than not in future periods.

Revenue Recognition: The Company has generated revenue from a collaboration agreement as well as service agreements with related parties.

To determine revenue recognition, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. At contract inception the Company assesses the goods or services promised within each contract and determine those that are performance obligations, then assesses whether each promised good or service is distinct. When the Company offers options for additional goods or services, such as to receive a license for intellectual property or for additional goods or services, the Company evaluates whether such options contain material rights that should be treated as additional performance obligations. Once performance obligations are identified, the Company then recognizes as revenue the amount of the transaction price that the Company allocated to the respective performance obligation when (or as) each performance obligation is satisfied, either at a point in time or over time. If the performance obligation is satisfied over time, the Company recognizes revenue based on the use of an input method.

Amounts received prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

As of December 31, 2023, the Company had one collaborative agreement with Bristol-Myers Squibb, which the Company entered into in January 2019. For a complete discussion of the accounting related to Bristol-Myers Squibb Collaboration Agreement, see Note 8, Collaboration Agreement and Stock Purchase Agreement with Bristol-Myers Squibb.

Research and Development Expense: Research and development costs are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries, stock-based compensation and benefits, facilities costs, depreciation, third-party license fees, acquisition of technology, and external costs of outside vendors engaged to conduct preclinical development activities and trials.

Stock-based Compensation: The Company's stock-based compensation program grants awards that may include stock options, restricted stock awards, restricted stock units, and other stock-based awards. The fair values of stock option grants are estimated as of the date of grant using a Black-Scholes option valuation model. The fair values of restricted stock awards and restricted stock units are based on the fair value of the Company's common stock on the date of grant. The estimated fair values of the awards are expensed over the requisite service period, which is generally the vesting period of the award. For service-based awards that are subject to graded vesting, the Company has elected to recognize compensation expense for these awards on a straight-line basis. The Company accounts for forfeitures as they occur. The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified.

The Company's expected stock price volatility assumption is based on volatilities of similar entities whose share or option prices are publicly available. The Company uses the simplified method to estimate the expected life assumption. The risk-free interest rate is based on the yield of U.S. Treasury securities consistent with the expected life of the option. No dividend yield was assumed as the Company does not intend to pay dividends on its common stock.

Leases: Under Accounting Standards Codification (ASC) 842 *Leases*, the Company determines if an arrangement is or contains a lease at inception. For leases with a term of 12 months or less, the Company does not recognize a right-of-use asset or lease liability. The Company's operating leases are recognized on its consolidated balance sheet as other long-term assets, other current liabilities, and other long-term liabilities. The Company does not have any finance leases.

Right-of-use 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 right-of-use assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. As the Company's leases typically do not provide an implicit rate, the Company uses an estimate of its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of lease payments. Operating lease right-of-use assets also include the effect of any lease prepaid or deferred lease payments and are reduced by lease incentives. The lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Lease expense is recognized on a straight-line basis over the lease term. The Company has elected to utilize the practical expedient to not separate lease components from non-lease components.

Comprehensive Loss: Comprehensive loss is comprised of the net loss and other comprehensive income or loss. Other comprehensive income or loss consists of unrealized gains or losses on marketable securities.

Accumulated Other Comprehensive Loss: Comprehensive loss is defined as the change in the equity of a business entity during a period from transactions and other events and circumstances from non-owner sources. It includes all changes in equity during a period except those resulting from investments by owners and distributions to owners. Comprehensive loss consists of: (i) all components of net loss and (ii) all components of comprehensive loss other than net loss, referred to as other comprehensive loss. Other comprehensive income or loss is comprised of unrealized gains and losses on debt securities.

Contingent Value Rights: The Company evaluates the CVR to determine if it qualifies as a derivative under ASC 815, *Derivatives and Hedging* ("ASC 815"). For derivative financial instruments that are accounted for as liabilities, the derivative instrument is initially recorded at its fair value and is then re-valued at each reporting date. Any changes in fair value are recorded as other income or expense for each reporting period. Derivative instrument liabilities are classified in the balance sheet as current or non-current based on whether or not net-cash settlement of the derivative instrument is probable within the next 12 months from the balance sheet date.

The Company determined that certain contingent payments under the Acquisition qualified for the scope exception under ASC 815, and as such, were not recorded as a derivative on the balance sheet as of December 31, 2023. Upon resolution of the CVR, the Company will recognize the payment consistent with the guidance in ASC 450. As of December 31, 2023, the contingent consideration cannot be reasonably estimated, and the contingency was not resolved.

Emerging Growth Company Status: The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such a time as those standards apply to private

companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that the Company no longer is an emerging growth company or affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, these financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

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

3. FAIR VALUE MEASUREMENTS

The following table presents information about the Company's financial assets measured or disclosed at fair value by level within the fair value hierarchy (in thousands):

	As of December 31, 2023	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets				
Cash equivalents:				
Money market funds	$ 53,613	$ 53,613	$ —	$ —
Marketable securities				
Corporate debt securities	55,571	—	55,571	—
Total assets	$ 109,184	$ 53,613	$ 55,571	$ —

	As of December 31, 2022	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets				
Cash equivalents:				
Money market funds	$ 55,861	$ 55,861	$ —	$ —
Marketable securities				
U.S. treasury securities	22,606	—	22,606	—
Corporate debt securities	74,422	—	74,422	—
Total assets	$ 152,889	$ 55,861	$ 97,028	$ —

For the years ended December 31, 2023 and 2022, there were no transfers into or out of Level 3.

4. MARKETABLE SECURITIES

The following table summarizes the Company's marketable securities (in thousands):

	As of December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Corporate debt securities	55,624	27	(80)	55,571
Total	$ 55,624	$ 27	$ (80)	$ 55,571

	As of December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	22,630	—	(24)	22,606
Corporate debt securities	75,161	—	(739)	74,422
Total	$ 97,791	$ —	$ (763)	$ 97,028

In accordance with the Company's investment policy, it places investments in investment grade securities with high credit quality issuers, and generally limits the amount of credit exposure to any one issuer. The Company evaluates securities for impairment at the end of each reporting period. Factors considered include whether a decline in fair value below the amortized cost basis is due to credit-related factors or non-credit-related factors, the financial condition and near-term prospects of the issuer, and the Company's intent and ability to hold the investment to allow for an anticipated recovery in fair value.

As of December 31, 2023, the Company held 23 marketable securities in an unrealized loss position, four of which were in an unrealized loss position for greater than 12 months. The total unrealized loss of securities in a loss position for greater than 12 months was $22.5 thousand as of December 31, 2023. Based on factors such as historical experience, market data, issuer-specific factors, and current economic conditions, the Company did not record an allowance for credit losses at December 31, 2023 and December 31, 2022, related to these securities. The Company also believes that it will be able to collect both principal and interest amounts due at maturity.

Marketable securities fair value by contractual maturity were as follows (in thousands):

	As of December 31, 2023
Due in one year or less	$ 22,233
Due after one year through five years	33,338
Total	$ 55,571

5. PREPAID EXPENSES AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets consisted of the following (in thousands):

	As of December 31,	
	2023	2022
Clinical, manufacturing and scientific development	$ 1,482	$ 1,372
Prepaid Insurance	565	727
Other	1,150	964
Total	$ 3,197	$ 3,063

6. PROPERTY AND EQUIPMENT, NET

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

	As of December 31,	
	2023	2022
Property and equipment:		
Lab equipment	$ 2,988	$ 2,858
Leasehold improvements	1,219	1,216
Electronic equipment and software	454	481
Furniture and fixtures	411	475
Total property and equipment	5,072	5,030
Less: accumulated depreciation	(2,737)	(1,825)
Property and equipment, net	$ 2,335	$ 3,205

Depreciation expense for the years ended December 31, 2023 and 2022 was $1.0 million and $0.9 million, respectively. There were no impairments for the years ended December 31, 2023 and 2022.

7. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

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

	As of December 31,	
	2023	2022
Employee compensation	$ 3,311	$ 3,236
Research and development expenses	3,964	4,462
Professional fees	1,221	526
Other current liabilities	85	119
Total	$ 8,581	$ 8,343

8. COLLABORATION AGREEMENT AND STOCK PURCHASE AGREEMENT WITH BRISTOL-MYERS SQUIBB

In January 2019, the Company entered into the Bristol-Myers Squibb Collaboration Agreement with Celgene Corporation, which was acquired by Bristol-Myers Squibb in November 2019, whereby the Company will carry out initial research and development activities with the goal of identifying and developing drug candidates for certain cancer types. Concurrent with execution of the Bristol-Myers Squibb Collaboration Agreement, the Company entered into a stock purchase agreement with Bristol-Myers Squibb, which resulted in the issuance of 14,545,450 shares of Series A-1 Preferred Stock (the “Stock Purchase Agreement”). In connection with the Company’s IPO, the series A-1 preferred stock converted into common stock.

Agreement Structure

Under the Bristol-Myers Squibb Collaboration Agreement, the Company will conduct exploratory and discovery activities, with the goal of identifying product candidates for certain targets, which are in the kynurenine pathway, which the Company is developing as IK-412, and the aryl hydrocarbon receptor (“AHR”), which the Company is developing as IK-175. The Company is obligated to advance research and development activities through the earlier of January 2024 or the completion of a Phase 1b clinical trial for each program ("the research term"). Bristol-Myers Squibb had the option to receive a global-development, manufacture and commercialization license for the product candidate, which expired in January 2024. Subsequent to the delivery of a license, Bristol-Myers Squibb would have been responsible for the worldwide development, manufacturing and commercialization of these product candidates.

Bristol-Myers Squibb paid the Company a total of $95.0 million in aggregate upfront consideration related to the Bristol-Myers Squibb Collaboration Agreement and Stock Purchase Agreement. The Company was eligible to receive $50.0 million, in case of an exercise of its option with respect to IK-175, and $40.0 million, in case of an exercise of its option with respect to IK-412. Upon the exercise of the delivery of each license, the Company would have been eligible to receive up to $450 million in milestone payments as well as a tiered royalty on worldwide sales from the high single to low teen digits.

Accounting Considerations of the Agreement

The Bristol-Myers Squibb Collaboration Agreement and the Stock Purchase Agreement were executed concurrently and in contemplation of each other. The issuance of Series A-1 Preferred Stock was initially accounted for at fair value. The purchase price for the Series A-1 Preferred Stock was considered to be at a discount from fair value, and therefore $1.8 million of the upfront from the Bristol-Myers Squibb Collaboration Agreement was allocated to the equity arrangement.

The Company determined that the Bristol-Myers Squibb Collaboration Agreement represented a contract with a customer and should be accounted for in accordance with ASC 606. The Company identified the two performance obligations, which are research and development services for IK-175 and IK-412. The options to receive worldwide development and commercialization licenses for the two targets and the option to receive manufacturing services in the future were determined to not provide any material rights to the customer and are therefore not considered to be performance obligations. The arrangement also contains certain di minimis items, including participation on joint oversight committees.

The Company identified $78.7 million of total transaction price which represents the upfront consideration allocated to the revenue arrangement. Additional consideration to be paid to the Company upon exercise of a right to receive a license or potential milestone and royalty payments are excluded from the transaction price as they relate to amounts that can only be achieved subsequent to the exercise of an options and are outside of the initial contact term.

Based on the distinct performance obligations identified above, the Company allocated the $78.7 million transaction price based on relative estimated standalone selling prices of each of its performance obligations as follows:

- $41.2 million for research and development services for IK-175; and
- $37.5 million for research and development services for IK-412.

The Company determined the estimated standalone selling price for the research and development services based on internal estimates of the costs to perform the services, including expected internal expenses and expenses with third parties, adjusted to include a reasonable profit margin. Significant inputs used to determine the total expense of the research and development activities include the length of time required and the number and cost of various studies that will be performed to complete the applicable development plan.

The Company is recognized revenue related to each of its performance obligations as the research and development services are performed through December 2023. The Company recognizes revenue related to research and development services performed using an input method by calculating costs incurred at each period end relative to total costs expected to be incurred.

In December 2021, the Company re-assessed the IK-412 program, which experienced manufacturing delays as a key component required in the manufacturing of IK-412, is similarly essential to the manufacturing of COVID-19 vaccines and therapies. As such, the availability of the component was delayed as resources were allocated towards vaccine production. Considering these delays and the timeline of the Bristol-Myers Squibb partnership, the Company made the strategic decision to pause IK-412 development activities for the remainder of the Bristol-Myers Squibb research term outside of the committed manufacturing efforts, which were completed in 2022.

During the year ended December 31, 2023 and 2022, the Company recognized revenue of $9.2 million and $15.6 million, respectively, from the Bristol-Myers Squibb Collaboration Agreement. The consolidated balance sheet as of December 31, 2023 includes no deferred revenue related to this agreement. The revenue recognized in 2023 was included in the deferred revenue balance as of December 31, 2022.

On January 17, 2024, Bristol-Myers Squibb notified the Company of its decision not to opt-in on the IK-175 program. In addition, Bristol-Myers Squibb did not provide an opt-in exercise for the IK-412 program. As a result, the Company has regained full global rights to the IK-175 and IK-412 programs. The IK-412 program remains IND ready. The Phase 1b study of IK-175 in urothelial carcinoma was completed and closed in 2023, and study data will be submitted for presentation at a future medical meeting. The Company will not invest further in the clinical development of IK-175 or IK-412, but will pursue strategic business development opportunities, including out-licensing.

9. ACQUISITION OF PIONYR

On August 4, 2023, the Company acquired Pionyr, pursuant to the Pionyr Acquisition Agreement. Under the terms of the Pionyr Acquisition Agreement, the Company issued to the stockholders of Pionyr 1,800,652 shares of the Company’s common stock (including 153,121 shares of the Company’s non-voting common stock), and 4,153,439 shares of Series A Preferred Stock, which was a newly designated series of preferred stock that is intended to have economic rights equivalent to the Company’s common stock, but with only limited voting rights. The Series A Preferred Stock converted to shares of the Company’s common stock pursuant to stockholder approval at a special meeting of stockholders held on October 11, 2023. Each stockholder of Pionyr at the time of closing also received one contractual CVR for each share of Pionyr stock held at closing. The CVR entitles the holder to receive 50% of net proceeds, outside of royalties, for any potential monetization of Pionyr legacy programs within two years.

Acquisition Accounting

The Company concluded that the Acquisition should be accounted for as a capitalization transaction, primarily based on the following facts and circumstances:

- The purpose of the transaction was for the Company to acquire the cash, cash equivalents and marketable securities of Pionyr;
- A nominal amount of Pionyr’s other assets were acquired, primarily related to the right-of-use-asset for Pionyr’s office and lab space lease located in San Francisco, California. The Company is actively seeking a tenant to sublease the space;
- Prior to the Acquisition, Pionyr was finalizing the wind down of all development activities that were ongoing. There will be no continuing operations of Pionyr other than the remaining wind down activities;

- No value has been ascribed to the legacy intellectual property assets acquired; and
- No assembled workforce or substantive processes were acquired that together could significantly contribute to the ability to create outputs.

Under the recapitalization accounting model, the assets acquired and liabilities assumed were recognized at their fair value on August 4, 2023. The equity issued by the Company was recognized on the basis of the net fair value of the assets acquired and liabilities assumed. Cash consideration transferred and transaction costs incurred attributable to the Acquisition are reflected as reductions to equity. The Company incurred $1.3 million of transaction costs that were direct and incremental to the Acquisition.

The following table summarizes the estimated fair values of the assets acquired and liabilities assumed at the Acquisition date (in thousands):

Assets Acquired	**As of August 4, 2023**
Cash and cash equivalents	$ 40,926
Marketable securities	20,362
Prepaid expenses and other current assets	1,359
Right-of-use-asset	3,889
Deposits and other assets	406
Total assets acquired	$ 66,942
Liabilities Assumed	
Accounts payable	(2,844)
Accrued expenses and other current liabilities	(8,097)
Operating lease liability	(1,485)
Long-term portion of operating lease liability	(5,647)
Other long-term liabilities	(852)
Total liabilities assumed	$ (18,925)
Net assets acquired [(1)]	$ 48,017

(1) Net assets acquired does not include the remaining costs to complete the wind down of Pionyr development activities and operations.

Fair value of equity issued and consideration transferred in connection with the Acquisition (in thousands):

	As of August 4, 2023
Issuance of Series A Preferred Stock	$ 32,837
Issuance of common stock	14,236
Cash consideration paid to settle Pionyr restricted stock units ("RSUs") and stock options	738
Cash consideration paid to Pionyr unaccredited stockholders	206
Total	$ 48,017

The CVR was not accounted for as a derivative on the date of merger, nor was it included in the consideration transferred to acquire Pionyr. As of December 31, 2023, the contingent consideration cannot be reasonably estimated, and the contingency was not resolved.

10. STOCKHOLDER'S EQUITY

Common Stock

As of December 31, 2023 and 2022, the Company had 150,000,000 shares of common stock authorized, respectively, of which 48,258,111 and 36,257,493 were issued and outstanding as of December 31, 2023 and 2022, respectively.

Voting: The holders of shares of common stock are entitled to one vote for each share of common stock held at all meetings of stockholders and written action in lieu of meetings; there is no cumulative voting. The holders of outstanding shares of common stock shall be entitled to elect two directors of the Company.

Dividends: The holders of shares of common stock are entitled to receive dividends, if and when declared by the Board of Directors. No dividends have been declared or paid by the Company since its inception.

Liquidation: After payment to the holders of shares of Preferred Stock of their liquidation preferences, the remaining assets of the Company are distributed to the holders of common stock.

Preferred Stock

On August 4, 2023, the Company filed a Certificate of Designation of Preferences, Rights and Limitations of Series A Non-Voting Convertible Preferred Stock ("Certificate of Designation") with the Secretary of State of the State of Delaware in connection with the Acquisition, which provides for the issuance of shares of Series A Preferred Stock. Pursuant to the Acquisition, the Company agreed to issue 4,153,439 shares of Series A Preferred Stock to Pionyr stockholders. The Company agreed to hold a special meeting of stockholders to submit the approval of the conversion of the Series A Preferred Stock into shares of common stock, pursuant to which each share of Series A Preferred Stock would be convertible into one share of voting common stock, provided, however, that if such stockholder already held shares of the Company's non-voting common stock prior to the conversion, such holder would receive shares of non-voting common stock in lieu of shares of voting common stock to the extent the issuance of shares of voting common stock to such holder would result in such holder, when aggregated with its affiliates for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), beneficially owning more than 9.99% of the Company's voting common stock (the "Non-Voting Beneficial Ownership Limitation"). If stockholders had not approved the conversion of the Series A Preferred Stock into common stock by February 4, 2024 (six (6) months from the closing of the Acquisition), then, upon any attempted conversion, holders of Series A Preferred Stock may have thereafter required the Company to repurchase the Series A Preferred Stock at the then-current fair value of the underlying Common Stock.

On September 25, 2023, the Company filed a Definitive Proxy Statement with the SEC to solicit approval of the issuance of common stock upon conversion of the Series A Preferred Stock at a special meeting of stockholders.

The Company classified convertible preferred stock as temporary equity in the accompanying consolidated statement of Convertible Preferred Stock and Stockholders' Equity due to terms that allow for redemption of the shares in cash upon certain events that are outside of the Company's control, including failure to obtain stockholder approval of the conversion of the Series A Preferred Stock. The Company did not accrete the value of the convertible preferred stock to the redemption values since a liquidation event was not considered probable prior to the conversion date.

The Series A Preferred Stock was subsequently converted to shares of the Company's common stock pursuant to stockholder approval at a special meeting of stockholders held on October 11, 2023.

11. STOCK BASED COMPENSATION

In March 2016, the Company's board of directors and stockholders adopted the 2016 Stock Incentive Plan which was amended and restated in December 2020, (as so amended and restated, the "2016 Plan") which permits the granting of (1) options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code, and (2) options that do not so qualify.

In March 2021, the Company's stockholders approved the 2021 Stock Incentive Plan (the "2021 Plan"), which became effective on March 30, 2021. The 2021 Plan replaced the 2016 Plan as the board of directors had determined it would not to make additional awards under the 2016 Plan following the closing of the IPO. However, the 2016 Plan will continue to govern outstanding equity awards granted thereunder. The shares of the Company's common stock subject to outstanding awards under the 2016 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right will be added back to the shares of common stock available for issuance under the 2021 Plan.

The 2021 Plan allows the Company to make equity-based and cash-based incentive awards to officers, employees, directors and consultants. The number of shares initially reserved under the 2021 Plan was 3,119,514 shares of the Company's common stock. The 2021 Plan contains an "evergreen" provision, which allows for an annual increase in the number of shares of common stock available for issuance under the 2021 Plan on the first day of each fiscal year during the period beginning in fiscal year 2022. The annual increase in the number of shares shall be equal to 4% of the number of shares of common stock outstanding on the immediately preceding December 31; and such lesser number of shares as determined by the Administrator as provided in the 2021 Plan. On January 1, 2023, the number of shares of common stock available for issuance under the 2021 Plan increased by 1,450,299 shares as a result of the automatic increase provision of the 2021 Plan. As of December 31, 2023, 3,413,255 shares of common stock remain available for future issuance under the 2021 Plan.

The vesting periods for equity awards, which generally is four years, are determined by the Board of Directors. The contractual term for stock option awards is ten years.

The total compensation expense recognized in the statements of operations associated with all the stock-based compensation awards granted by the Company is as follows (in thousands):

	Year Ended December 31,	
	2023	2022
Research and development	$ 3,937	$ 3,974
General and administrative	3,695	3,551
Total stock-based compensation expense	$ 7,632	$ 7,525

The weighted-average fair value of the stock options granted during the year ended December 31, 2023 and 2022 was $2.34 and $5.52 per share, respectively. As of December 31, 2023, the total unrecognized stock-based compensation balance for unvested options was $11.2 million which is expected to be recognized over 2.1 years.

The following table summarizes stock option activity under the Plan for the year ended December 31, 2023:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (thousands)
Outstanding as of December 31, 2022	6,589,479	$ 7.29	7.73	$ 362
Granted	1,750,224	3.13		
Exercised	(34,027)	4.01		
Cancelled or forfeited	(1,217,415)	6.91		
Outstanding as of December 31, 2023	7,088,261	$ 6.35	6.92	$ 94
Vested or expected to vest as of December 31, 2023	7,088,261	$ 6.35	6.92	$ 94
Options exercisable as of December 31, 2023	4,032,553	$ 6.61	5.98	$ 94

The intrinsic value of options exercised for the years ended December 31, 2023 and 2022 was $0.1 million and $1.2 million, respectively.

The fair value of each option award granted during the years ended December 31, 2023 and 2022 is estimated on the date of grant using the Black-Scholes option pricing model. This model incorporates various assumptions, including the expected volatility, expected term, and interest rates. The underlying assumptions used to value stock options granted to participants using the Black-Scholes option-pricing presented on a weighted-average basis were as follows:

	Year Ended December 31,	
	2023	2022
Risk-free interest rate	4.00%	2.42%
Expected dividend yield	0%	0%
Expected option term (in years)	6.04	5.94
Expected stock price volatility	87.0%	84.8%

Employee Stock Purchase Plan

On March 20, 2021, the Company's stockholders approved the 2021 Employee Stock Purchase Plan (the "ESPP"), which became effective on March 30, 2021. The ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of 346,613 shares of the Company's common stock. An annual increase in the number of shares of common stock reserved and available for issuance under the ESPP shall be equal to 1% of the number of shares of common stock outstanding on the immediately preceding December 31; and such lesser number of shares as determined by the Administrator as provided in the ESPP. As of December 31, 2023, no shares have been purchased by employees under the ESPP.

12. EMPLOYEE BENEFIT PLAN

The Company has a defined-contribution savings plan covering all eligible U.S. employees under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). Contributions to the plan by the Company totaled $0.5 million and $0.6 million for the years ended December 31, 2023 and 2022, respectively. Employees can designate the investment of their 401(k) accounts into several mutual funds. Administrative costs of the plan for each of the years ended December 31, 2023 and 2022, were immaterial.

13. INCOME TAXES

The components of income tax expense were as follows (in thousands):

	Year Ended December 31,	
	2023	2022
Current		
Federal	$ (237)	$ —
State	68	27
Total Current Provision	$ (169)	$ 27

The effective income tax rate differed from the amount computed by applying the federal statutory rate to the Company's loss before income taxes as follows:

	Year Ended December 31,	
	2023	2022
Tax effected at statutory rate	21.0%	21.0%
State taxes	6.4%	7.2%
Stock compensation	(1.2)%	(0.5)%
Non-deductible expenses	(0.6)%	(0.7)%
Federal research and development credits	4.2%	5.0%
Change in valuation allowance	(30.0)%	(32.0)%
Total	0.2%	—%

The Company's total deferred tax assets are as follows (in thousands):

	As of December 31,	
	2023	2022
Deferred tax assets:		
Federal net operating loss carryforward	$ 29,529	$ 22,875
State net operating loss carryforward	8,581	6,693
R&D credit carryforwards	14,589	10,667
Capitalized start-up costs	196	219
Accruals and reserves	802	823
Deferred revenue	—	2,502
Stock based compensation	2,381	1,900
Lease liability	2,934	1,556
Capitalized R&E	44,366	14,995
Total deferred tax asset	103,378	62,230
Deferred tax liability:		
Fixed assets	$ (603)	$ (761)
Right of use asset	(1,554)	(1,436)
Total deferred tax liability	(2,157)	(2,197)
Net deferred tax asset and liability before valuation allowance	101,221	60,033
Valuation allowance	(101,221)	(60,033)
Net deferred tax asset	$ —	$ —

The Company's 2023 income tax provision benefit related the current year acquisition of Pionyr, offset partially by state income taxes. ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more-likely-than-not that some portion or all the deferred tax assets will not be realized. The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on this, the Company has provided a valuation allowance for the full amount of the net deferred tax assets as the realization of the deferred tax assets is not determined to be more likely than not. During 2023, the valuation allowance increased by $41.2 million primarily due to the increase in the Company's book loss reported in the period and the Pionyr acquisition.

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

As of December 31, 2023, the Company had approximately $140.6 million and $135.8 million of Federal and State operating loss carryforwards respectively. The Federal net operating losses are not subject to expiration and the state net operating losses begin to expire in 2037. These loss carryforwards are available to reduce future federal taxable income, if any. As of December 31, 2023, the Company also has federal and state research and development tax credit carryforwards of approximately $11.7 million and $3.6 million respectively, to offset future income taxes, which will begin to expire beginning in December 2031. These loss carryforwards are subject to review and possible adjustment by the appropriate taxing authorities. The amount of loss carryforwards that may be utilized in any future period may be limited based upon changes in the ownership of the company's ultimate parent.

Uncertain Tax Positions

ASC 740 prescribes the accounting for uncertainty in income taxes recognized in the financial statements. We regularly assess the outcome of potential examinations in each of the taxing jurisdictions when determining the adequacy of the amount of unrecognized tax benefit recorded. We recognize tax benefits from uncertain tax positions only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities, based on the technical merits of the position. The tax benefits recognized in the financial statements from such positions are then measured based on the largest benefit which is more likely than not to be realized upon ultimate settlement. We recognize interest and penalties related to unrecognized tax positions in our provision for (benefit from) income taxes line of our Consolidated Statements of Operations.

The aggregate changes in the balance of our gross unrecognized tax benefits were as follows (dollars in thousands):

	Year Ended December 31,	
	2023	2022
Balance at the beginning of the year	$ —	$ —
Beginning balance adjustment	927	—
Increases related to tax positions taken from prior years	22	—
Ending balance	$ 949	$ —

As of December 31, 2023, the balance was adjusted by $0.9 million related to the acquisition of Pionyr.

As of December 31, 2023, $0.9 million of the unrecognized tax benefits, if recognized, would impact our effective tax rate. We do not expect a significant change in the amount of unrecognized tax benefits within the next 12 months. We recognized an immaterial amount of interest related to uncertain tax positions in our provision for (benefit from) income taxes during 2023.

The Company files U.S. federal and state income tax returns and is generally subject to income tax examinations by these authorities for all tax years after December 31, 2020. Currently, no federal or state income tax returns are under examination by the respective income tax authorities.

14. RESEARCH LICENSE AGREEMENTS

During 2015, the Company entered into an exclusive patent license agreement (the "UT Austin License") to license certain technologies and intellectual property rights from the University of Texas at Austin (the "University"), an entity affiliated with a director of the Company at the time of the agreement. The UT Austin License shall remain in effect until the expiration or abandonment of the last to expire technologies and intellectual property rights. The Company shall pay License Maintenance fees annually of $40 thousand. Additionally, the Company shall make additional milestone payments to the University upon meeting

certain development milestones in the aggregate of $4.7 million during the term of the UT Austin License. The Company will pay the University royalties as defined in the UT Austin License on any commercialized product sales related to the licensed technology in a percentage in the low single digits. The Company will also be responsible for reimbursing the University for certain patent-related costs incurred on its behalf.

In 2018, the Company acquired IPR&D on an Arrys' immune-oncology candidate based on the intellectual property associated with Arrys' AskAt License as part of the acquisition of Arrys. Total consideration allocated to the technology was $28.5 million and was recognized as research and development expense upon the acquisition. The AskAt License is intended to be used by the Company in its future development of therapeutic drug candidates for eventual clinical development and commercialization. The Company shall make additional milestone payments to AskAt upon meeting certain development milestones totaling $4.0 million, as well as certain sales event milestones ranging from $50 million to $250 million contingent on sales in a calendar year, during the term of the AskAt License. The Company will pay the AskAt royalties a percentage in the low single digits as defined in the AskAt License on any commercialized product sales related to the licensed technology. The Company intended to use the license granted pursuant to the AskAt Agreement in our future development of therapeutic drug candidates for eventual clinical development and commercialization. The AskAt Agreement will be terminated as of March 20, 2024, and all assets will be returned to AskAt, at which point no further costs will be incurred by the Company.

15. LEASE OBLIGATIONS

Boston Lease

On July 21, 2020, the Company entered into an operating lease agreement for 20,752 square feet of office, lab and animal care facility space located in Boston, Massachusetts for the Company's corporate headquarters. The commencement date of the lease was February 19, 2021 and the lease term is 63 months. The base rent at commencement is $0.1 million per month and escalates by 3% annually for total lease payments during the term of $9.3 million. The Company's lease agreement requires the Company to maintain a cash letter of credit to secure their obligations under the lease of $0.9 million. This balance is included in other assets on the accompanying consolidated balance sheets. The Company recognized a right of use asset of $7.5 million and an operating lease liability of $7.5 million upon the commencement of the lease.

San Francisco Lease

The Company also assumed an operating lease agreement for 28,029 square feet of office and lab space located in San Francisco, California from the Acquisition of Pionyr. The space is currently vacant and the Company is actively seeking a tenant to sublease. As of the Pionyr acquisition date, August 4, 2023, the remaining lease term was 44-months with base rent of $0.2 million per month with annual escalations of 3.5%. Total lease payments during the remaining 44-month lease term are $8.3 million. The Company's lease agreement requires the Company to maintain a cash letter of credit to secure its obligations under the lease of $0.4 million. The Company recognized a right of use asset of $3.9 million and an operating lease liability of $7.1 million upon the commencement of the lease. In December 2023, the Company re-assessed the sublease market for the San Francisco lease and recorded a right of use asset impairment of $1.7 million for a portion of the lease.

Other Lease Disclosures

The components of the lease costs which are included in the consolidated statements of operations and comprehensive loss were as follows (in thousands):

	Year Ended December 31,	
	2023	2022
Operating lease costs	$ 2,316	$ 1,764
Variable lease costs	889	466
Total lease costs	$ 3,205	$ 2,230

Variable lease cost primarily related to operating expenses, parking, taxes and insurance associated with the Company's operating leases.

Supplemental cash flow information relating to the Company's leases were as follows (in thousands):

	Year Ended December 31,	
	2023	2022
Cash paid for amounts included in the measurement of lease liabilities (operating cash flows)	$ 2,534	$ 1,774

The remaining lease terms and discount rates related to the Company's leases were as follows:

	As of December 31,	
	2023	2022
Remaining lease term	3.0 years	3.4 years
Discount Rate	7.8%	7.7%

The future minimum lease payments for the Company's operating lease as of December 31, 2023, were as follows (in thousands):

Fiscal Year	Operating Leases
2024	3,924
2025	4,212
2026	3,171
2027	719
2028	—
Total minimum lease payments	12,026
Less amounts representing interest or imputed interest	1,288
Present value of lease liabilities	$ 10,738

16. COMMITMENTS AND CONTINGENCIES

The Company is also party to various agreements, principally relating to licensed technology, that require future payments relating to milestones not met as of December 31, 2023 or royalties on future sales of specified products that have not yet occurred as of December 31, 2023.

17. RELATED PARTY TRANSACTIONS

The Company entered into several agreements with a director and an entity affiliated with a director:

1. As discussed in Note 14 above, the Company has entered into a license agreement with the University, which was affiliated with a director of the Company at the time of the license agreement. During the years ended December 31, 2023 and 2022 the Company recorded expenses in connection with University license fees and certain patent-related costs incurred on its behalf of $0.1 million and $0.2 million, respectively.
2. OrbiMed Advisors LLC ("OrbiMed"), a related party of the Company, was previously a stockholder of Pionyr. In connection with the Acquisition, OrbiMed was allocated 153,121 shares of non-voting common stock and 353,192 shares of Series A Preferred Stock, which converted to common stock pursuant to stockholder approval at a special meeting of stockholders held on October 11, 2023. As of December 31, 2023, OrbiMed beneficially owned approximately 8.9% of the Company's voting common stock outstanding.

18. NET LOSS PER SHARE ATTRIBUTABLE TO COMMON STOCKHOLDERS

The Company has generated a net loss in all periods presented, therefore the basic and diluted net loss per share attributable to common stockholders are the same as the inclusion of the potentially dilutive securities would be anti-dilutive.

The following table sets forth the outstanding potentially dilutive securities that have been excluded in the calculation of diluted net loss per share because to do so would be anti-dilutive:

	Year ended December 31,	
	2023	2022
Options to Purchase Common Stock	7,088,261	6,589,479
Total	7,088,261	6,589,479

19. SUBSEQUENT EVENTS

Workforce Reduction

On January 17, 2024, the Board of Directors of the Company approved a plan to reduce the Company's workforce by approximately 35% (the "Workforce Reduction"). The Workforce Reduction is designed to align the Company's workforce with its strategy to focus on its clinical stage, targeted oncology programs, IK-930 and IK-595. The Workforce Reduction generally affects employees working in the Company's discovery organization, as well as select employees working in development and general and administrative functions. The Workforce Reduction will result in the termination of approximately twenty (20) employees and is expected to be completed by March 31, 2024. The Company expects to incur exit costs related to the discontinuation of its discovery efforts and expects to recognize these charges during the three months ended March 31, 2024. Expenses related to the Workforce Reduction consist of employee severance and related termination benefits, and are expected to result in approximately $1.6 million in cash expenditures.

Bristol-Myers Squibb Collaboration Agreements

As previously disclosed, the Company's AHR antagonist IK-175 and kynureninase IK-412 programs, in development in collaboration with Bristol Myers Squibb, were eligible for opt-in through early 2024. On January 17, 2024, Bristol Myers Squibb notified the Company of its decision not to opt-in on the IK-175 program. In addition, Bristol Myers Squibb did not provide an opt-in exercise for the IK-412 program. As a result, the Company has regained full global rights to the IK-175 and IK-412 programs.

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President and Chief Executive Officer

Owen Hughes
Chief Executive Officer of XOMA Corporation

Iain D. Dukes, D.Phil.
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Former Chief Scientific Officer of Translate Bio, Inc.

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