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, 2021

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. ☐

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, 2021 was $296.7 million.

The number of shares of Registrant's Common Stock outstanding as of March 10, 2022 was 36,108,995.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's proxy statement for the 2022 annual meeting of stockholders to be filed pursuant to Regulation 14A within 120 days after the registrant's fiscal year ended December 31, 2021, are incorporated by reference in Part III of this Form 10-K.

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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.
- The COVID-19 pandemic, or a similar pandemic, epidemic, or outbreak of an infectious disease, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates.
- We have never successfully completed any clinical trials for our oncology programs, and we may be unable to do so for any product candidates we develop. Certain of our oncology programs are still in preclinical development and may never advance to clinical development.
- Our programs are focused on the development of oncology therapeutics for patients with genetically defined or biomarker-driven cancers, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs is novel and may never lead to approved or marketable products.
- Clinical product development involves a lengthy and expensive process, with an uncertain outcome.
- 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 company sponsored Phase 1 clinical trials of IK-930, IK-175, and IK-007 and expect to rely on third parties to conduct clinical trials for our other programs that enter clinical trials. In addition, our product candidates may be evaluated in investigator-sponsored clinical trials. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements, or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.
- We 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 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 prospectus 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 preclinical 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 to efficiently discover and develop product candidates;
- 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;
- developments relating to our competitors and our industry;
- the effect of the ongoing COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and clinical trials and any future studies or trials; and
- other risks and uncertainties, including those 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, that 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 targeted oncology company developing precision medicines tailored to biomarker-defined patient groups with specific unmet needs. With our robust biomarker and translational approach we aim to develop targeted treatments and define patient populations who are most likely to respond to treatment. Our current programs are across the Hippo pathway, RAS pathway, and key immune signals in the tumor-microenvironment (TME), with approaches to targeting both cancer driving targets and mechanisms of resistance to targeted therapies. Our focus on patient-driven development is platform and process agnostic, allowing us to research both known and novel targets, with a shared guiding principle of aiming to address the unmet need of a biomarker-defined patient population. Since we commenced operations in 2016, we have advanced multiple product candidates into clinical development. In addition, we have a robust pipeline of discovery-stage targeted oncology programs.

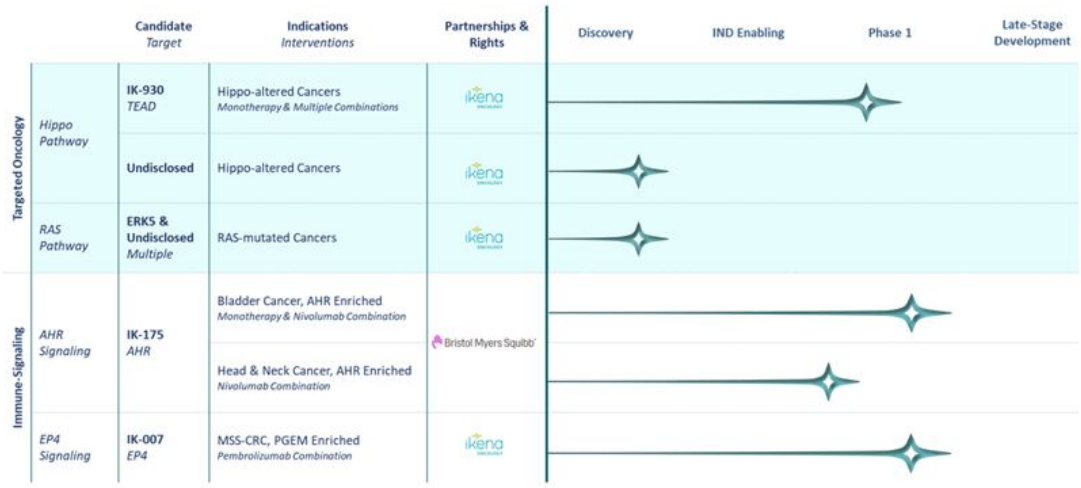
Our lead targeted oncology product candidate, IK-930, is an oral small molecule inhibitor of the transcriptional enhanced associate domain, or TEAD, transcription factor in the Hippo signaling pathway. The Hippo pathway is genetically altered in approximately 10% of human cancers and is widely accepted as a prevalent driver of cancer pathogenesis and a mediator of poor outcomes for patients. In our ongoing first-in-human clinical trial, we are focusing on indications that provide the potential for rapid clinical development to achieve proof-of-concept, such as NF2 deficient mesothelioma and solid tumors with YAP1 or TAZ gene fusions, including epithelioid hemangioendothelioma, or EHE, in which 100% of patients have Hippo pathway alterations. We also plan to assess IK-930 in combination with other targeted therapies across several indications, including EGFR mutated non-small cell lung cancer (NSCLC) and KRAS mutated cancers. In October 2021, our Investigational New Drug Application, or IND, for IK-930 was accepted by the U.S. Food and Drug Administration, or FDA, and we subsequently initiated a first in human Phase 1 clinical trial of IK-930 in patients with advanced solid tumors with a high frequency of Hippo pathway alternations. The first patient was dosed in January 2022, and we are currently recruiting patients in this ongoing Phase 1 clinical trial.

Our discovery efforts are focused on additional targeted oncology programs, following our philosophy of designing treatments for patients' populations identified through the genetic make-up of their tumors. Our pre-clinical pipeline is growing to include additional Hippo pathway and RAS pathway-targeting programs, including our program against the novel target extracellular signal related kinase 5 (ERK5). We are generating mechanistic and translational data to accompany our approaches and identify underserved RAS-mutated cancer patient populations.

Our clinical-stage programs also include product candidates in development to target immune signaling in the tumor microenvironment (TME). These programs are all built on the same foundation of biomarker-driven clinical trial design and patient enrichment, aiming to develop therapies that can precisely be used for specific cancer patients. IK-175 is an oral inhibitor of aryl hydrocarbon receptor, or AHR, which we are evaluating in a Phase 1a/1b clinical trial in solid tumors and in urothelial carcinomas as monotherapy and in combination with nivolumab. We expect to report initial clinical data from this trial in the second half of 2022. Additionally, we plan to initiate a second Phase 1b trial with IK-175 in head and neck squamous cell carcinoma (HNSCC) in the second half of 2022. The IK-175 program is partnered with Bristol-Myers Squibb Company. The partnership also includes our IK-412 program, which experienced manufacturing delays previously disclosed in 2021. Considering these delays and the timeline of the partnership, we made the strategic decision to pause IK-412 development activities for the remainder of the Bristol Myers Squibb collaboration agreement term once the ongoing committed Chemistry, Manufacturing, and Controls (CMC) work has been completed.

Also within TME immune signaling, IK-007, which inhibits the prostaglandin E receptor 4, or EP4, in the COX2 pathway, is being evaluated in a Phase 1b clinical trial in combination with pembrolizumab for the treatment of patients with MSS CRC. We recently completed enrollment in this trial and expect to report data at a medical conference in the second half of 2022.

Our current pipeline is shown below:



BMS has the right to exclusively license IK-175 and IK-412 (not shown) under a master collaboration agreement
Pembrolizumab provided through a clinical trial collaboration agreement with Merck for IK-007 clinical program
Ikena has a worldwide exclusive license to IK-007 except with respect to China and Taiwan from AskAt

Our Strategy

We are dedicated to bringing next generation targeted oncology therapies to cancer patients. We plan to achieve this goal with diverse approaches to targeted oncology and immune signaling and through our deep understanding of complex biologic pathways, biomarker-driven discovery, our experience and skills in drugging novel and previously intractable targets, and robust translational research informing clinical development. The key components of our current strategy are as follows:

- **Advance IK-930 through clinical development.** We are developing IK-930, an oral small molecule inhibitor of TEAD, to evaluate its potential to bring single agent therapeutic benefit to patients with tumors harboring genetic mutations in the Hippo signaling pathway. IK-930 as monotherapy is currently being evaluated in a Phase 1 clinical trial in cancer patients. Our clinical development strategy is designed to achieve clinical proof-of-concept in genetically defined subset of solid tumors where significant unmet medical need exists, to leverage the potential for fast-to-market opportunities in orphan indications, and to evaluate combination of IK-930 with other targeted therapies to address therapeutic resistance, such as with an epidermal growth factor receptor, or EGFR, inhibitor in broader indications.
- **Progress our research in both the Hippo pathway and RAS pathway towards identification of potential development candidates and advancement through clinical development.** We have a robust discovery effort to continue to identify potential opportunities for targeted oncology pipeline growth, including additional programs within the Hippo and RAS pathways. Our continued efforts in the Hippo pathway have the potential to result in additional candidates that could complement IK-930 and further our leadership in the space. Our discovery efforts in RAS are aiming to develop therapies for RAS-driven cancers, including KRAS mutated cancers, where there is significant unmet need. This work includes targeting multiple nodes in the pathway. For example, we are studying small molecules targeting ERK5 in the RAS signaling pathway that we believe may have the potential to bring therapeutic benefit to patients with KRAS mutant cancers that are not currently addressed by existing KRAS inhibitors.

- **Continue advancing IK-175, a BMS-partnered program, through Phase 1b clinical trials aiming to achieve key near-term financial milestone.** Bristol Myers Squibb, our strategic partner, has the exclusive right to exclusively license each of IK-175 and IK-412 worldwide through completion of Phase 1b clinical trials. The IK-412 program experienced manufacturing delays previously disclosed in 2021. Considering these delays and the timeline of the partnership, we made the strategic decision to pause IK-412 development for the remainder of the BMS contract term once the ongoing committed CMC work has been completed. IK-175 is being evaluated in a Phase 1 clinical trial in bladder cancer enriched for nuclear AHR positive patients using our proprietary AHR biomarker assay. We are currently recruiting patients in the expansion cohorts of both the combination and monotherapy arms of the trial. If Bristol Myers Squibb exercises their option to exclusively license IK-175, we would receive $50 million in opt-in fees, which would provide a meaningful source of non-dilutive capital. We would be eligible to receive clinical, regulatory, and commercial milestone payments and royalties on worldwide net sales.
- **Maximize the value of our pipeline through continued discovery efforts and growth; generating a pipeline of programs supported by robust translational research and designed for biomarker-defined patient populations.** As we seek to expand our targeted oncology pipeline and advance it through proof-of-concept clinical trials, we plan to build a fully integrated biotechnology company. As we grow, we plan to advance programs that fit with our philosophy of patient-driven development and identify biomarker-defined populations in need that can benefit from targeted therapeutics. 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 internally identified targets, we are open to opportunistically in-license or acquire discovery and clinical programs for which we can leverage our expertise in drug discovery and structural biology-guided chemistry, with a focus on mechanisms of actions targeting cancer drivers that complement our existing targeted oncology programs.

Our Programs

Targeted Oncology Programs

IK-930, a TEAD inhibitor

IK-930 is an internally discovered oral small molecule inhibitor of the TEAD family of transcription factors in the Hippo signaling pathway. TEAD functions as the ultimate step in the Hippo signal transduction pathway by driving expression of genes involved in cell proliferation and survival. The Hippo pathway is widely accepted as a key and prevalent driver of cancer pathogenesis and is genetically altered in approximately 10% of all cancers, and such genetic alterations are often associated with poor clinical outcomes.

IK-930 is a novel inhibitor of TEAD that exploits a recently discovered and promising 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 that targeted protein-to-protein interactions, or PPIs, 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 activity. By selecting IK-930 based upon these characteristics, we believe IK-930 has the potential to bring therapeutic benefit to patients with tumors harboring genetic mutations 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.

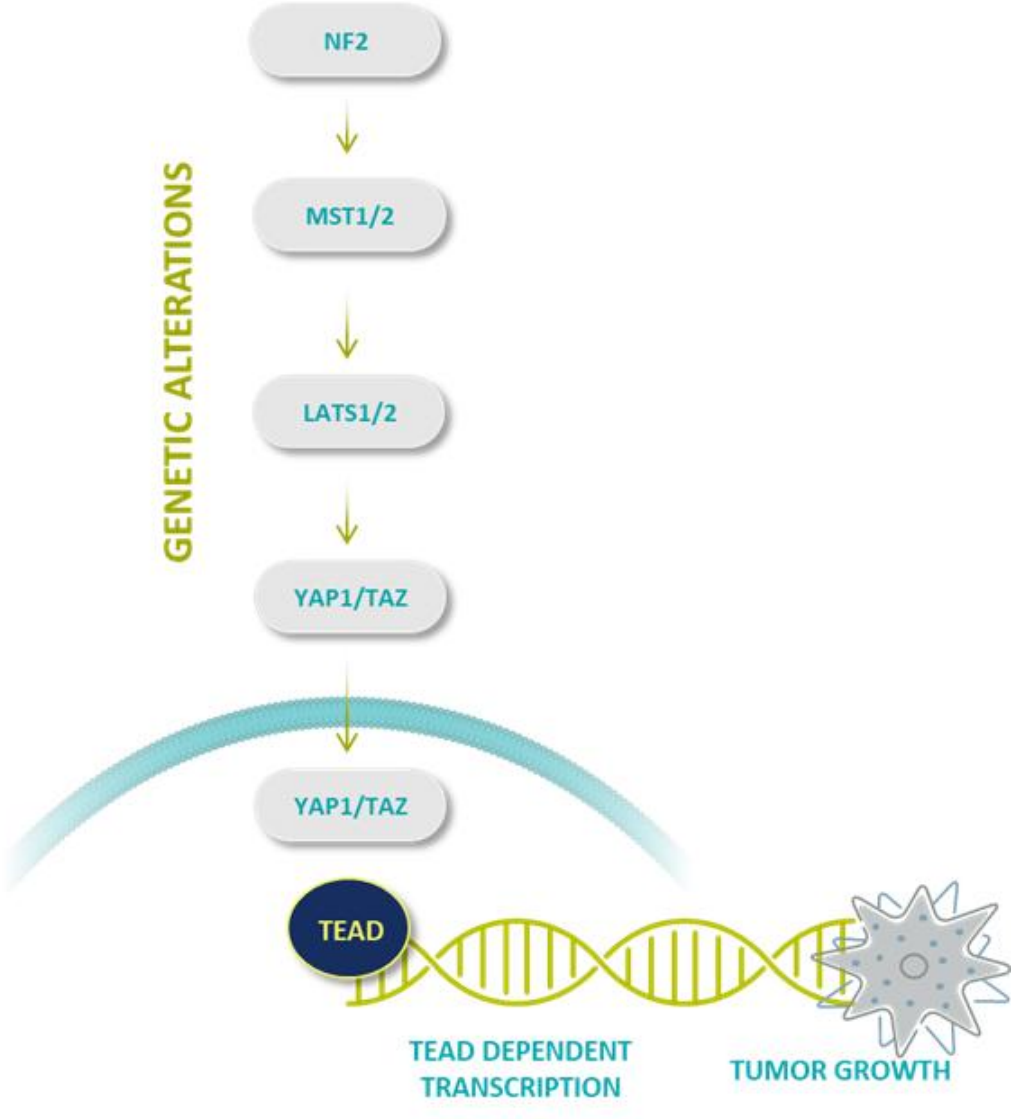
We are currently evaluating IK-930 in a first-in-human Phase 1 clinical trial as a monotherapy in Hippo-mutated cancers. The study aims to evaluate the safety and preliminary antitumor activity of IK-930 in Hippo-mutated cancers in orphan indications such as NF2-deficient malignant pleural mesothelioma and EHE, a rare type of vascular sarcoma. The FDA granted IK-930 orphan designation for the treatment mesothelioma in the first quarter of 2022. In addition, we plan to evaluate IK-930 in combination with other targeted agents in the Phase 1 clinical trial, with the aim of potentially addressing therapeutic resistance in more prevalent tumor indications characterized by genetic alterations, including EGFR mutant NSCLC.

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.

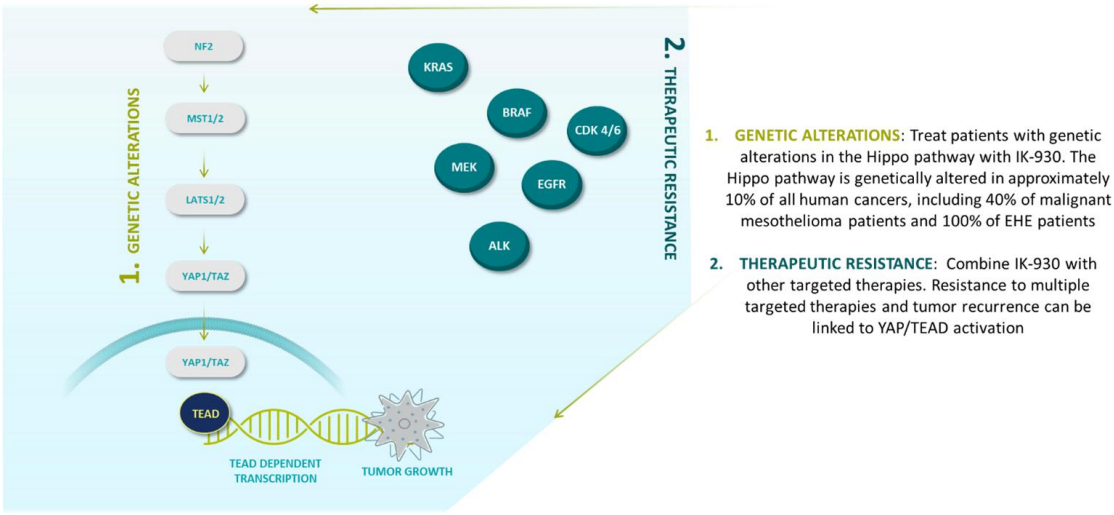
The Hippo signaling cascade begins with NF2, a gene that encodes the scaffold protein merlin, which links multiple extracellular cues to an intracellular signaling cascade. Merlin activates the kinases MST1 and MST2, or MST1/2, which subsequently phosphorylate and activate the kinases LATS1 and LATS2, or 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.

Hippo Pathway Diagram



Nuclear YAP1 was observed to lead to increased TEAD activity as measured by higher levels of TEAD gene transcription. 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 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.

Two Clinical Strategies to Inhibit the Hippo Pathway with IK-930 to Address Multiple Cancer Patient Populations



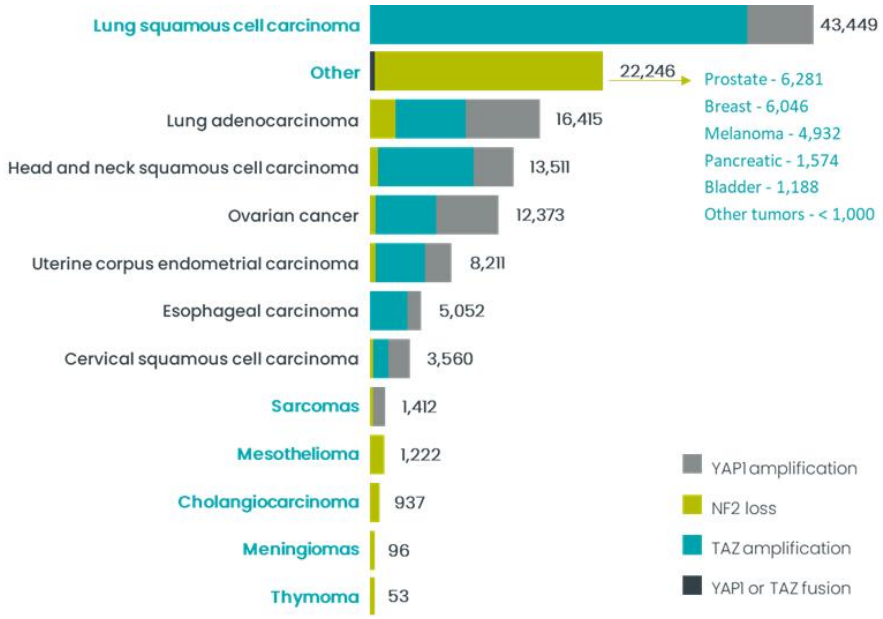
Epidemiology of Hippo pathway driven cancers

Published literature suggests that approximately 10% of all solid tumors present with dysregulated Hippo pathway and subsequent activation of TEAD. 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. Moreover, there is cross-talk between the Hippo pathway and multiple other signal transduction pathways, such as EGFR, which can lead to aberrant TEAD activation.

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

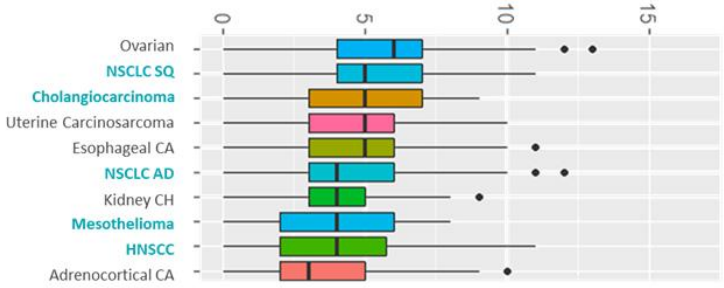


Genetic alterations in the Hippo pathway are present in diverse cancer types but there are certain cancers, including more prevalent indications such as lung squamous cell carcinoma, and rarer indications such as mesothelioma and sarcoma, which are reported to have a particularly high incidence of genetic alterations in the Hippo pathway and 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 has orphan designation for the treatment of mesothelioma.
- Multiple soft tissue sarcomas have YAP1 and TAZ gene fusions. For example, approximately 90% of epithelioid hemangioendothelioma, or EHE, have TAZ-CAMTA1 fusions and the remaining 10% have YAP1-TFE3 fusions, which are directly linked to the etiology of these cancers.
- In squamous lung cancer, 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.

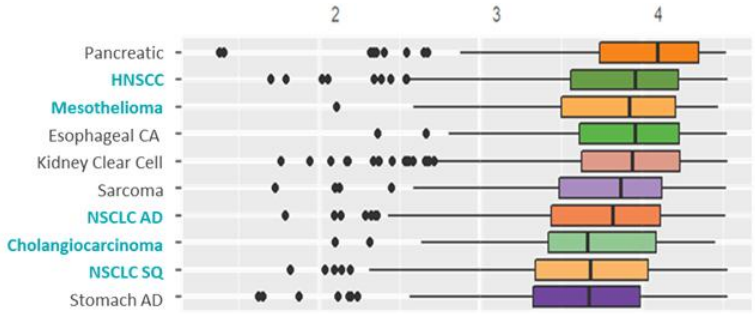
As part of our translational strategy, we have conducted bioinformatics analyses of the genomic and transcription profiles of cancer patients, broadening our understanding of the pathway's role in certain cancers, and supporting our indication selection and clinical development plan.

Results of Genetic Analysis of Indications with Hippo Alterations



We conducted genetic (top image) and transcriptional analysis (bottom image) of Hippo pathway dependency that identified a common subset of cancers. The data show the results from the genetic analysis of Hippo pathway alterations and the transcription analysis of YAP/TAZ activation. The overlapping cancer types present as indications with high potential for impact through Hippo pathway inhibition. For example, mesothelioma, head & neck squamous cell carcinoma, cholangiocarcinoma, and non-small cell lung cancers demonstrate high frequencies of Hippo pathway alterations as well as high YAP/TAZ activity scores.

Results of Transcriptional Analysis of YAP/TAZ Activity Scores



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. Approximately 30% of patients with non-small-cell lung carcinoma, or NSCLC, will have EGFR mutations. Tagrisso (osimertinib) 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. Early use of osimertinib raises the question of the optimal management of osimertinib resistance and the role of targeted agent combinations in this patient population. We believe this population also represents a substantial opportunity for TEAD inhibitors. Published data from patient tumor samples shows that, upon acquired resistance to EGFR inhibitors through specific mutations in EGFR, there is an increase in nuclear YAP1 in tumors as compared to baseline. 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. 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.

- 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. Even with this newly approved treatment, the median overall survival of these patients is 18 months, with most of the patients eventually progressing and dying from their disease. IK-930 has orphan designation for the treatment of mesothelioma. Approximately 40% of malignant mesothelioma patients are associated to 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 central nervous system, or CNS, tumor, accounting for approximately one-third of primary CNS tumors. Surgery and/or radiation therapy, or 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 continue to be poor, underscoring the substantial need for new therapies.
- Soft Tissue Sarcomas, or 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). This cancer can occur anywhere in the body with the most common sites being the liver, lungs, and bone. It 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.

- 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

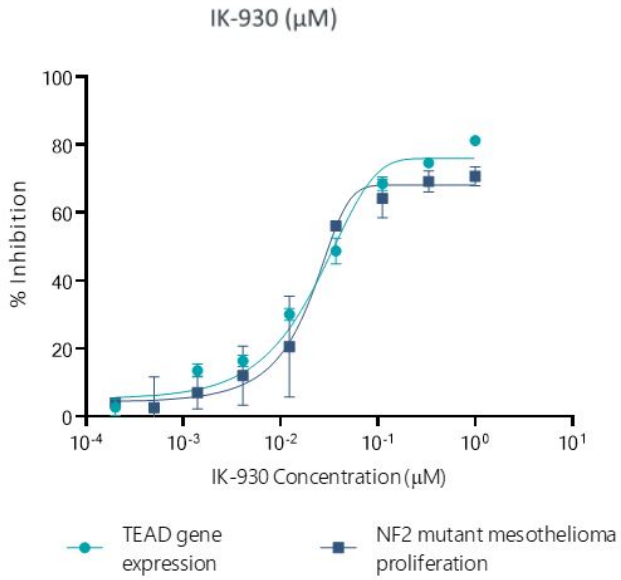
IK-930 is an oral small molecule inhibitor of TEAD that binds to a recently discovered lipid binding pocket on TEAD itself. TEAD activity is dependent on binding of the fatty acid palmitate to a central lipid pocket. IK-930 blocks palmitate from binding TEAD, thereby disrupting TEAD-dependent gene transcription. The mechanism of action of IK-930 is differentiated from historically unsuccessful attempts that targeted PPIs using either small molecules or cyclic peptides. It is often difficult to discover compounds that disrupt PPIs with sufficient potency due to the typically undruggable shallow PPI pockets and large surface areas that make up tight PPIs. We believe that targeting the lipid binding pocket of TEAD has the potential to yield more potent and selective molecules as compared to these historical attempts. Using structural biology-guided chemistry, we were able to generate novel TEAD inhibitor compounds, including IK-930, 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 activity. 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. In addition to primary cancers linked to the Pathway we plan to evaluate IK-930 in patients with the potential for acquired resistance to other targeted therapies. We have generated preclinical data supporting our belief of the clinical opportunity to treat EGFR and MEK resistant patients with IK-930.

We believe our ongoing translational work coupled with our clinical development strategy positions us to select patients most likely to benefit from TEAD inhibition.

Based on our preclinical studies, we believe IK-930 is a potent, well tolerated and selective TEAD inhibitor with favorable pharmacologic properties. In a TEAD reporter cell line, IK-930 inhibited TEAD-dependent transcription with an EC50 of 25 nM, and inhibited proliferation of H226 cells, an NF2 mutant mesothelioma cell line, with an EC50 of 21 nM, demonstrating that IK-930 has high potency in inhibiting activated Hippo signaling in cultured cancer cells.

The figure below illustrates the inhibition of TEAD by IK-930.

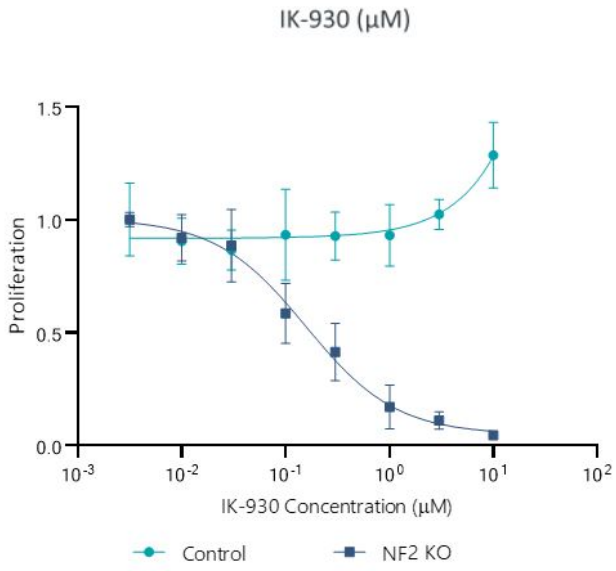
Inhibition of TEAD by IK-930 blocks TEAD-Dependent Transcription and Proliferation in H226 Cells Containing an NF2 Mutation



The ability of IK-930 to selectively inhibit proliferation in Hippo pathway mutated cells was demonstrated in the H28 mesothelioma cell line which does not have any Hippo pathway mutations. This cell line is insensitive to IK-930. However, knockdown of NF2 using CAS9-CRISPR converts H28 into an IK-930 sensitive tumor.

The figure below illustrates IK-930 blocking the proliferation of cells with NF2 loss but not in cells with normal NF2.

IK-930 Blocks Proliferation in Cells with NF2 Loss but Not in Cells with Normal NF2

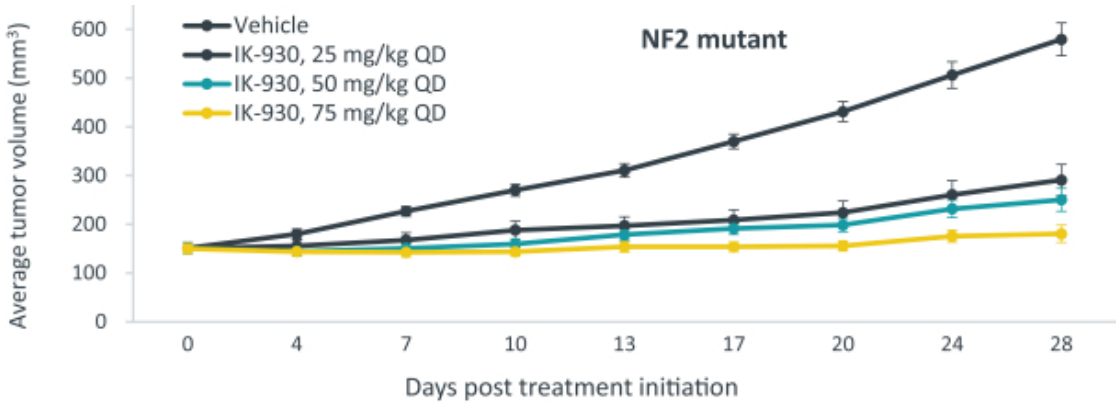


We also observed that IK-930 was significantly selective for TEAD as assessed in these cell-based assays relative to a safety panel of 45 receptors, enzymes and ion channels, a human ether-a-go-go related gene, or hERG, assay and a panel of Cytochrome P450, or CYP, inhibition assays.

We observed favorable PK/PD of IK-930 in preclinical studies. We observed that IK-930 exhibited antitumor activity in preclinical tumor models with Hippo pathway mutations. IK-930 dosed in a H226 NF2 mutant mouse xenograft model led to antitumor activity throughout the treatment period. We observed similar activity in a xenograft model using a LATS1 fusion/LATS2 deleted tumor model. IK-930 dosed in NF2 mutant and LATS1 fusion/LAT2 deleted mouse xenograft models led to tumor growth inhibition compared to vehicle.

The figures below illustrate the antitumor activity of IK-930 in Hippo mutant xenograft models.

Antitumor Activity of IK-930 in Hippo Mutant Xenograft Models

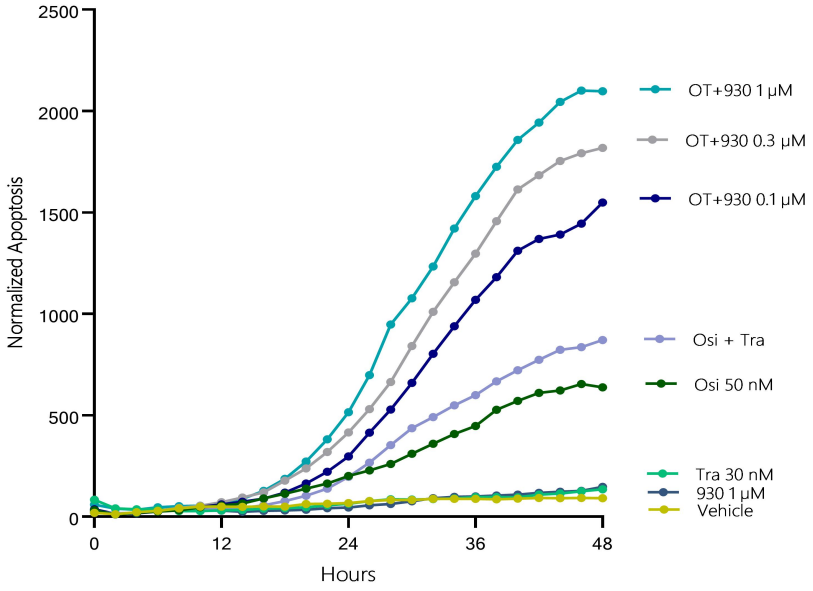


In addition to potential for single agent activity in tumors with genetic alterations in the Hippo pathway, we believe there is an opportunity for IK-930 to be beneficial in combination with other targeted therapies in the therapeutic resistance setting. Alterations in the Hippo pathway have been connected 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.

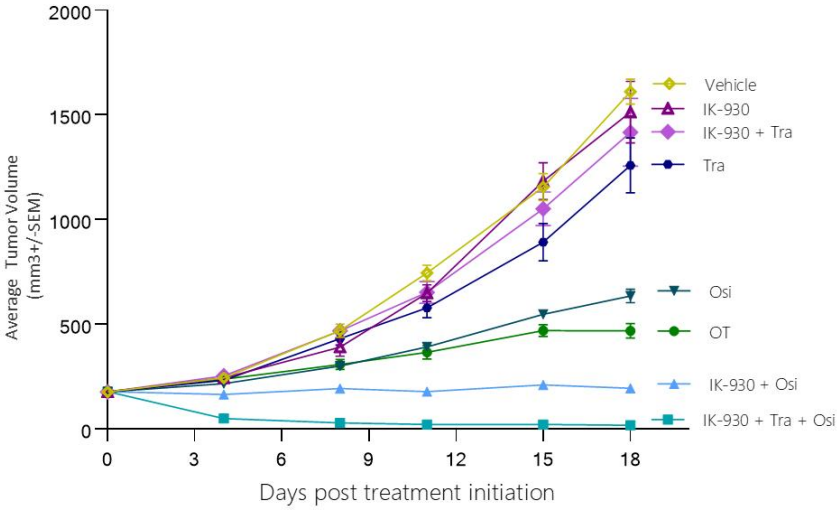
We have generated robust preclinical data supporting our confidence in the clinical opportunity to treat EGFR resistant patients with IK-930. We observed *in vitro* that inhibitors of EGFR (osimertinib) promote YAP1 nuclear localization in EGFR mutant NSCLC cells. Moreover, we observed that IK-930 is able to kill EGFR resistant lung cancer cells *in vitro* in combination with osimertinib. We observed increased apoptosis *in vitro* and activity *in vivo* of IK-930 combined with EGFR inhibition. In the H1975 EGFR mutant lung cancer xenograft mouse model, we observed 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, or MAPK, survival pathway further leads to antitumor activity.

The figure below illustrates *in vitro* (top) and *in vivo* (bottom) models of IK-930 in EGFR mutant lung cancer.

IK-930 in EGFR Mutant Lung Cancer

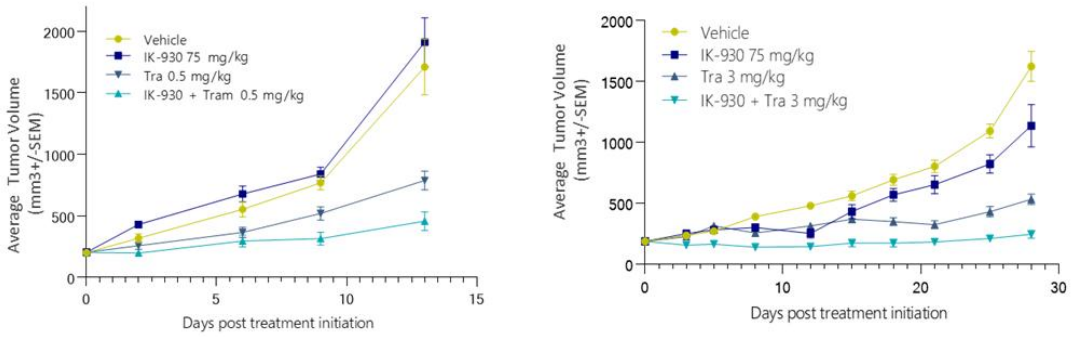


Tra: Trametinib
Osi: Osimertinib
OT: Osi + Tra Combo



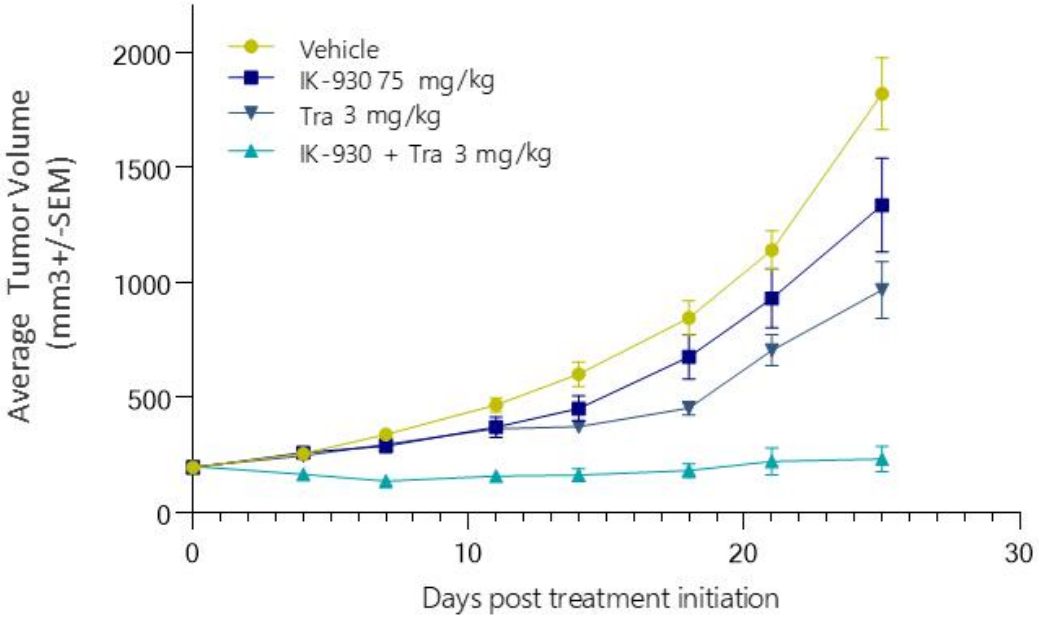
We also conducted studies in several tumor models of KRAS-mutant cancers assessing the combination of IK-930 with trametinib. In two models of KRAS G13D, HCT116 and LoVo IK-930 combined with trametinib demonstrated robust anti-tumor activity than either single agent alone.

IK-930 Combination with Trametinib in two KRAS G13D CRC Models



In a mouse model of KRAS G12S model A549 combination of IK-930 with trametinib showed significant impact on tumor inhibition.

IK-930 Combination with Trametinib in KRAS G12S NSCLC Model



Importantly, in all three of these models, IK-930 added activity only when treatment with trametinib was present, suggesting the resistance of the tumor is linked to the Hippo pathway and could benefit from TEAD inhibition. These data support studying IK-930 in combination with targeted therapies in multiple tumor types, including EGFR and KRAS mutant tumors.

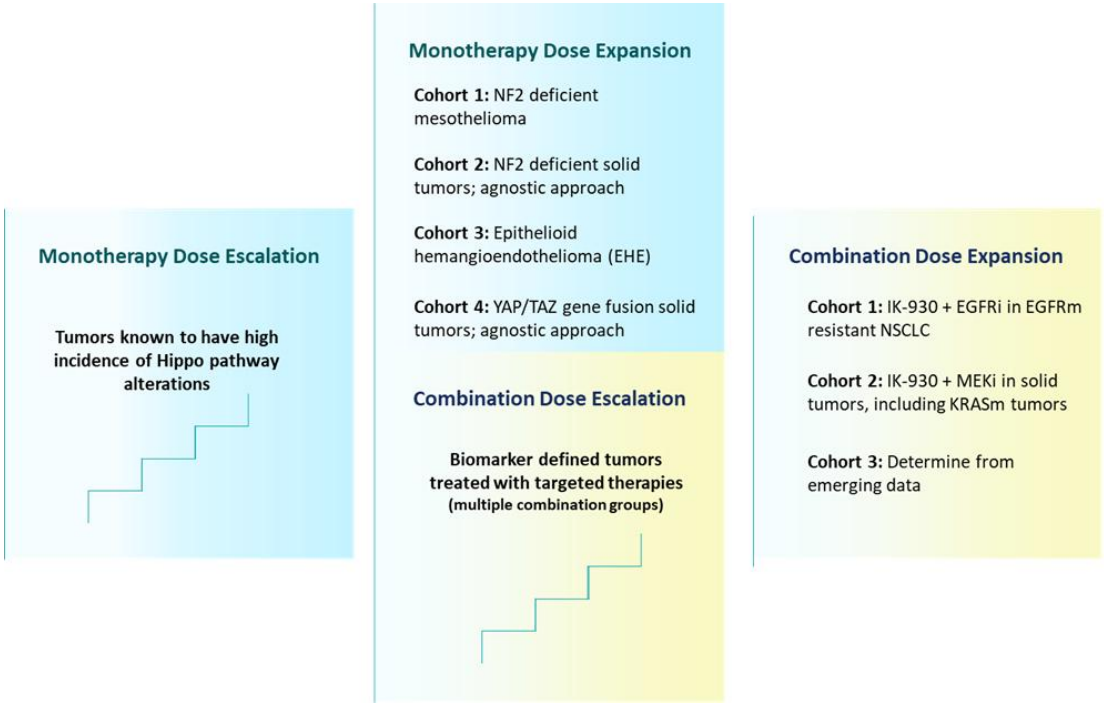
IK-930 clinical development strategy

Given the broad role of the Hippo signaling pathway on tumor biology and cancer progression, we plan to focus development of IK-930 on biomarker selected patient populations based on NF2 loss, and/or YAP1 and TAZ gene fusion or gene amplification in patients with solid tumors. We plan to utilize a comprehensive clinical development strategy focused on genetically defined patient populations targeting indications of high unmet medical need, which includes the following components:

- Assessing potential in rapid proof-of-concept and fast-to-market opportunities of IK-930 monotherapy for patients with solid tumors harboring genetic alterations in the Hippo pathway in rare and orphan disease indications; and
- Expanding our clinical development plan into combinations with other targeted therapies as well as broader indications.

Our ongoing Phase 1 clinical trial of IK-930 is exploring IK-930 as a monotherapy and is planned to also assess IK-930 in combinations with other targeted therapies. The monotherapy arm 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, as illustrated in the figure below. The first patient in this trial was dosed with IK-930 in January 2022. Currently, we are enrolling the monotherapy dose escalation cohort with patients with tumors known to have high incidence of Hippo pathway alterations. In the monotherapy dose expansion we plan to include multiple cohorts and select patients prospectively based on specific Hippo genetic alterations such as NF2 loss and/or YAP1 and TAZ gene fusion.

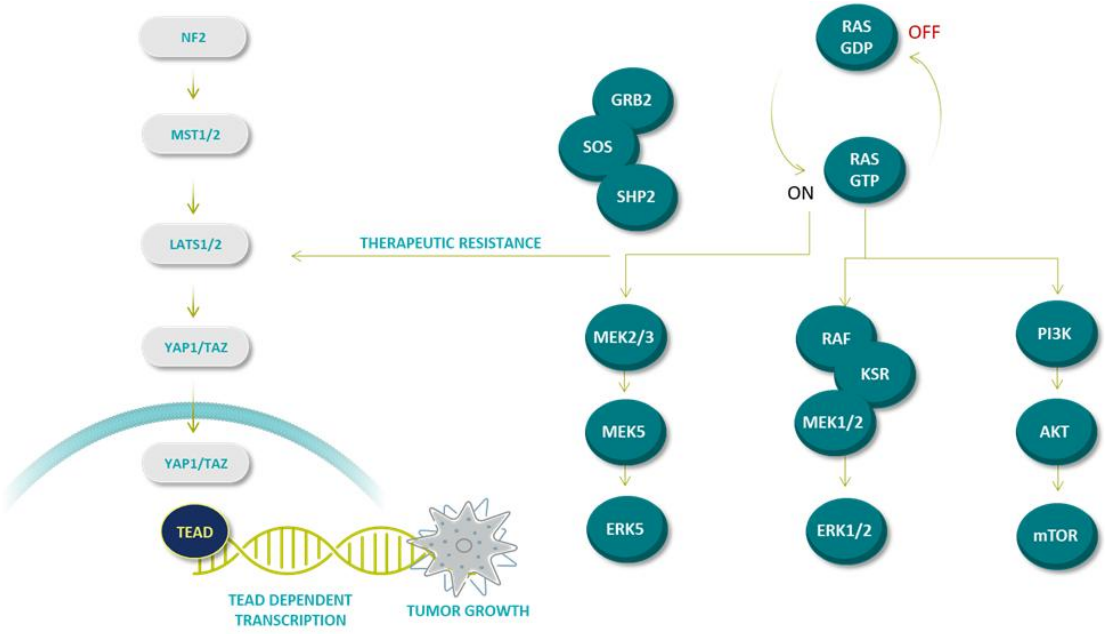
Phase 1 Clinical Trial of IK-930



In the combination arm of the Phase 1 clinical trial, we plan to include three different cohorts and explore indications based on emerging efficacy data from the monotherapy arm, as well as biomarker defined tumors with known mechanisms of tumor escape where IK-930 may be able to overcome resistance to targeted therapies, such as EGFR resistant NSCLC, and potentially improve effectiveness of targeted therapies. We expect to provide a clinical data update from this trial in 2023.

Early-Stage Research to Expand Targeted Oncology Portfolio

Across our early-stage pipeline, we are conducting work in both the Hippo and RAS pathway in the effort to develop therapies for cancers that target key nodes and feedback connections between mutations and alterations. The image below is a depiction of select areas of the RAS pathway and Hippo pathway.



Our Efforts in the RAS Pathway

This work is across multiple nodes in the pathway, both known and novel. We believe that positive clinical data from the recently approved KRAS G12C inhibitors provide support for modulating targets in the KRAS pathway, including potentially G12D, G12V, and others that are not being addressed by current product candidates or approved therapies. In addition, clinical therapeutic resistance to G12C inhibitors has developed and emerging data suggests cancer cells continue to rely on MAPK signaling pointing toward a need for vertical combinations within the pathway.

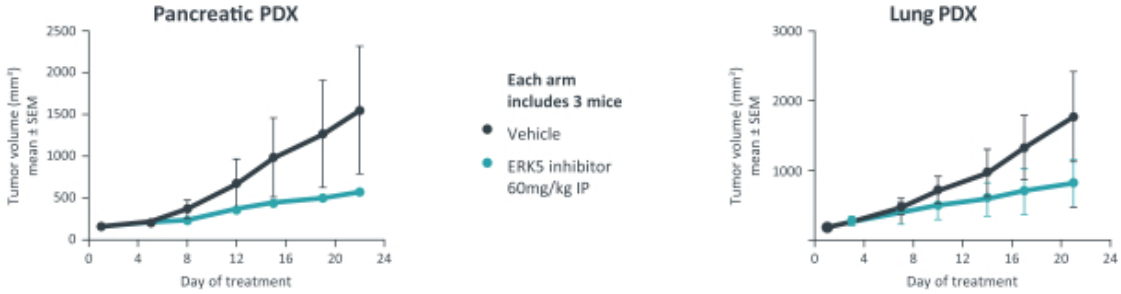
We are developing small molecule inhibitors of ERK5 for the potential to treat patients with KRAS mutant cancers. We believe that ERK5 provides an opportunity to address unmet medical need in the RAS pathway by modulating a key target that is downstream of RAS and therefore applicable to cancers with oncogenic KRAS mutations.

ERK5 Rationale

ERK5 is a member of the MAPK family. It is composed of an N-terminal kinase domain and a C-terminal tail responsible for sub-cellular localization and transcriptional activation. ERK5 can be activated in response to a range of mitogenic stimuli such as growth factors, G protein-coupled receptor agonists, cytokines and cellular stresses (e.g., hypoxia, shear stress). Through the MAPK signaling cascade, mitogen-activated protein kinase 5, or MEK5 activates ERK5 by phosphorylating the N-terminal domain, thereby enabling ERK5 kinase activity. ERK5 is an important mediator of tumorigenesis and metastatic progression, and a fundamental component of drug resistance in cancer.

As illustrated in the figure below, we observed single agent antitumor activity in both a pancreatic and lung patient derived xenografts in mice using a small-molecule ERK5 inhibitor. This inhibitor is a potent and selective tool compound with an IC50 *in vitro* of 35 nM with high selectivity for ERK5 but has a short half-life and short PD effect.

ERK5 inhibition reduces tumor growth in patient-derived mouse xenograft models of pancreatic and lung cancer



Moreover, we observed increased antitumor activity with dual ERK5 and MEK inhibition in KRAS mutant cancers in preclinical studies. In a three dimensional cell culture system, we observed that combined ERK5 and MEK inhibition led to synergistic antitumor activity (synergy score > 1.5) in two mutant KRAS lung cancer cell lines, NCI-H2122 (G12C KRAS mutation) and A-549 (G12S KRAS mutation), but not in the wildtype KRAS lung cancer cell line NCI-H520.

Synergy of ERK5 and MEK inhibition in KRAS mutant but not wild type cells in 3D cell culture system

In preclinical studies in KRAS primary human tumor models of lung and pancreatic cancer, we observed synergistic effects on tumor inhibition by combining this inhibitor tool compound of ERK5 and trametinib. These models contained mutations in the RAS pathway. These data, as illustrated in the figure below, suggest that, in addition to single agent potential in KRAS-mutated cancers, there is potentially a clinical opportunity for ERK5 inhibitors to be used in combination with MEK inhibitors and other targeted therapies to address therapeutic resistance in these patient populations.

Synergistic combination of MEK inhibitor and ERK5 inhibitor in KRAS mutant pancreatic (right) and lung (left) primary human tumor xenografts

RAS Signaling Opportunity

Despite continuous industry efforts in the past several decades to develop therapies for KRAS mutant cancers, therapies directly targeting KRAS G12C are only now beginning to show clinical promise. In the United States, about 13% of patients with NSCLC harbor the KRAS G12C mutation. Although there has been recent progress with these compounds that directly inhibit mutant KRAS, the majority of the KRAS space remains open. At this time, 85% of KRAS mutations (G12D, G12V, G13, others) are not being addressed by clinical stage product candidates or approved therapies. KRAS mutations are estimated to occur in about 26% of all cancers, including 25% of lung cancers, 90% of pancreatic cancers and between 27% and 56% of colorectal cancers. We believe that new approaches to key nodes and novel targets, like ERK5, represent differentiated opportunities to address these high unmet medical need segments.

As we continue to narrow in on potential targets and product candidates, we are looking extensively at the patient populations that have the potential to benefit from new therapies. There are three indications we believe represent unmet needs despite the recent advancement in the space: NSCLC, pancreatic cancer and CRC.

- *NSCLC*: There are an estimated 228,000 new cases of lung cancer diagnosed and approximately 135,000 deaths in the United States annually. NSCLC is estimated to account for approximately 80% to 85% of lung cancer cases and KRAS mutations are estimated to occur in about 25%. Previously, patients were treated primarily with radiation therapy or combinations of cytotoxic drugs. In the past 15 years, a number of targeted agents have been developed based on alterations in the genes for EGFR and anaplastic lymphoma kinase gene, or ALK, significantly improving the outcome of patients with NSCLC harboring these genetic alterations. Furthermore, in the last five years, the introduction of immunotherapy for the treatment of NSCLC patients has also improved the outcome of the treatment in patients, especially those with high PD-L1 expression. However, a significant proportion of NSCLC patients are ineligible for these novel therapies or develop resistance to existing treatments, representing an important unmet medical need. Approximately two-thirds of NSCLC patients are ineligible for treatment with EGFR or ALK targeted therapies, representing an important unmet medical need. Despite the availability of these new therapies, the prognosis in NSCLC remains poor, with an overall five-year survival for all patients diagnosed with NSCLC estimated to be approximately 19% and until recently there were no specific therapeutic options for this subset of patients. Even with the emergence of KRAS inhibitors targeting G12C mutations, most NSCLC patients with KRAS mutations will eventually progress and die due to their disease.
- *Pancreatic cancer*: The American Cancer Society estimates that about 57,600 patients will be diagnosed with pancreatic cancer in 2020. The tendency of pancreatic cancer to spread silently before diagnosis makes it one of the deadliest cancer diagnoses. In metastatic pancreatic cancer, surgery and radiation are

used only for symptom control. Chemotherapy, such as gemcitabine and 5-FU/leucovorin/oxaliplatin/irinotecan, can help improve pancreatic cancer symptoms and survival. The drug olaparib (Lynparza) has been approved for metastatic patients with the BRCA gene mutation whose cancer has responded well to chemotherapy. Unfortunately, in spite of the development of new treatments for pancreatic cancer, deaths due to this tumor are on the rise. The National Cancer Institute has identified targeting oncogenic RAS as one of the four major priorities for pancreatic cancer research.

- *CRC*: CRC is the second leading cause of cancer deaths in the United States. Despite the reduction of incidence and improvement of early detection in the United States, approximately 86% of patients are diagnosed after the onset of symptoms when their disease is relatively advanced. Patients with advanced CRC are treated with radiation and chemotherapy drugs such as 5-fluorouracil, oxaliplatin and capecitabine, as well as recently approved antibodies, that inhibit angiogenesis, such as bevacizumab. In a subset of CRC patients, treatment with antibodies targeting epidermal growth factor receptor, or EGFR, (for example, the agent cetuximab) has been shown to be effective both as monotherapy and in combination with chemotherapy. However, approximately 40% of patients have a mutation in the KRAS gene that renders cetuximab ineffective.

Immune Signaling Programs

In addition to our programs targeting the RAS and Hippo pathways, we are also advancing programs that target immune-signaling pathways that contribute to the TME. These programs, like our targeted oncology pipeline, are supported by robust biomarker research that allow us to prospectively select patients.

Two of our immune signaling programs, IK-175 and IK-412, are partnered with BMS. Through our strategic partnership, Bristol Myers Squibb has the exclusive right to license each of IK-175 and IK-412 through completion of Phase 1b clinical trials. IK-175 is an inhibitor of AHR and both unselected patients and those with activated AHR are currently being enrolled in the dose expansion cohort of a Phase 1 clinical trial of patients with locally advanced or metastatic solid tumors, including bladder cancer. IK-412 is an enzyme therapy designed to lower levels of immunosuppressive kynurenine in the TME. The IK-412 program experienced manufacturing delays previously disclosed in 2021. Considering these delays and the timeline of the partnership we have made the strategic decision to pause IK-412 development for the remainder of the Bristol Myers Squibb collaboration agreement term once the ongoing CMC work has been completed.

IK-175, an AHR antagonist

IK-175 is a potent, selective oral antagonist of AHR. We observed evidence of antitumor activity of IK-175 as a monotherapy and in combination with an anti-PD-1 antibody in preclinical models. We are currently enrolling patients with bladder cancer in a Phase 1 clinical trial of IK-175, evaluating it as both a monotherapy and in combination with nivolumab in both unselected population and enriched with patients whose tumors have activated AHR . Pursuant to our master collaboration agreement with Celgene Corporation (now Bristol Myers Squibb), or the Bristol Myers Squibb Collaboration Agreement, we are responsible for development of IK-175 through the completion of a Phase 1b clinical trial, through the completion of which Bristol Myers Squibb has an exclusive right to exclusively license IK-175 worldwide. See “—License and Collaboration Agreements—Master Collaboration Agreement with Bristol-Myers Squibb” for additional information.

Dual role of AHR in cancer progression

AHR is a ligand-dependent transcription factor that drives tumor progression through direct cancer cell and immunosuppressive effect in the TME. In some tumors, such as bladder cancer, high levels of AHR lead to constitutive, always-on activation and direct stimulation of tumor cell growth. AHR is also a critical component of a dominant immunosuppressive pathway in cancer, a pathway that modulates the function of cells in both the innate and adaptive components of the immune system. AHR is, in its inactive form, found in the cytosol, outside the nucleus. Upon binding of a signaling molecule or ligand, AHR migrates to the nucleus and functions as a transcription factor.

AHR is overexpressed and constitutively activated in a number of tumors, including, but not limited to, bladder cancer and advanced breast cancer. Constitutive activation of AHR also has been reported in head and neck squamous cell carcinoma as well as castration-resistant prostate cancer. In melanoma, constitutive activation of AHR is believed to represent a significant mechanism of resistance to approved inhibitors of BRAF kinase. Inhibition of constitutively active AHR in patient-derived acute myeloid leukemia cells has been shown to sensitize these cells to killing by natural killer cells.

Bladder cancer overview

We prioritized patients with bladder cancer as a lead indication for the development of IK-175 based on the following:

- Poor prognosis of patients with bladder cancer is associated with a high AHR transcript profiling score;
- High levels of AHR mRNA and protein as measured by immunohistochemistry and RNAscope are found in bladder cancers;
- AHR amplifications have been described in approximately 5% to 22% of bladder cancer patients; and
- Nuclear localization of AHR is high in bladder cancers.

Bladder cancer is the most common malignancy involving the urinary system and there were an estimated 81,400 new cases of bladder cancer and 17,980 deaths in the United States in 2020. The five-year survival for patients with early-stage disease is 88%; however, for patients with metastatic disease or cancer that has spread to other parts of the body, the five-year survival drops to 5%.

The most common treatment for patients diagnosed with advanced or metastatic bladder cancer is chemotherapy with platinum-based drugs such as carboplatin or cisplatin in combination with gemcitabine. Patients with metastatic disease that progresses during or after platinum-based chemotherapy are increasingly being treated with checkpoint immunotherapy. A number of PD-1 and PD-L1 checkpoint inhibitors have been approved by the FDA for the treatment of patients with refractory bladder cancer. Objective response rates in clinical trials with checkpoint inhibitors have generally been between 13% and 29%. The median overall survival of patients with advanced or metastatic bladder cancer from the start of initial therapy is 12.7 months. Other drugs have been recently approved for use in patients with metastatic bladder cancer after failure to platinum based regimens and checkpoint inhibitors including Enfortumab vedotin and Sacituzumab govitecan (antibody directed conjugates or ADCs).

Our solution, IK-175

IK-175 is an internally discovered small molecule AHR antagonist that we are developing for the treatment of advanced or metastatic solid tumors, including bladder cancer where AHR-activation is known to lead to poor prognoses. We observed that IK-175 is potent and selective for AHR in multiple *in vitro* assays and species.

We have an ongoing, open-label Phase 1 clinical trial evaluating IK-175 as a monotherapy and in combination with nivolumab. The dose-escalation cohorts enrolled locally advanced or metastatic solid tumor patients. Currently we are enrolling in our expansion cohorts for patients with bladder cancer, including selection for patients who are AHR biomarker positive. Clinical pharmacokinetic and pharmacodynamic data supports once-daily clinical dosing in patients.

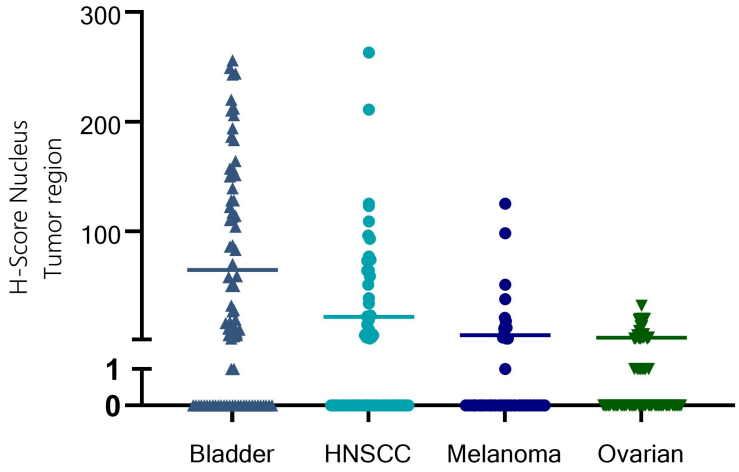
IK-175 indication and patient selection strategy

Our IK-175 clinical development strategy is focused on enrolling patients who are most likely to respond to an AHR antagonist. As part of our robust translational strategy, we have explored three tumor profiling technologies centered on AHR to help guide indication selection and/or candidate patients:

- AHR gene amplification: Increases in the number of copies of the AHR gene as assessed by Fluorescent In Situ Hybridization, or FISH, are observed in over 5% of multiple cancers such as esophageal, bladder and lung cancers.

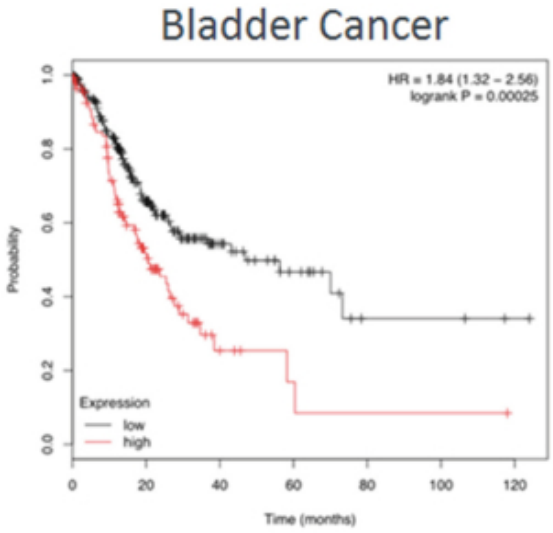
- Nuclear AHR positivity: Constitutive activation of AHR leads to its localization to the nucleus, which can be directly measured by a proprietary immunohisto chemical staining assay that we developed. In the monotherapy expansion cohort, we are prospectively enriching for patients with tumors that exhibit activated AHR using this assay. With the proprietary assay we developed, we assessed multiple tumor samples and found bladder cancer has the highest percentage of nuclear AHR positivity of those sample test. Head and neck cancer, melanoma, and ovarian cancer also resulted in higher-than-average scores, as displayed in the image below. The assay also is being used in our ongoing clinical trial to select patients with high nuclear-AHR positivity.

Immunohistochemistry Tumor Microarray Results



AHR-dependent gene transcription: Activation of AHR leads to changes in transcription of many genes which can be quantified by standard mRNA transcription profiling technologies. We discovered this gene transcription expression signature. We generated a profile of the transcriptional changes induced by AHR activation across a panel of cell lines. We then used this profile to score tumors based on available transcript profiling data in public databases. We found that bladder cancer patients with transcriptional profiles that scored highest using our activated AHR profile had poorer prognoses compared to those with low scores, as illustrated in the figure below.

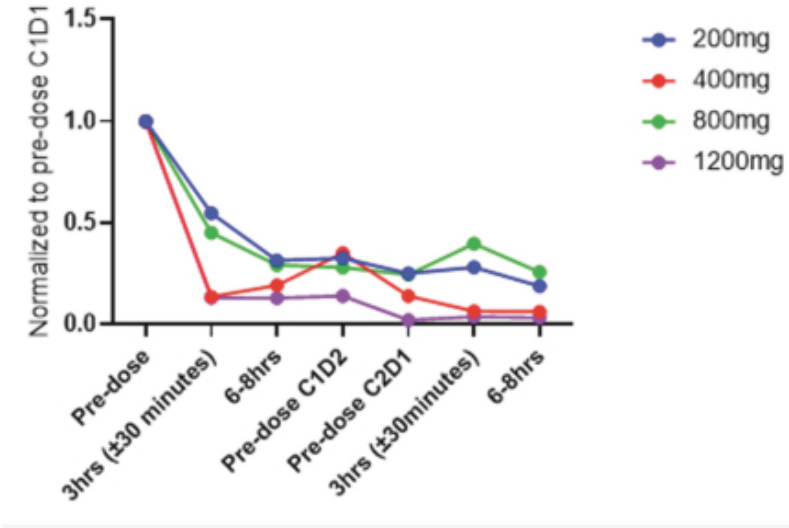
AHR-activated Gene Transcription Signature is Associated with Poor Overall Survival in Bladder Cancer Patients (c)



Ongoing Phase 1 clinical trial and clinical development

We are currently enrolling patients with locally advanced or metastatic solid tumors in an open-label Phase 1 clinical trial evaluating IK-175 as a monotherapy and in combination with nivolumab, including dose expansion cohorts for patients with bladder cancer in both all comers and AHR positive tumors. The primary endpoint of this trial is safety and tolerability. As of February 1, 2022, we have completed the dose escalation of both treatment we are currently enrolling patients in both the monotherapy and combination dose expansion cohorts. To date, we have not observed any dose limiting toxicities, or DLTs, to date and have not reached the maximum tolerated dose in both treatment arms. In the first four dose cohorts, we observed dose responsive target gene inhibition in whole blood assay from patient samples, as set forth in the graph below.

IK-175 Target Modulation in Patients



We plan to present initial clinical data from this program in the second half of 2022. Additionally, we plan to initiate a clinical trial in HNSCC as second indication to explore for IK175 in the second half of 2022.

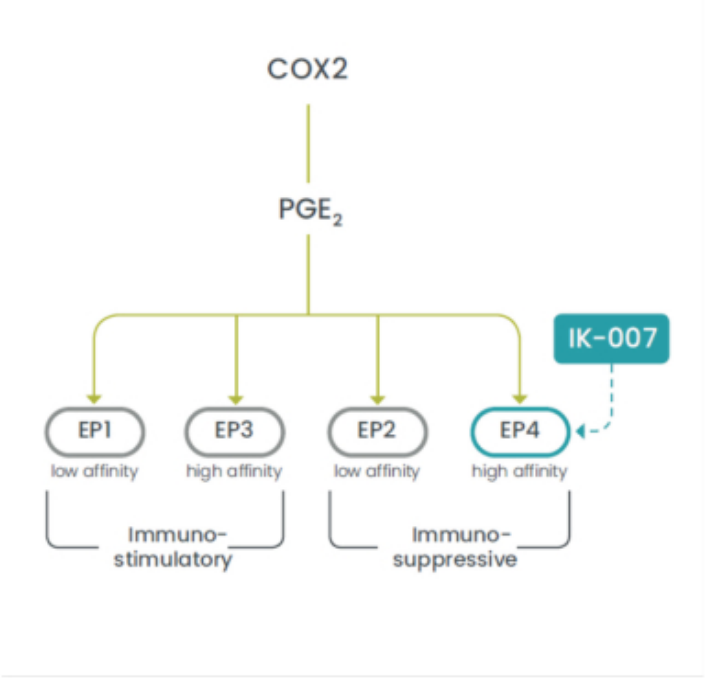
IK-007, an EP4 antagonist

IK-007 is an oral selective antagonist of the EP4 receptor. IK-007 has been well tolerated in over 900 subjects to date in non-oncology clinical trials. We are conducting a Phase 1b clinical trial of IK-007 in combination with pembrolizumab for the treatment of patients with MSS CRC, which represents approximately 85% of patients with CRC. In this Phase 1b clinical trial, we observed encouraging preliminary evidence of tolerability and antitumor activity and did not observe any DLTs in the initial dose escalation cohort. In addition, we have identified higher baseline levels of urinary PGEM, a metabolite in the EP4 pathway, as a potential biomarker that we believe is associated with clinical benefit. The trial completed enrollment in the fourth quarter of 2021. We anticipate presenting clinical data from this program in the second half of 2022.

Role of EP4 Pathway in cancer

Prostaglandin-endoperoxide synthase 2, or COX2, is an enzyme that is responsible for the production of prostaglandins during inflammation, including Prostoglandin E2 or PGE2. PGE2 sends its signals through four distinct receptors, known as EP1 through EP4, and these receptors in immune cells can have either stimulatory or suppressive activities. We believe that blocking immunosuppressive activity by inhibiting EP4, the higher affinity immunosuppressive receptor of PGE2, could be valuable in treating cancer. We also believe that selectively blocking PGE2 signaling through EP4 could lower the likelihood of toxicities that may result from fully blocking this fundamental pathway. The figure below illustrates the mechanism of action of IK-007.

IK-007 selectively blocks EP4, the high affinity immunosuppressive receptor in the COX2/PGE2 pathway.



A large body of literature demonstrates that activation of the PGE_2 pathway in cancer augments tumor initiation, progression and therapeutic resistance. Increased expression of pathway components, including EP4, is associated with decreased survival, therapeutic and preventive precedent in a number of cancer types, including CRC. When activated, EP4 affects the activity of a broad range of cells within the innate and adaptive immune system culminating in an immunosuppressive TME. Preclinical studies suggest that a selective antagonist of EP4 has the potential to bring therapeutic benefit to tumors such as CRC by changing the immunosuppressive TME so that tumors can become more accessible to the penetration of immune cells and more susceptible to the activity of checkpoint inhibitors.

MSS CRC Overview

CRC is the second leading cause of cancer deaths in the United States. The National Cancer Institute estimates that there were 147,950 new cases of CRC and 53,200 CRC related deaths in the United States in 2020. Approximately 35% of patients newly diagnosed with CRC will die within five years. PD-1 checkpoint inhibitors have been approved in a subset of CRC known as microsatellite instability-high, or MSI-H, tumors. MSI-H tumors are found in about 15% of CRC patients, with microsatellite stability, or MSS, tumors representing the remaining 85% of patients. The prognosis of MSS CRC patients is significantly poorer than that of MSI-H patients. MSS CRC represents a large unmet clinical need. Interim data of single agent treatment with pembrolizumab showed an overall response rate in MSS CRC of 0% (0/18).

Our solution, IK-007

IK-007 is a selective EP4 antagonist originally discovered by Pfizer that we licensed to explore as a potential cancer therapy. IK-007 has been dosed in over 900 adults in previous non-oncology clinical trials, including in two Phase 2 clinical trials on the treatment of osteoarthritic knee pain. In normal healthy volunteers studies, IK-007 was found to be well tolerated when administered as a single dose up to 1000 mg and as multiple doses up to 300 mg twice a day for 14 days. Based on the biological rationale for PGE_2/EP4 in CRC and the high unmet medical need in MSS CRC, in particular given that single agent pembrolizumab is inactive in these patients, we are currently conducting a Phase 1b clinical trial of IK-007 in combination with pembrolizumab for the treatment of patients with MSS CRC. Encouraging preliminary evidence of antitumor activity and higher baseline levels of a potential predictive PGE2 metabolite biomarker, called PGEM, are emerging from the ongoing trial.

At the end of 2021, the trial completed enrollment and patients continue in follow-up. We anticipate presenting clinical data from this program in the second half of 2022.

Ongoing Phase 1b trial

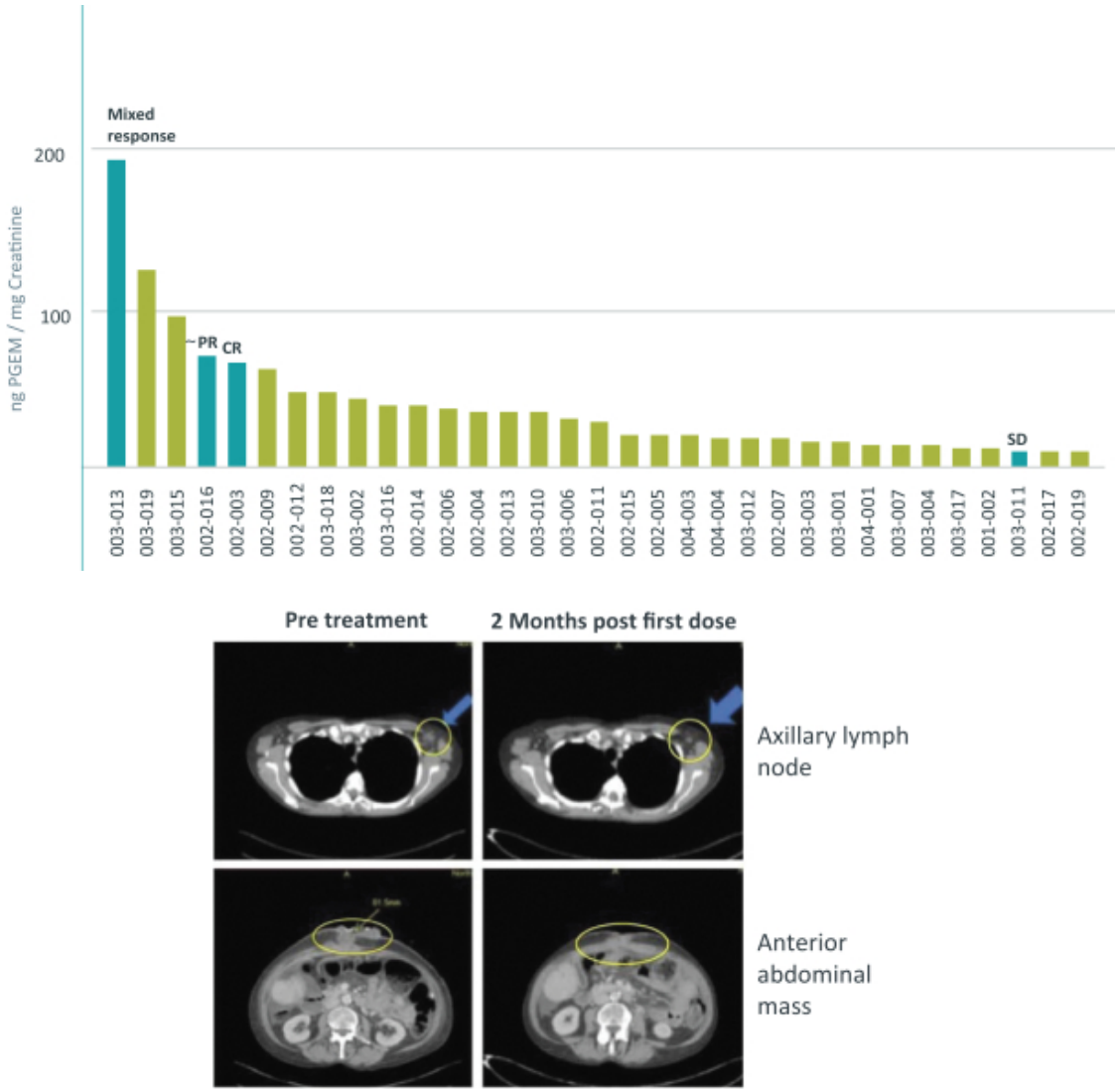
We are conducting a single arm Phase 1b clinical trial of IK-007 in combination with pembrolizumab in patients with MSS CRC patients who have received at least two lines of prior systemic therapy and progressed, and therefore unlikely to respond to pembrolizumab monotherapy. The primary endpoint of this trial is safety and tolerability of IK-007 alone and in combination with pembrolizumab.

While early in development, we are encouraged by the observed antitumor activity of IK-007 in combination with pembrolizumab. As of the last data cut in 2021, we observed evidence of clinical benefit (complete response, or CR, partial response, or PR, and stable disease, or SD, for 16 weeks) in four out of 20 evaluable patients treated at 300 mg bid p.o. as follows:

- One patient had a CR and remained on study for 22 months;
- One patient experienced 29% tumor shrinkage that was close to meeting the criteria for a PR;
- One patient had durable stable disease for over six months (prolonged SD); and
- One patient had a mixed response with shrinkage of some but not all tumors and stable disease for 17 weeks (prolonged SD).

The patient who reached a CR had received five prior lines of therapy. This highly refractory patient’s tumor also exhibited low tumor mutational burden, or TMB, reducing the likelihood that the antitumoral response could be due to pembrolizumab treatment alone as high TMB is often associated with response to anti-PD-1 therapies. Tumor response was observed soon after commencement of dosing with IK-007. A significant shrinkage of 48% of the tumor size was observed by CT scan after approximately two months of combined therapy. With additional cycles of treatment, evidence of tumor in this patient disappeared and the patient was classified as a complete responder, as illustrated in the figure below. This patient was on treatment for 22 months.

Complete response in an MSS CRC patient treated with 300 mg IK-007 and 200 mg pembrolizumab, and association with high urinary PGEM levels.



Moreover, we have identified a biomarker in the EP4 pathway, higher baseline levels of urinary PGEM, that we believe can help us select for patients who may benefit the most from IK-007. An ad hoc analysis of the first 33 patients enrolled in the study showed that there was a significant correlation between higher baseline levels of urinary PGEM and clinical benefit observed and with prolonged time on treatment (defined as over 16 weeks on study drug). High urine levels of PGEM (> 50 ng/mg creatinine) were present in approximately 20% (21.2% with 95% CI 9.0-38.9) of the first 33 CRC patients tested for PGEM in the study.

The most common related adverse events were Grade 1 or Grade 2 fatigue, pruritus and Grade 3 or Grade 4 increased gamma-glutamyl transferase, a liver enzyme.

Given the early positive tolerability profile of IK-007 in the first two cohorts (300 mg BID) in combination with pembrolizumab as well as encouraging signs of activity at this dose, we amended the protocol to explore three more

dose escalation levels of IK-007: 450 mg, 600 mg and 900 mg BID in combination with pembrolizumab. No DLTs in the three additional dose escalation cohorts were observed up to 900 mg BID. Most adverse events observed included myalgia, anemia, decrease appetite, insomnia and diarrhea, mostly Grade 1 or Grade 2. We also observed transient elevations of liver function tests, or LFTs, that in a few cases required IK-007 dose modifications.

Based on these data, we selected the dose of 900 mg BID of IK-007 in combination with pembrolizumab (200 mg) every three weeks for the dose expansion cohort. The trial is fully enrolled and patients are currently undergoing follow-up.

In selecting patients to receive IK-007, our objective is to focus treatment on patients who are most likely to respond. We generated a validated urine PGEM biomarker assay. We used it to measure baseline PGEM urinary levels to select patients who are more likely to respond in our MSS CRC dose expansion cohort.

We also conducted a second open-label single arm Phase 1b clinical trial of IK-007 in combination with pembrolizumab in patients with advanced or metastatic post anti-PD-1/L1 treatment in NSCLC. Based on the combined data generated in the interim period for efficacy and safety, we decided not to further explore this combination in NSCLC and terminated this clinical trial in December 2020.

We believe that IK-007 may have the potential to bring therapeutic benefit beyond MSS CRC and we may expand into certain additional indications in which there is high unmet medical need and biological rationale for the key role of EP4 pathway in cancer progression.

IK-007 in Inflammatory Breast Cancer

Inflammatory breast cancer, or IBC is a rare, aggressive form of breast cancer with high unmet medical need. While it represents less than 5% of all breast cancers, it progresses quickly and is most often diagnosed when it has already reached stage 3 or 4. There is a higher incidence of IBC in younger women as it can go undetected in early stages without the regularity of mammograms seen in older patients. Additionally, IBC has a higher incidence in African American women. Increased COX-2 is expressed in the EP4 pathway is in 40-50% of IBC patients and has been associated with poor prognosis.

In September 2021, an investigator-initiated trial (IIT) of IK-007 in combination with the chemotherapy agent eribulin was launched in metastatic IBC led by Naoto Ueno, M.D., of the University of Texas MD Anderson Cancer Center and it is currently enrolling patients.

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 the segments of the pharmaceutical, 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., Cedilla Therapeutics, Inc., BridGene Biosceiences, Sanofi, and Roche/Genentech. Vivace Therapeutics, Inc. and Novartis are both in Phase 1 clinical trials with their programs. All other programs are preclinical.

IK-175

We are aware of one other AHR antagonist in clinical development under development by Bayer AG, or Bayer. Bayer is currently enrolling patients with advanced solid tumors in a Phase 1 trial for BAY-2416964 in advanced solid tumors.

IK-007

IK-007 is one of the EP4 antagonists currently in clinical development. The other programs in clinical development are from Ono Pharmaceutical (ONO-4578), Adlai Nortye/Eisai (AN-0025 / E-7046), and Ionova (INV-1120) which are in Phase 1 clinical trials. Tempest Therapeutics'TPST-1495, a dual antagonist that selectively blocks EP2 and EP4, is in Phase 1 clinical trials.

License and Collaboration Agreements

Master Collaboration Agreement with Bristol-Myers Squibb

In January 2019, we entered into the BMS Collaboration Agreement with Celgene Corporation (which was acquired by BMS in November 2019) under which BMS may 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 except for inverse agonists, or the Collaboration Candidates, which we are developing as IK-175 and IK-412. The BMS 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.

On a program-by-program basis, through the completion of a Phase 1b clinical trial for each of IK-175 and IK-412, BMS has 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. Additionally, if we do not complete a Phase 1b clinical trial by the end of the research term (as defined below), we may elect to provide a data package to BMS upon which BMS may exercise the foregoing option for an additional $0.25 million fee.

As previously disclosed in 2021, the IK-412 program 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. Considering these delays and the timeline of the BMS partnership, we have made the strategic decision to pause IK-412 development activities for the remainder of the BMS contract term once the ongoing committed CMC work has been completed.

If and when BMS exercises its rights for a Collaboration Candidate, and as a result of the timing of our submission of INDs with respect to each Collaboration Candidate, BMS is required to pay us $50.0 million, in the case of an exercise of its option with respect to IK-175, and $40.0 million, in the case of an exercise of its option with respect to IK-412. The option exercise fees are payable within fifteen (15) days after the execution of each license agreement. Upon the execution of each license agreement, we will become eligible to receive up to $265.0 million under such license agreement in regulatory milestones and $185.0 million in commercial milestones as well as a tiered royalties at rates ranging from the high single to low teen percentages based on worldwide annual net sales by BMS, subject to specified reductions.

BMS will continue to pay royalties on a Collaboration Candidate-by-Collaboration Candidate and country-by-country basis, until the latest of (i) there being no valid claim under the licensed patents covering the Collaboration Candidate, (ii) expiration of all regulatory exclusivity for the Collaboration Candidate in such country, and (iii) twelve (12) years after the first commercial sale of the Collaboration Candidate in the applicable country (the Royalty Term), after which the applicable license granted to BMS in such country will become non-exclusive, fully paid-up, perpetual, irrevocable and royalty-free.

The research term under the BMS Collaboration Agreement continues for a period of five (5) years from its effective date. The term of any license agreement described above would continue on a Collaboration Candidate-by-Collaboration Candidate and country-by-country basis until the expiration of all Royalty Terms under such agreement, unless earlier terminated as described below.

The BMS Collaboration Agreement may be terminated (i) by either party on a program-by-program basis if the other party remains in material breach of the BMS Collaboration Agreement following a cure period to remedy the material breach, (ii) by BMS at will on a program-by-program basis or in its entirety, (iii) by either party, in its entirety, upon bankruptcy or insolvency of the other party, or (iv) automatically, on a program-by-program basis if BMS fails to timely deliver an opt-in notice to us.

Each license agreement may be terminated (i) by either party if the other party remains in material breach of the license agreement following a cure period to remedy the material breach, (ii) by BMS at will, (iii) by either party, in its entirety, upon bankruptcy or insolvency of the other party, or (iv) by us, in its entirety, if BMS challenges a patent licensed by us to BMS under the license agreement or any jointly-owned collaboration patents.

Upon our termination of a license agreement for BMS' breach, bankruptcy or insolvency or patent challenge, we would receive (i) upon our timely request, a nonexclusive worldwide license under BMS' know-how and patents covering the applicable licensed compound to the extent that such compound (or product or diagnostic product containing such compound) has been or is in active development or commercialization as of termination; and (ii) subject to determination of an applicable license payment in accordance with the license agreement, an exclusive license for the foregoing. If BMS terminates a license agreement for our breach or bankruptcy or insolvency, BMS' license will survive for six (6) months. Additionally, in the event of our material breach, BMS may elect to have the license agreement continue, with all future payments under that license agreement reduced by 50%.

Patent License Agreement with the University of Texas at Austin

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

Pursuant to the License Agreement, and 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 Licensed 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., or Arrys, in December 2018, we acquired in-process research and development assets related to AskAt Inc.’s, or AskAt, selective EP4 antagonists, namely IK-007 which we are currently developing in a Phase 1b clinical trial in MSS CRC and IK-008 which is a backup molecule, based on the intellectual property associated with a License Agreement, or 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. Please see “Business—Intellectual Property—EP4 Antagonist Patent Families,” for additional information concerning the intellectual property related to the AskAt Agreement.

The term of the AskAt Agreement expires on licensed product-by-licensed product and country-by-country basis upon the expiration of the royalty term for such licensed product, unless earlier terminated as described below.

The License Agreement may be terminated (i) by either party if the other party remains in material breach of the license agreement following a cure period to remedy the breach, (ii) by us for convenience upon 180 days’ notice or (iii) by either party, in its entirety, upon bankruptcy or insolvency of the other party.

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 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 United States Patent and Trademark Office 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 March 1, 2022, our overall patent portfolio includes forty-nine (49) 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 March 1, 2022, we solely own ten patent families related to TEAD inhibitors and degraders, 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 2042, not including any patent term adjustment, patent term extension, or supplementary protection certificate (SPC). The non-provisional 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 March 1, 2022, this TEAD patent family contains two pending U.S. applications, and pending applications in foreign jurisdictions, such as Europe, Japan, Australia, Canada, India, South Korea, Mexico, Argentina, and Taiwan. For one of our pending U.S. patent applications, the United States Patent & Trademark Office has mailed an Issue Notification stating that a U.S. patent is set to issue on March 15, 2022 based on this patent application. This application includes composition of matter claims encompassing IK-930. 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 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 March 1, 2022, this TEAD patent family contains a pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, Australia, Canada, India, South Korea, Mexico, Argentina, and Taiwan. 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 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 March 1, 2022, 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 2041, not including any patent term adjustment, patent term extension, or SPC.
- We have one TEAD patent family directed to a fourth collection of TEAD inhibitors, compositions thereof, and methods of their use. As of March 1, 2022, 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 2041, not including any patent term adjustment, patent term extension, or SPC.
- We have one TEAD patent family directed to a collection of TEAD degrader compounds, compositions thereof, and methods of their use. As of March 1, 2022, 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 2041, 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 covered by our solely owned pending U.S. and foreign patent applications that, if granted and all appropriate maintenance fees paid, are expected to expire from 2040 to 2042, not including any patent term adjustment, patent term extension, or SPC.

ERK5 and RAS Signaling Pathway Program Patent Families

As of March 1, 2022, we exclusively own fifteen patent families related to inhibitors targeting the ERK5 and RAS signaling pathway, compositions thereof, and methods of their use. For the ERK5 program, we exclusively own four pending PCT applications and over two pending U.S. provisional patent applications. For the RAS signaling pathway program, we exclusively own over nine 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 2041 to 2042, not including any patent term adjustment, patent term extension, or SPC.

EP4 Antagonists Patent Families

As of March 1, 2022, we have an exclusive license 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. These patent families are described in more detail below.

- We have one EP4 in-licensed patent family directed to crystal forms of EP4 antagonists, compositions thereof, and methods of their use. As of March 1, 2022, this EP4 in-licensed patent family contains a U.S. patent and patents in foreign jurisdictions, such as Europe, Japan, Canada, India, South Korea, and Mexico. The U.S. and foreign patents in this EP4 in-licensed patent family, if all appropriate maintenance fees paid, are expected to expire in 2026, not including any patent term adjustment, patent term extension, or SPC.
- We have one EP4 in-licensed patent family directed to EP4 antagonists, compositions thereof, and methods of their use. As of March 1, 2022, this EP4 in-licensed patent family contains a U.S. patent and patents in foreign jurisdictions, such as Europe, Japan, Canada, South Korea, Mexico, and Brazil. These U.S. and foreign patents in this EP4 in-licensed patent family, if all appropriate maintenance fees paid, are expected to expire in 2024, not including any patent term adjustment, patent term extension, or SPC.
- We have one EP4 in-licensed patent family directed to use of certain EP4 antagonists for treating cancer. As of March 1, 2022, this EP4 in-licensed patent family contains U.S. patents, patents in foreign jurisdictions, such as Europe, Japan, Canada, South Korea, and Mexico, and pending applications in the U.S. and Europe. These U.S. and foreign patents and any further U.S. or foreign patents that may issue from this EP4 in-licensed patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2030, not including any patent term adjustment, patent term extension, or SPC.
- We have one EP4 in-licensed patent family directed to use of certain EP4 antagonists for treating NASH-associated liver cancer. As of March 1, 2022, this EP4 in-licensed patent family contains U.S. patents, patents in foreign jurisdictions such as Europe, Japan, Canada, and Mexico, and pending applications in foreign jurisdictions, such as India. These U.S. patents, if all appropriate maintenance fees are paid, are expected to expire in 2036, not including any patent term extension, or patent term extension. These foreign patents and any further foreign patents that may issue from this EP4 in-licensed patent family, if granted and all appropriate maintenance fees paid, are expected to expire in 2037, not including any patent term adjustment, patent term extension, or SPC.
- We have two additional EP4 in-licensed patent families directed to use of EP4 antagonists for (i) treating immune disease or allergy and (ii) treating cartilage disease. As of March 1, 2022, these EP4 in-licensed patent families contained three U.S. patents, patents in foreign jurisdictions such as Europe, Japan, Canada, South Korea, and Mexico, and pending applications in foreign jurisdictions such as Japan, Europe, India, and South Korea. These U.S. and foreign patents and any further foreign patents that may issue from these EP4 in-licensed patent families, if granted and all appropriate maintenance fees paid, are expected to expire in 2031 and 2034, respectively, not including any patent term adjustment, patent term extension, or SPC.

As of March 1, 2022, 2022, 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. These patent families are described in more detail below.

- EP4 jointly-owned patent family one is directed to use of EP4 antagonists in combination with an immuno-oncology agent for treating cancer. As of March 1, 2022, EP4 jointly-owned patent family one contains one U.S. patent, and pending applications in the U.S. and foreign jurisdictions, such as Europe, Japan, China, Australia, and Canada. The U.S. parent and any further any U.S. or foreign patents that may issue from EP4 jointly-owned patent family one, 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.

- EP4 jointly-owned patent family two is directed to methods of making certain EP4 antagonists and the compositions thereof. As of March 1, 2022, EP4 jointly-owned patent family two contains a pending U.S. application, and pending applications in foreign jurisdictions, such as Europe, Japan, China, Canada, and India. Any U.S. or foreign patents that issue from EP4 jointly-owned patent family two, 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.
- EP4 jointly-owned patent family three is directed to certain EP4 antagonist formulations, and the methods of use thereof. As of March 1, 2022, EP4 jointly-owned patent family three 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 EP4 jointly-owned 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.

As of March 1, 2022, we solely own two patent families directed to EP4 antagonist salts and crystal forms, and methods of using EP4 antagonists. 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 2039 to 2041, not including any patent term adjustment, patent term extension, or SPC. These patent families are described in more detail below.

- EP4 solely-owned patent family one is directed to crystal forms of certain EP4 antagonists. As of March 1, 2022, this EP4 solely-owned patent family contains pending U.S. and European applications. Any U.S. or foreign patents that issue from this EP4 solely-owned 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.
- EP4 solely-owned patent family two is directed to methods for selecting patients for EP4 antagonist treatment. As of March 1, 2022, this EP4 solely-owned patent family contains a pending PCT application. Any U.S. or foreign patents that issue from this EP4 solely-owned 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.

As of March 1, 2022, our current lead EP4 antagonist IK-007 salt and crystal forms thereof, compositions thereof, and uses of IK-007 or a salt or crystal form thereof are covered by select patents and/or patent applications described above. These select patents and patent applications include over seven (7) issued U.S. patents, multiple pending U.S. patent applications, a PCT international patent application, and issued patents and pending patent applications in foreign jurisdictions that, if granted and all appropriate maintenance fees paid, are expected to expire from 2024 to 2041, not including any patent term adjustment, patent term extension, or SPC, as described in more detail above.

AHR Antagonists Patent Families

As of March 1, 2022, 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 2041, not including any patent term adjustment, patent term extension, or SPC. The non-provisional 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 March 1, 2022, this AHR antagonists patent family contains two U.S. patents, patents in foreign jurisdictions such as Singapore, and pending applications in the U.S. and foreign jurisdictions, such as Europe, Japan, China, Australia, Canada, India, South Korea, and Mexico. 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 March 1, 2022, this AHR antagonists patent family contains one U.S. patent, and pending applications in the U.S. and foreign jurisdictions, such as Europe, Japan, China, Australia, Canada, India, South Korea, and Mexico. This U.S. patent and any further U.S. or 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 March 1, 2022, 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 March 1, 2022, AHR antagonists patent family four contains a pending U.S. application and a pending PCT application. 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 March 1, 2022, this AHR antagonists patent family contains a pending PCT application. 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 March 1, 2022, this AHR antagonists patent family contains a pending PCT application. 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 March 1, 2022, this AHR antagonists patent family contains a pending PCT application. 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 March 1, 2022, we and Oregon Health & Science University (OHSU) jointly own one patent family related to methods of using AHR antagonists, which contains a pending U.S. provisional application. 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 2042, not including any patent term adjustment, patent term extension, or SPC.

As of March 1, 2022, our solely owned patents and patent applications covering current lead AHR antagonist IK-175, salts and crystal forms thereof, compositions thereof, and methods of the use include two issued U.S. patents, multiple pending U.S. and PCT international patent applications, patents in foreign jurisdictions such as Singapore, and pending patent applications in Europe, Japan, Australia, Canada, China, and other foreign jurisdictions, all of which are described above where, if granted and all appropriate maintenance fees paid, are expected to expire from 2038 to 2041, not including any patent term adjustment, patent term extension, or SPC.

IK-412

We own and exclusively license patents and patent applications related to our IK-412 program. Our in-licensed patent portfolio related to this program includes three patent families that include patents and patent applications covering our IK-412 biologic drug product as a composition of matter and methods of using the same, alone or in combination with other therapeutic agents. The three exclusively licensed patent families are licensed from the University of Texas at Austin.

As of March 8, 2022, the first in-licensed patent family includes two issued patents in the U.S., which are projected to expire in 2034 and 2035, respectively, excluding any patent term extensions, if applicable. The first in-licensed

patent family also includes issued patents in Europe, Hong Kong, Australia, China, Israel, India, Japan, Korea, New Zealand, and South Africa, and such patents are expected to expire in 2034, excluding any patent term extensions, if applicable. Within this first in-licensed patent family, patent applications are pending in the U.S., Brazil, Canada, China, Europe, Japan, Korea, and South Africa.

As of March 8, 2022, the second in-licensed patent family includes two issued patents in the U.S., which are projected to expire in 2035, excluding any patent term extensions, if applicable. Within this second in-licensed patent family, patent applications are pending in the U.S., Canada, Europe, Israel, and Japan.

As of March 8, 2022, the third in-licensed patent family includes patent applications in the U.S., Argentina, Australia, Brazil, Canada, Chile, China, Colombia, Eurasian Patent Organization, Hong Kong, Europe, Israel, India, Japan, Korea, Mexico, New Zealand, Singapore, Thailand, Taiwan, and South Africa. Patents that issue from these applications are projected to expire in 2039, excluding any patent term adjustments or extensions, if applicable.

As of March 8, 2022, we also solely own patent applications related to our IK-412 program. The company-owned patent portfolio related to this program consists of one patent family that currently includes one U.S. patent application and one PCT international patent application covering our IK-412 biologic drug product as a composition of matter and methods of using the same, alone or in combination with other therapeutic agents. Patents issuing from the company-owned patent family are projected to expire in 2040, excluding any patent term adjustments or extensions, if applicable.

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 filed for and obtained Notices of Allowance for trademark protection with the U.S. Patent and Trademark Office for the IKENA and IKENA ONCOLOGY word marks for goods and services.

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 undergoing preclinical testing, 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 and biologics. We, along with our vendors, contract research organizations, or CROs, clinical investigators and contract manufacturing organizations, or 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 biologics 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, or FD&C Act, and biologics under the FD&C Act and the Public Health Service Act, or PHSA, as amended, their implementing regulations. Both drugs and biologics 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 revocation of approved applications, warning or untitled letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

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

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice, or GLP, requirements;

- completion of the manufacture, under current Good Manufacturing Practices, or 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 investigational new drug application, or 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, or 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, or GCP, requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- preparation and submission to the FDA of an NDA or BLA;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to file the application for review;
- satisfactory completion of one or more FDA pre-approval or pre-license 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 or biological 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 or BLA; and
- FDA review and approval of the NDA or BLA, 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 and biologics

Before testing any drug or biologic 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 or BLA.

In August 2018, the FDA released a draft guidance entitled "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 or BLA 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 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 and biologics

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 or BLA 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. A BLA is a request for approval to market a new biologic for one or more specified indications and must contain proof of the biologic's safety, purity and potency 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, or the safety, purity and potency of the investigational biologic, to the satisfaction of the FDA. FDA must approve an NDA or BLA before a drug or biologic may be marketed in the United States.

The FDA reviews all submitted NDAs and BLAs 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 or BLA 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 or BLA. The FDA reviews an NDA or BLA 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, or PDUFA, the FDA targets ten months, from the filing date, in which to complete its initial review of a new molecular entity NDA or BLA and respond to the applicant, and six months from the filing date of a new molecular entity NDA or BLA for priority review. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs or BLAs, and the review process is often extended by FDA requests for additional information or clarification.

Further, under PDUFA, as amended, each NDA or BLA 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 or BLAs 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, or 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 or biologic 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 or BLA, 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 or BLA, 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 or BLA 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 or BLA, 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 or biologic 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 or BLA. 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 and biologics

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

A new drug or biologic 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 or biologic 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 or biologic, alone or in combination with one or more other drugs or biologics, 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 or BLA 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 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 studies to verify and describe the product's clinical benefit. The FDA may 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, or PREA, as amended, certain NDAs and BLAs and certain NDA and BLA 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, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies 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 or biologic for an indication for which orphan designation has been granted, except that PREA will apply to an original NDA or BLA for a new active ingredient that is orphan-designated if the drug or biologic 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 and biologics

Drugs and biologics 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 where products are obtain reimbursement under federal health care programs. Promotional materials for approved drugs and biologics must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the drug or biologic, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or BLA or NDA or BLA 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 or BLA. 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 and biologics 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 revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs; or mandated modification of promotional materials and labeling and issuance of corrective information.

Regulation of companion diagnostics

Companion diagnostics identify patients who are most likely to benefit from a particular therapeutic product; identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness. Companion diagnostics are regulated as medical devices by the FDA. In the United States, the FD&C Act, and its implementing regulations, and other federal and

state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption or FDA exercise of enforcement discretion applies, diagnostic tests generally require marketing clearance or approval from the FDA prior to commercialization. The two primary types of FDA marketing authorization applicable to a medical device are clearance of a premarket notification, or 510(k), and approval of a premarket approval application, or PMA.

To obtain 510(k) clearance for a medical device, or for certain modifications to devices that have received 510(k) clearance, a manufacturer must submit a premarket notification demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or to a pre-amendment device that was in commercial distribution before May 28, 1976, or 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, or 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.

On July 31, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance document, for novel therapeutic products that depend on the use of a diagnostic test and where the diagnostic device could be essential for the safe and effective use of the corresponding therapeutic product, the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic, although the FDA recognizes that there may be cases when contemporaneous development may not be possible. However, in cases where a drug cannot be used safely or effectively without the companion diagnostic, the FDA's guidance indicates it will generally not approve the drug without the approval or clearance of the diagnostic device. The FDA also issued a draft guidance in July 2016 setting forth the principles for co-development of an in vitro companion diagnostic device with a therapeutic product. The draft guidance describes principles to guide the development and contemporaneous marketing authorization for the therapeutic product and its corresponding *in vitro* companion diagnostic.

Once cleared or approved, the companion diagnostic device must adhere to post-marketing requirements including the requirements of the FDA's QSR, 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, or CMS, other divisions of the U.S. Department of Health and Human Services, 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 prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus 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 Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act, or 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 False Claims Act, 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, or 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 federal Anti-Kickback Statute, a person or entity may be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it.

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, impose, among other things, specified requirements on covered entities and their respective business associates relating to the privacy and security of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates in some cases, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.
- The Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, imposed new annual reporting requirements for certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, for certain payments and "transfers of value" provided to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations extend to include transfers of value made in the previous year to certain non-physician providers such as physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives.
- 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 the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or 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," or 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. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. 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, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030 unless additional Congressional action is taken. The Coronavirus Aid, Relief and Economic Security Act, or CARES Act, as well as subsequent legislation, these reductions have been suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Then, a one percent (1%) payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the two percent (2%) payment reduction will resume on July 1, 2022. . In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three (3) to five (5) years.

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. At a federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. 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. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates would have been be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on December 29, 2021, CMS rescinded the Most Favored Nations rule. Additionally, on November 30, 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. 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.

On May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug sponsor to make its drug products available to eligible patients as a result of the Right to Try Act.

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 and biologics 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. 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, or 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 marketing authorization of a product candidate for a therapeutic indication under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use, or CHMP, is responsible for conducting an initial assessment of whether a product meets the required quality, safety and efficacy requirements, and whether a product has a positive benefit/risk ratio. Under the centralized procedure the maximum timeframe for the evaluation of a marketing authorization application, or MAA, by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of 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 make the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of 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 authorization 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 EEA Member States in a procedure whereby the countries concerned recognize the validity of the original, national marketing authorization.

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

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized marketing authorizations (under the Northern Ireland Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). All medicinal products with a current centralized marketing authorization were automatically converted to Great Britain marketing authorizations on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare Products Regulatory Agency (MHRA), the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required. The MHRA also has the power to have regard to marketing authorizations approved in EU Member States through decentralized or mutual recognition procedures with a view to more quickly granting 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 or biosimilar applicants from referencing the preclinical and clinical trial data contained in the dossier of the innovator product when applying for a generic or biosimilar marketing authorization in the 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 or biosimilar 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 marketing authorization based on a MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

The criteria for designating an “orphan medicinal product” in the EEA are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, in the EEA a medicinal product may be designated as orphan if it meets the following criteria (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; and (2) either (a) such condition affects no more than five in 10,000 persons in the EEA when the application is made, or (b) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EEA to justify the investment needed for its development; and (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 significant benefit to those affected by the condition. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. During this ten-year orphan market exclusivity period, no marketing authorization application shall be accepted, and no marketing authorization shall be granted for a similar medicinal product for the same indication, although similar, is safer, more effective or otherwise clinically superior than the authorized product; (ii) the marketing authorization holder of the authorized product consents to a second orphan medicinal product application; or (iii) the marketing authorization holder of the authorized product cannot supply enough orphan medicinal product. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. 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. 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, or 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, or 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 Supplementary Protection Certificate or 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, or IVDR, which will become applicable on 26 May 2022 and will repeal Directive 98/79/EC on in vitro diagnostic medical devices. Devices that comply with the requirements of the IVDR will be 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 new 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 in to 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 new Clinical Trials Regulation offer sponsors the possibility to choose between the requirements of the previous Clinical Trials Directive and the Clinical Trials Regulation if the request for authorization of a clinical trial is submitted in the year after the new Clinical Trials Regulation became applicable. If the sponsor chooses to submit under the Clinical Trials Directive, the clinical trial continues to be governed by the Directive until three years after the new Clinical Trials Regulation became applicable. The new 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, or 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 European Economic Area, or EEA, which consists of the EU Member States, plus Norway, Liechtenstein and Iceland.

Government regulation of data collection outside of the United States

Internationally, numerous jurisdictions have their own data security and privacy legal framework with which we will be required to comply if we conduct clinical trials in those jurisdictions or otherwise conduct jurisdictions in those jurisdictions. In the event we conduct clinical trials in the European Union or otherwise collect personal data from data subjects in the European Union, we will be subject to additional privacy restrictions. The collection and use of personal health data in the EEA is governed by the General Data Protection Regulation, or the GDPR, which became effective on May 25, 2018. The GDPR applies to the processing of personal data by any company established in the EEA and to companies established outside the EEA to the extent they process personal data in connection with the offering of goods or services to data subjects in the EEA or the monitoring of the behavior of data subjects in the EEA. The GDPR enhances data protection obligations for data controllers of personal data, including stringent requirements relating to the consent of data subjects, expanded disclosures about how personal data is used, enhanced requirements for securing personal data, requirements to conduct privacy impact assessments for "high risk" processing, limitations on retention of personal data, mandatory data breach notification and "privacy by design" requirements, and creates direct obligations on service providers acting as processors. The GDPR also imposes strict rules on the transfer of personal data outside of the EEA to countries that do not ensure an adequate level of protection, like the United States. Failure to comply with the requirements of the GDPR and the related national data protection laws of the European Union Member States and Norway, Iceland and Liechtenstein, which may deviate slightly from the GDPR, may result in fines of up to 4% of a company's global revenue for the preceding financial year, or €20,000,000, whichever is greater. Moreover, the GDPR grants data subjects the right to claim material and non-material damages resulting from infringement of the GDPR. Given the breadth and depth of changes in data protection obligations, maintaining compliance with the GDPR will require significant time, resources and expense, and we may be required to put in place additional controls and processes ensuring compliance with the new data protection rules. There continues to be a level of uncertainty as to the exact interpretation of the new requirements on any future trials and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the new law.

In addition, further to the UK's exit from the EU on January 31, 2020, the GDPR ceased to apply in the UK at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law, referred to as the UK GDPR. The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Although the UK is regarded as a third country under the EU's GDPR, the European Commission ("EC") has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

To enable the transfer of personal data outside of the EEA or the UK, adequate safeguards must be implemented in compliance with European and UK data protection laws. On June 4, 2021, the EC issued new forms of standard contractual clauses for data transfers from controllers or processors in the EU/EEA (or otherwise subject to the GDPR) to controllers or processors established outside the EU/EEA (and not subject to the GDPR). The new standard contractual clauses replace the standard contractual clauses that were adopted previously under the EU Data Protection Directive. The UK is not subject to the EC's new standard contractual clauses but has published a draft version of a UK-specific transfer mechanism, which, once finalized, will enable transfers from the UK. We will be required to implement these new safeguards when conducting restricted data transfers under the EU and UK GDPR and doing so will require significant effort and cost.

Data protection authority activity differs across the EU, with certain authorities applying their own agenda which shows there is uncertainty in the manner in which data protection authorities will seek to enforce compliance with GDPR. For example, it is not clear if the authorities will conduct random audits of companies doing business in the EU, or if the authorities will wait for complaints to be filed by individuals who claim their rights have been violated. Enforcement uncertainty and the costs associated with ensuring GDPR compliance are onerous and may adversely affect our business, financial condition, results of operations and prospects.

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

On June 23, 2016, the electorate in the UK voted in favor of leaving the EU, commonly referred to as Brexit, and the UK formally left the EU on January 31, 2020. There was a transition period during which EU pharmaceutical laws continued to apply to the UK, which expired on December 31, 2020. However, the EU and the UK have concluded a trade and cooperation agreement, or 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 foresee 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 will continue to apply in Northern Ireland). The regulatory regime in Great Britain therefore broadly aligns with current EU regulations, however it is likely that these regimes will diverge in 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.

Human Capital

As of February 28, 2022, we had 67 full-time employees, of which 34 have M.D. or Ph.D. degrees. Within our workforce, 46 employees are engaged in research and development and 21 are engaged in business development, finance, legal, and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements. 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 Securities Exchange Act of 1934, as amended, or the Exchange Act, are available through the "Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the 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. Our targeted oncology programs are still in preclinical development. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on 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 $34.1 million and $44.3 million for the years ended December 31, 2021 and 2020, respectively. We had an accumulated deficit of $145.5 million as of December 31, 2021. 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, including as a result of the COVID-19 pandemic; and
- future accounting pronouncements or changes in our accounting policies.

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

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 preclinical studies for our targeted oncology and TME programs;
- timely file and the acceptance of our investigational new drug applications, or IND, for our programs in order to commence our planned clinical trials or 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;
- implement measures to help minimize the risk of the COVID-19 pandemic to our employees as well as patients and subjects enrolled in our clinical trials; 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 currently advancing multiple targeted oncology programs through preclinical development toward identification of potential therapeutic candidates and subsequent planned IND filings. Additionally, we are conducting Phase 1 clinical trials of three of our candidates, IK-930, IK-007 and IK-175. Consequently, we expect our expenses to significantly increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate and complete clinical trials of, and seek regulatory approval for, our product candidates. 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 have begun to and expect to 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 March 30, 2021, we completed our initial public offering of our common stock, or IPO, and expect that the net proceeds from the IPO, together with our existing cash and cash equivalents will be sufficient to fund our operations through mid-2024. 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 product discovery, preclinical and clinical development, laboratory testing and clinical trials for our product candidates;
- the potential additional expenses attributable to adjusting our development plans (including any supply related matters) to the COVID-19 pandemic;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and 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 our existing collaboration agreements or any additional 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 more recently due to the COVID-19 pandemic 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 risk 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.

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

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

Public health crises such as pandemics or similar outbreaks could adversely impact our business. Since late 2019, a novel strain of a virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes COVID-19 has spread to most countries across the world, including all 50 states within the U.S., including Boston, Massachusetts, where our primary office and laboratory space is located. The coronavirus pandemic continues to evolve, with new variants of the SARS-CoV-2 virus identified, and has led to the implementation of various responses, including government-imposed quarantines, travel restrictions, mask and vaccine mandates and other public health safety measures. The extent to which COVID-19 impacts our operations or those of our third party partners, including our preclinical studies or clinical trial operations, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the outbreak, new information that will emerge concerning the variants of the coronavirus and the actions to contain the coronavirus or treat its impact, among others. The continued spread of COVID-19 globally and the continued identification of new variants of the SARS-CoV-2 virus could adversely impact our preclinical or clinical trial operations in the U.S., including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography. For example, similar to other biopharmaceutical companies, we may experience delays in initiating IND-enabling studies, protocol deviations, enrolling our clinical trials, or dosing of patients in our clinical trials as well as in activating new trial sites. COVID-19 may also affect employees of third-party CROs located in affected geographies that we rely upon to carry out our clinical trials. In addition, as a result of medical complications associated with microsatellite stable colorectal cancer, or MSS CRC, the patient populations that our most advanced and other product candidates target may be particularly susceptible to COVID-19, which may make it more difficult for us to identify patients able to enroll in our current and future clinical trials and may impact the ability of enrolled patients to complete any such trials. Any negative impact COVID-19 has to patient enrollment or treatment or the execution of our product candidates could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, and have a material adverse effect on our financial results.

As previously disclosed in 2021, the IK-412 program 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. Considering these delays and the timeline of the BMS partnership, we have made the strategic decision to pause IK-412 development activities for the remainder of the BMS contract term once the ongoing committed CMC work has been completed.

We will continue to monitor the impact of COVID-19 related supply chain issues relating to the rest of our business. Additionally, timely enrollment in planned clinical trials is dependent upon clinical trial sites the rest of which could be adversely affected by global health matters, such as pandemics. We are currently and plan to conduct clinical trials for our product candidates in geographies which are currently being affected by the ongoing COVID-19 pandemic. Some factors from the COVID-19 pandemic that have delayed and may continue to delay, or have otherwise adversely affected enrollment in the clinical trials of our product candidates, as well as our business generally, include:

- the potential diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our prospective clinical trials;
- limitations on travel that could interrupt key trial and business activities, such as clinical trial site initiations and monitoring, domestic and international travel by employees, contractors or patients to clinical trial sites, including any government-imposed travel restrictions or quarantines that will impact the ability or willingness of patients, employees or contractors to travel to our clinical trial sites or secure visas or entry permissions, a loss of face-to-face meetings and other interactions with potential partners, any of which could delay or adversely impact the conduct or progress of our prospective clinical trials;

- the potential negative affect on the operations of our third-party manufacturers;
- interruption in global shipping affecting the transport of clinical trial materials, such as patient samples, investigational drug product and conditioning drugs and other supplies used in our prospective clinical trials;
- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments;
- operations, staffing shortages, travel limitations or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees and other important agencies and contractors;
- diversion of components required in our manufacturing process for certain of our programs due to COVID-19 related vaccination and treatment efforts;
- changes in federal, state and local regulations as part of a response to the ongoing COVID-19 pandemic, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether; and
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines.

We have taken precautionary measures intended to help minimize the risk of the virus to our employees, including requiring certain of our employees to work remotely, suspending all non-essential travel worldwide for our employees and discouraging employee attendance at industry events and in-person work-related meetings, as indicated and necessary, and which could negatively affect our business. We cannot presently predict the scope and severity of the planned and potential shutdowns or disruptions of businesses and government agencies, such as the Securities and Exchange Commission, or the SEC, or FDA.

These and other factors arising from COVID-19 and any variants could worsen in countries that are already afflicted with COVID-19 or could continue to spread to additional countries. Any of these factors, 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 the economy of the United States and other economies, which could impact our ability to raise the necessary capital needed to develop and commercialize our programs and product candidates.

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

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. IK-930 is in clinical development, however, our other targeted oncology programs are still in preclinical development and may never advance to clinical development. We are currently advancing multiple targeted oncology programs through preclinical development toward potential therapeutic candidates and subsequent IND, including targeting ERK5 as part of our RAS pathway research. We may not be able to file such IND or INDs for any of our other product candidates on the timelines we expect, if at all. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that require us to suspend or terminate clinical trials. Commencing each of these clinical trials is subject to finalizing 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 a new drug application, or NDA, or a biologics license application, or BLA, to the FDA, a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, or other marketing applications to regulatory authorities in other

jurisdictions, for each product candidate and, consequently, the regulatory approval of each product candidate. We currently have two product candidates from our TME program in clinical development. We are conducting a Phase 1 trial with IK-175 in patients with bladder cancer with activated aryl hydrocarbon receptor, or AHR, and a Phase 1b trial with IK-007 in combination with pembrolizumab for the treatment of patients with advanced or progressive microsatellite stable colorectal cancer, or MSS CRC. We initiated a Phase 1 clinical trial of IK-930 in the first quarter of 2022. However, we do not know whether these or any of our future clinical trials will begin on time or be completed on schedule, if at all.

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 preclinical studies and future and ongoing clinical trials may not be successful. Currently, we have three programs in early clinical development and our other targeted oncology programs are in preclinical 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 preclinical studies and 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 our preclinical studies or clinical trials, including as a result of delays in obtaining, or failure to obtain, the FDA's clearance to initiate clinical trials under future INDs. Additionally, we cannot be certain that preclinical studies or clinical trials for our product candidates will not 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, preclinical 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 preclinical studies or clinical trials or to delay or terminate a clinical trial;
- regulators or institutional review boards, or 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 clinical research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- preclinical studies or clinical trials of our product candidates may fail to show safety or efficacy or otherwise produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials, or we may decide to abandon product research or development programs;
- preclinical studies or clinical trials of our product candidates may not produce differentiated or clinically significant results across tumor types or indications;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls, be unable to provide us with sufficient product supply to conduct or complete preclinical studies or clinical trials, fail to meet their contractual obligations to us in a timely manner, or at all, 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;
- clinical trials of our product candidates may be delayed due to complications associated with the COVID-19 and related variants;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;

- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our product candidates; and
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate

We could encounter delays if a clinical trial is suspended or terminated by us, including upon the recommendation of the Safety Monitoring Committee, or SMC, 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, including those caused by the COVID-19 pandemic and related variance, also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates and may significantly harm our business, operating results, financial condition and prospects.

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

We may not be able to initiate 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. In particular, because we are focused on patients with specific genetic mutations for the development of our targeted oncology programs, and on patients with specific biomarkers for the development of our TME 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. Furthermore, our ability to enroll patients may be significantly delayed by the ongoing COVID-19 and variant pandemic, and we cannot accurately predict the extent and scope of such delays at this point.

In addition to the competitive trial environment, the eligibility criteria of our 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, including the impacts of the COVID-19 pandemic, that may limit patients, principal investigators or staff or clinical site availability.

We anticipate that certain of our current product candidates and future product candidates 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 checkpoint inhibitor immunotherapies or other standards of care like chemotherapies, targeted therapies or radiotherapy. For example, we plan to explore IK-930 in combination with epidermal growth factor receptor, or EGFR inhibition, and in combination with a mitogen-activated protein kinase, or MEK inhibitor, in certain indications and we are currently evaluating IK-175 in combination with nivolumab, which is marketed by Bristol-Myers Squibb Company, or BMS. We are also currently conducting a Phase 1b clinical trial of IK-007 in combination with pembrolizumab, which is marketed by Merck. Our ability to develop and ultimately commercialize our current programs and product candidates and any future programs or product candidates used in combination with EGFR inhibitors, nivolumab, pembrolizumab, or other 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 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 BMS, Merck or any future collaborator or supplier cannot continue to supply their products on commercially reasonable terms, we would need to identify alternatives for accessing checkpoint inhibitor immunotherapies. 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 and TME programs or our product candidates may not necessarily be predictive of the results from later preclinical studies and clinical trials. Similarly, even if we are able to complete our planned preclinical studies and clinical trials of our product candidates according to our current development timeline, the results from such preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

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

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

We plan to nominate multiple development candidates stemming from our RAS-pathway and additional Hippo pathway research programs. We plan to progress candidates to IND, however, we may not be able to file such INDs or INDs for future product candidates for our targeted oncology or other programs on the timelines we expect. For example, due to supply chain issues in manufacturing of IK-412 due to the ongoing COVID-19 pandemic, we previously delayed the IND submission to the FDA and have now paused development. 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 to a new IND. Any failure to file INDs on the timelines we expect or to obtain

regulatory approvals for our planned clinical trials may prevent us from initiating or completing our clinical trials or commercializing our product candidates on a timely basis, if at all.

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

Before obtaining regulatory approvals for the commercial sale of any products, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. Clinical testing is expensive and can take many years to complete, and outcomes are inherently uncertain. Failure can occur at any time during the clinical trial process. Because our 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. For example, we conducted a second open-label single arm Phase 1b clinical trial of IK-007 in combination with pembrolizumab in patients with advanced or metastatic post anti-PD- 1/L1 treatment in non-small-cell lung carcinoma, or NSCLC, but based on the combined data generated in the interim period for efficacy and safety, we decided not to further explore this combination in NSCLC and terminated this clinical trial in December 2020. 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. While we have initiated a clinical trial of IK-930, our lead targeted oncology program, in the first quarter of 2022, and are in early stages of clinical trials for IK-175 and IK-007, our TME programs, 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 pathway 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 may in the future conduct clinical trials for our product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We may in the future choose to conduct additional clinical trials outside the United States, including in Europe, Australia or 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. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving regulatory approval or clearance for commercialization in the applicable jurisdiction.

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

Research programs to pursue the development of our existing and planned product candidates for additional indications and to identify new product candidates and disease targets require substantial technical, financial and human resources whether or not they are ultimately successful. Our research programs may initially show promise in identifying potential indications and/or product candidates, 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 and/or product candidates;
- 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 or to develop suitable potential product candidates through internal research programs, 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 or to develop suitable product candidates through internal research programs, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential product candidates or 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, BLA, premarket approval application, or PMA, or equivalent application types, may cause delays in the approval or rejection of an application. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may 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, BLA 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.

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 lead targeted oncology product candidate, IK-930, is an oral small molecule inhibitor of the transcriptional enhanced associate domain, or TEAD, transcription factor in 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. We are developing a small molecule inhibitor program against ERK5 in the RAS signaling pathway. KRAS mutations in the RAS signaling pathway occur in approximately 26% of all cancers. Additionally, we are currently evaluating the safety and tolerability of IK-175 in a Phase 1 dose expansion clinical trial in patients with solid tumors and intend to pursue development in patients with bladder cancer with activated AHR. AHR amplifications have been described in approximately 5% to 22% of bladder cancer patients. We are also developing IK-007 in a Phase 1b clinical trial in patients with MSS CRC. Patients with MSS CRC represent approximately 80% of all colorectal cancer patients, and these patients generally do not respond to approved checkpoint inhibitors. 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 cancer immunotherapies 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;
- the commercial success of the checkpoint blockade drugs 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 risk evaluation and mitigation strategy, or 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 the Centers for Medicare & Medicaid Services, or 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, or ASP, 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 on third parties to conduct our Phase 1 clinical trials of IK-930 and IK-175 and Phase 1b clinical trial of IK-007 and expect to rely on third parties to conduct clinical trials for our other targeted oncology and other TME programs, 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, including our Phase 1 clinical trials of IK-930 and IK-175 and Phase 1b clinical trial of IK-007, as well as any other current product candidates or future product candidates that may emerge from our targeted oncology and TME programs.

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 Good Clinical Practices, or GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any products in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we, our principal investigators or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our future clinical trials will comply with GCPs. In addition, our clinical trials must be conducted with product candidates produced under current Good Manufacturing Practice, or 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 Phase 1 clinical trials of IK-930 and IK-175 and Phase 1b clinical trial of IK-007 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. For example, in September 2021, an investigator-initiated trial (IIT) of IK-007 in combination with the chemotherapy agent eribulin was launched in metastatic IBC led by Naoto Ueno, M.D., of the University of Texas MD Anderson Cancer Center.

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, including the existing collaboration that we have with Celgene Corporation (now part of BMS), 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. For example, although BMS provided us with an $80.5 million upfront payment and a $14.5 million equity investment upon entering into that certain master collaboration agreement with Celgene Corporation (now BMS), we might need additional funding to advance product candidates prior to the completion of a Phase 1b clinical trial, the clinical milestone when BMS must decide whether to exercise its exclusive license rights to IK-175 or IK-412. On November 20, 2019, BMS acquired Celgene Corporation and BMS may take a different approach to our collaboration or determine not to continue 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 cGMPs 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 contract manufacturing organization, or 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 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, or 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 such as the COVID-19 pandemic 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.

The manufacture of biologics is complex and our third-party manufacturers may encounter difficulties in production. If any of our third-party manufacturers encounter such difficulties, our ability to provide supply of product candidates for clinical trials or products for patients, if approved, could be delayed or prevented.

Manufacturing biologics, especially in large quantities, is often complex and may require the use of innovative technologies to handle living cells. Each lot of an approved biologic must undergo thorough testing for identity, strength, quality, purity and potency. Manufacturing biologics requires facilities specifically designed for and validated for this purpose, and sophisticated quality assurance and quality control procedures are necessary. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business.

In addition, there are risks associated with large scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with good manufacturing practices, lot consistency and timely availability of raw materials. Even if we obtain regulatory approval for any of our current product candidates or any future product candidates, there is no assurance that our manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential commercial launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

We 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 U.S. Patent and Trademark Office (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, IK-007, IK-175, and IK-412, or future product candidates, such as against our RAS signaling target, ERK5, 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, 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. Recent patent reform legislation in the U.S. and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a "first inventor to file" system. The first-inventor-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, 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 EU, the European Commission, upon the recommendation of the EMA's Committee for Orphan Medicinal Products, grants orphan designation to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the EU and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized for marketing in the EU (or the product would be a significant benefit to those affected by the condition). Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the product in the EU would generate sufficient return to justify the necessary investment in developing the product. In the EU, orphan drug 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 mesothelioma. 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 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.

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 for any of our product candidates, may not lead to a faster development, regulatory review or approval process, and each designation does not increase the likelihood that any of our product candidates will receive regulatory approval in the United States.

We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. 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 may seek fast track designation for some of our product candidates. 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. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

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, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA requires that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence. 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.

If approved, our investigational products regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biologic products that are biosimilar to or interchangeable with an FDA-licensed reference biologic product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of the other company's product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that any of our product candidates approved as a biologic product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our investigational medicines to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once licensed, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If competitors are able to obtain regulatory approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

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

The FDA, the EMA and regulatory authorities in other countries have each expressed interest in further regulating biotechnology products. Agencies at both the federal and state level in the United States, as well as 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. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new 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. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, since March 2020, when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestic and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission-critical work, prioritize other higher-tiered inspectional needs (e.g., for-cause inspections), and carry out surveillance inspections using risk-based approaches for evaluating public health. On July 16, 2020, the FDA noted that it was continuing to expedite oncology product development with its staff

teleworking full-time. As of May 26, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluate to be adequate, the FDA has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Additionally, regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption 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. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

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

Payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs and those methods are not always specifically adapted for new technologies such as gene therapy and therapies addressing rare diseases such as those we are developing. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars; 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; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government's comparative effectiveness research.

Since enactment of the ACA, there have been numerous judicial, administrative, executive, and legislative 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. Prior to the Supreme Court's decision, President Biden issued an Executive Order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The Executive Order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administrations or other efforts by third parties, if any, to challenge repeal or replace the ACA, will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted:

- On August 2, 2011, the U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect

through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the temporary suspension, a 1% payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022. In January 2013, the American Taxpayer Relief Act of 2012 became law, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding 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.

- On January 2, 2013, the U.S. American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.
- On April 13, 2017, CMS published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.
- On May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.
- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.
- On December 20, 2019, former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repealed the Cadillac tax, the health insurance provider tax, and the medical device excise tax. It is impossible to determine whether similar taxes could be instated in the future.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

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 local state Medicaid programs could have a significant impact on our business.

We expect that the ACA, as well as other 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. This could 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 the ACA 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 U.S. 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, once we begin commercializing our product candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain regulatory approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our product candidates for which we obtain regulatory approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order, arrangement, or recommendation of, any good, facility, item or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment of up to ten years, and exclusion from government healthcare programs. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers, on the other. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA, or federal civil money penalties. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;
- the federal civil and criminal false claims and civil monetary penalties laws, including the FCA, imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act. 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;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme or artifice to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses,

representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) , and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services information related to certain payments and other transfers of value to physicians, nurse practitioners, certified nurse anesthetists, physician assistants, clinical nurse specialists, and certified nurse midwives as well as teaching hospitals. Manufacturers are also required to disclose ownership and investment interests held by physicians and their immediate family members;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations including the Final Omnibus Rule published in January 2013, which impose obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the creation, maintenance, receipt, use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, 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. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- federal price reporting laws, which would require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above, among others, some of which may be broader in scope and may apply regardless of the payor. Many U.S. states have adopted laws similar to the federal AKS and FCA, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives. State and foreign laws, including for example the European Union General Data Protection Regulation, or GDPR, which became effective May 2018 also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties. Finally, there are state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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 a 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 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 can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the 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 cGMPs and GCPs 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 voluntary or mandatory product recalls;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- clinical trial holds;
- fines, warning letters or other regulatory enforcement action;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

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

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

In the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials, we may be subject to additional privacy restrictions. Most notably, in the European Union and the UK, the collection, use, storage, disclosure, transfer, or other processing of personal data, including personal health data, is subject to the GDPR and the UK GDPR, respectively, as well as applicable national data protection requirements. The GDPR and UK GDPR are wide-ranging in scope and impose numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. Compliance with the GDPR and UK 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, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

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

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

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or 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 sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees, including temporary loss due to illness, could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also

experience competition for the hiring of scientific 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 may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential or proprietary information, including personal data, damage our reputation, and subject us to significant financial and legal exposure.

We rely on information technology systems that we or our third-party providers operate to process, transmit and store electronic information in our day-to-day operations. In connection with our product discovery efforts, we may collect and use a variety of personal data, such as names, mailing addresses, email addresses, phone numbers and clinical trial information. A successful cyberattack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under state (e.g., state breach notification laws), federal (e.g., HIPAA, as amended by HITECH), and international law (e.g., the GDPR) and may cause a material adverse impact to our reputation, affect our ability to conduct new studies and potentially disrupt our business.

We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. If we or our third-party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third-party providers could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in the losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenue or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business. By way of example, the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020, creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal data. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. In March 2020, the California State Attorney General has proposed varying versions of companion draft regulations which are not yet finalized. Despite the delay in adopting regulations, the California State Attorney General became empowered to commence enforcement actions against violators beginning July 1, 2020. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability. Some observers have noted

that the CCPA could mark 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.

Further, a new California privacy law, the California Privacy Rights Act, or CPRA, was passed by California voters on November 3, 2020. The CPRA will create additional obligations with respect to processing and storing personal information that are scheduled to take effect on January 1, 2023 (with certain provisions having retroactive effect to January 1, 2022). Additionally, some observers have noted that the CCPA and CPRA could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business. Already, in the United States, we have witnessed significant developments at the state level. For example, on March 2, 2021, Virginia enacted the Consumer Data Protection Act (the "CDPA") and, on July 8, 2021, Colorado's governor signed the Colorado Privacy Act ("CPA"), into law. The CDPA and the CPA will both become effective January 1, 2023. While the CDPA and CPA incorporate many similar concepts of the CCPA and CPRA, 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.

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

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.

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 Therapeutics or Amplify Medicines, 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 February 28, 2022, we had 67 full-time employees. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly as we function as a public company and in the areas of product development, regulatory affairs and, if any of our product candidates receives regulatory approval, sales, 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 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. 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 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage point change (by value) in the ownership of its equity by certain stockholders 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, 2021, we had federal and state net operating loss carryforwards of approximately $18.2 million and $5.3 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.

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, or 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. 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 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 Risks

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

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners 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 current COVID-19 pandemic has caused significant volatility and uncertainty in U.S. and international markets. See “Risks Related to the Development of our Targeted Oncology and Other Programs and Product Candidates—The COVID-19 pandemic, or a similar pandemic, epidemic, or outbreak of an infectious disease may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates.” In addition, the current military conflict between Russia and Ukraine could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions that may be initiated by nations including the U.S., 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 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. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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 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 Jumpstart Our Business Startups Act of 2012, or 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 $1.07 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 Securities and Exchange Commission, 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.

Although we are still evaluating the JOBS Act, we currently intend to take advantage of some, but not all, of the available exemptions available to us so long as we qualify as an "emerging growth company." 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 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 incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, and particularly after we are no longer an "emerging growth company" 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 additional, 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 Securities Exchange Act of 1934, or 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 2. PROPERTIES

Our corporate headquarters is located in Boston, Massachusetts. We previously leased approximately 13,170 square feet of office and laboratory space, or the Boston Lease. The term of our Boston Lease expired on February 28, 2021. We entered into a lease to move our corporate headquarters and occupy approximately 20,752 square feet of office, laboratory and animal care space, or the New Lease. The New Lease commenced on February 19, 2021, and the term is expected to expire on May 31, 2026.

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 10, 2022, there were approximately 20 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.

Use of Proceeds from Initial Public Offering

On March 30, 2021, we closed our initial public offering, or IPO, in which we issued and sold 8,984,375 shares of common stock, including the exercise in full by the underwriters of their option to purchase up to 1,171,875 additional shares of common stock, at a public offering price of $16.00 per share. All of the shares of common stock issued and sold in our initial public offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (Registration No. 333-253919), which was declared effective by the SEC on March 25, 2021. The offering terminated upon the closing of the IPO. Jefferies LLC, Cowen and Company, LLC, Credit Suisse Securities (USA) LLC and William Blair & Company, L.L.C. acted as joint book-running managers for the offering. The aggregate gross proceeds to us from our initial public offering, inclusive of the over-allotment exercise, were $143.8 million.

The aggregate net proceeds to us from the IPO, inclusive of the over-allotment exercise, was approximately $131.3 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10% or more of any class of our equity securities or to any other affiliates.

There has been no material change in the planned use of IPO proceeds from that described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act of 1933, as amended, on March 26, 2021.

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 entitled "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 targeted oncology company developing precision medicines tailored to biomarker-defined patient groups with specific unmet needs. With our robust biomarker and translational approach we aim to develop targeted treatments and define patient populations who are most likely to respond to treatment. Our current programs are across the Hippo pathway, RAS pathway, and key immune signals in the tumor-microenvironment (TME), with approaches to targeting both cancer driving targets and mechanisms of resistance to targeted therapies. Our focus on patient-driven development is platform and process agnostic, allowing us to research both known and novel targets, with a shared guiding principle of aiming to address the unmet need of a biomarker-defined patient population. Since we commenced operations in 2016, we have advanced multiple product candidates into clinical development. In addition, we have a robust pipeline of discovery-stage targeted oncology programs.

Our lead targeted oncology product candidate, IK-930, is an oral small molecule inhibitor of the transcriptional enhanced associate domain, or TEAD, transcription factor in 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 clinical trial, we are focusing on indications that provide the potential for rapid clinical development to achieve proof-of-concept, such as NF2 deficient mesothelioma and solid tumors with YAP1 or TAZ gene fusions, including epithelioid hemangioendothelioma, or EHE, in which 100% of patients have Hippo pathway alterations. We also plan to assess IK-930 in combination with other targeted therapies across several indications, including EGFR mutated non-small cell lung cancer (NSCLC) and KRAS mutated cancers. In October 2021, our Investigational New Drug Application, or IND, for IK-930 was accepted by the U.S. Food and Drug Administration, or FDA, and we subsequently initiated a first in human Phase 1 clinical trial of IK-930 in patients with advanced solid tumors with a high frequency of Hippo pathway alternations. The first patient was dosed in January 2022, and we are currently recruiting patients in this ongoing Phase 1 clinical trial.

Our discovery efforts are focused on additional targeted oncology programs, following our philosophy of designing treatments for patients' populations identified through the genetic make-up of their tumors. Our pre-clinical pipeline is growing to include additional Hippo pathway and RAS pathway-targeting programs, including our program against the novel target extracellular signal related kinase 5 (ERK5). We are generating mechanistic and translational data to accompany our approaches and identify underserved RAS-mutated cancer patient populations.

Our clinical-stage programs also include product candidates in development to target immune signaling in the tumor microenvironment (TME). These programs are all built on the same foundation of biomarker-driven clinical trial design and patient enrichment, aiming to develop therapies that can precisely be used for specific cancer patients. IK-175 is an oral inhibitor of aryl hydrocarbon receptor, or AHR, which we are evaluating in a Phase 1a/1b clinical trial in solid tumors and in urothelial carcinomas as monotherapy and in combination with nivolumab. We expect to report initial clinical data from this trial in the second half of 2022. Additionally, we plan to initiate a second Phase 1b trial with IK-175 in head and neck squamous cell carcinoma (HNSCC) in the second half of 2022. The IK-175

program is partnered with Bristol-Myers Squibb Company. The partnership also includes our IK-412 program, which experienced manufacturing delays previously disclosed in 2021. Considering these delays and the timeline of the partnership, we made the strategic decision to pause IK-412 development activities for the remainder of the Bristol Myers Squibb collaboration agreement term once the ongoing committed Chemistry, Manufacturing, and Controls (CMC) work has been completed.

Also within TME immune signaling, IK-007, which inhibits the prostaglandin E receptor 4, or EP4, in the COX2 pathway, is being evaluated in a Phase 1b clinical trial in combination with pembrolizumab for the treatment of patients with MSS CRC. We recently completed enrollment in this trial and expect to report data at a medical conference in the second half of 2022.

We were incorporated as a Delaware corporation on March 2, 2016, and our headquarters is located in Boston, Massachusetts. Since our inception, we devoted 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. On March 30, 2021, we completed an IPO, in which we issued and sold 8,984,375 shares of our common stock at a public offering price of $16.00 per share, including 1,171,875 shares of common stock sold pursuant to the underwriters' exercise of their option to purchase additional shares of common stock, for aggregate gross proceeds of $143.8 million. We raised approximately $131.3 million after deducting underwriting discounts and commissions and offering expenses payable by us.

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

We have incurred significant net losses in every year since our inception and expect to continue to incur significant expenses and increasing net losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year and could be substantial. Our ability to generate product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our current or future product candidates. Our net losses were $34.1 million and $44.3 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $145.5 million. We anticipate that our expenses will increase significantly 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;
- establish agreements with contract research organizations, or CROs, and contract manufacturing organizations, or 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, including personnel to support our research and development programs, any future commercialization efforts and our transition to operating 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.

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

As of December 31, 2021, we had cash and cash equivalents of $232.2 million. We believe the existing cash and cash equivalents on hand as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements through mid 2024. To date, we have primarily financed our operations through proceeds from private placements of preferred stock, payments from a collaboration agreement, related party revenue and completion of the IPO. 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 that would otherwise be expected. There can be no assurance that we will be able to obtain additional funding on acceptable terms, if at all.

Impact of COVID-19 Pandemic

We continue to monitor the impacts of the COVID-19 pandemic and its potential impact on our business including in our clinical trials, manufacturing capabilities, and ability to access necessary resources. We have taken important steps to ensure the safety of our employees and their families and to reduce the spread of COVID-19. We have established a work-from-home policy for all employees while ensuring essential staffing levels in our operations remain in place, including maintaining key personnel in our laboratories. For employees working in our facilities, we have implemented stringent safety measures designed to comply with applicable federal, state and local guidelines instituted in response to the COVID-19 pandemic. We have also maintained efficient communication with our partners and clinical sites as the COVID-19 situation has evolved. We have taken these precautionary steps while maintaining business continuity so that we can continue to progress our programs.

In the first half of 2021, we were notified that a key component required in the manufacturing of IK-412, our novel kynurenine-degrading enzyme, is similarly essential to the manufacturing of COVID-19 vaccines and therapies. As such, the availability of the component has been delayed as resources have been allocated towards vaccine production in the near-term. With this information and manufacturing lead times, the IND submission for IK-412 was delayed. Considering these delays and the timeline of the BMS collaboration partnership we have made the strategic decision to pause IK-412 development for the remainder of the BMS contract term once the ongoing committed CMC work has been completed. We will continue to monitor the impact of COVID-19 related supply chain issues relating to our business.

See “Risk Factors” for a discussion of the potential adverse impact of the COVID-19 pandemic on our business, financial condition, and results of operations.

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 BMS Collaboration Agreement.

Collaboration Agreement and Stock Purchase Agreement with BMS

In January 2019, we entered into the BMS Collaboration Agreement with Celgene Corporation (which was acquired by BMS in November 2019), pursuant to which BMS may 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 aryl hydrocarbon receptor, or AHR, excluding AHR agonists for inverse agonists, which we are developing as IK-412 and IK-175, respectively. On a program-by-program basis, through the completion of a Phase 1b clinical trial for each of IK-175 and IK-412, BMS has the exclusive option to exclusively license to develop, commercialize and manufacture the relevant product candidate worldwide. Concurrent with execution of the BMS Collaboration Agreement, we entered into a stock purchase agreement with Celgene Corporation (now BMS) in November 2019, or the Stock Purchase Agreement, pursuant to which we issued Celgene Corporation 14,545,450 shares of Series A-1 preferred stock.

BMS paid a total of $95.0 million in aggregate upfront consideration related to the BMS Collaboration Agreement and Stock Purchase Agreement. We are 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. If we do not complete a Phase 1b clinical trial by the end of the research term, we may elect to provide a data package to BMS upon which BMS may exercise the foregoing option for an additional $0.25 million fee. Upon the delivery of each license, we become eligible to receive up to $265.0 million in regulatory milestones and $185.0 million in commercial milestones as well as a tiered royalties at rates ranging from the high single to low teen digits percentages based on worldwide annual net sales by BMS, subject to specified gross sale reductions.

In the first half of 2021, we were notified that 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 has been delayed as resources have been allocated towards vaccine production in the near-term. With this information and manufacturing lead times, the IND submission for IK-412 was delayed. Considering these delays and the timeline of the BMS collaboration partnership we have made the strategic decision to pause IK-412 development for the remainder of the BMS contract term once the ongoing committed CMC work has been completed.

Operating Expenses

Our operating expenses since inception have consisted 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 and clinical 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 the ongoing COVID-19 pandemic 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 and headcount needed 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 to 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 Securities and Exchange Commission, or SEC, requirements, director and officer insurance costs, and investor and public relations costs.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations:

	Year Ended December 31,			
(In thousands, except percentages)	**2021**	**2020**	**Dollar Change**	**Percent Change**
Revenue:				
Research and development revenue under collaboration agreement	$ 30,985	$ 9,194	$ 21,791	237 %
Operating expenses:				
Research and development	47,108	44,847	2,261	5 %
General and administrative	18,015	8,866	9,149	103 %
Total operating expenses	65,123	53,713	11,410	21 %
Loss from operations	(34,138)	(44,519)	10,381	-23 %
Other income	23	263	(240)	(91)%
Net loss	$ (34,115)	$ (44,256)	$ 10,141	-23 %

Revenue

The research and development revenue under collaboration agreement of $31.0 million and $9.2 million for the years ended December 31, 2021 and 2020, respectively, is related to an increase of revenue from the BMS Collaboration Agreement for the IK-175 and IK-412 programs which was executed in January 2019.

The revenue increase on IK-412 is due to a decrease in our estimate of the total services to be performed on the IK-412 program during the remainder of the BMS Collaboration Agreement term. In December 2021, the Company re-assessed the IK-412 program, which experienced manufacturing delays previously disclosed in 2021. Considering

these delays and the timeline of the BMS partnership, the Company made the strategic decision to pause IK-412 development activities for the remainder of the BMS research term once the ongoing committed CMC work has been completed. As a result of the decision to pause, the Company recorded a change in estimate during the three months ended December 31, 2021 and recognized $16.5 million of research and development revenue.

The revenue also increased on IK-175 is due to continued progression of the program during the year ended December 31, 2021.

Research and Development Expenses

The following table summarizes our research and development expenses:

	Year Ended December 31,			
(In thousands, except percentages)	**2021**	**2020**	**Dollar Change**	**Percent Change**
Direct research and development expenses by program:				
IK-930	$ 8,351	$ 4,911	$ 3,440	70 %
IK-175	5,844	7,161	(1,317)	(18)%
IK-412	2,984	3,699	(715)	(19)%
IK-007	2,632	4,943	(2,311)	(47)%
Other discovery stage programs	11,708	3,556	8,152	229 %
Acquisition of in-process research and development assets	—	11,140	(11,140)	(100)%
Research and development personnel and overhead expenses	15,589	9,437	6,152	65 %
Total research and development expenses	$ 47,108	$ 44,847	$ 2,261	5 %

Research and development expense was $47.1 million for the year ended December 31, 2021, compared to $44.8 million for the year ended December 31, 2020. Included within research and development personnel and overhead expenses is stock-based compensation expense of $2.4 million and $0.8 million for the years ended December 31, 2021 and 2020, respectively. The increase in research and development expense of $2.3 million was primarily attributable to the IND-enabling studies, manufacturing development costs and clinical trial start-up costs for IK-930, and research activities for other discovery stage programs. In addition, research and development expenses related to personnel and overhead expenses increased due to an increase in headcount. This increase in research and development expenses was partially offset by the write-off for the acquisition of in process research and development assets of $11.1 million as a result of the acquisition of Amplify in October 2020, and a net decrease in development activities for IK-175, IK-412, and IK-007.

General and Administrative Expenses

General and administrative expense was $18.0 million for the year ended December 31, 2021, as compared to $8.9 million for the year ended December 31, 2020. General and administrative expense includes $2.7 million and $1.0 million of stock-based compensation expense for the years ended December 31, 2021 and 2020, respectively. The increase was primarily attributable to an increase in compensation expense due to an increase in headcount, as well as general increases in legal and consulting expenses.

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 BMS Collaboration Agreement, from cash obtained from acquisitions, and most recently, from common stock in our IPO. In March 2021, we completed our IPO in which we received net proceeds, inclusive of the exercise by the underwriters of their option of purchase additional

shares, of approximately $131.3 million, after deducting underwriting discounts and commissions and estimated offering expenses.

As of December 31, 2021, we had cash and cash equivalents of $232.2 million. Based upon our current operating plans, we expect that our existing cash and cash equivalents balances will enable us to meet our planned operating expenses and capital expenditure requirements into mid-2024.

Cash Flows

The following table summarizes our sources and uses of cash for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
(In thousands)	**2021**	**2020**
Net cash provided (used in) by operating activities	$ (60,252)	$ (37,826)
Net cash (used in) provided by investing activities	(1,760)	2,922
Net cash provided by financing activities	131,738	116,184
Net increase in cash and cash equivalents	$ 69,726	$ 81,280

Operating Activities

During the year ended December 31, 2021, we used $60.3 million of cash in operating activities. The net cash used in operating activities primarily consisted of our net loss of $34.1 million which includes non-cash charges of $5.2 million of stock-based compensation expense, and the realization of $31.0 million of previously deferred revenue recognized as a result of the BMS Collaboration Agreement.

During the year ended December 31, 2020, we used $37.8 million of cash in operating activities. We utilized cash to fund our net loss of $44.3 million, which includes non-cash expense recognized related to the acquisition of in process research and development assets of $11.1 million as a result of the acquisition of Amplify in October 2020 and the realization of $9.2 million of previously deferred revenue recognized as a result of the BMS Collaboration Agreement. There was $3.1 million of other non-cash expenses and a net use of $1.4 million to fund changes in prepaid expenses and other current assets, accounts payable, accrued expenses and other current liabilities and lease liability.

Investing Activities

The net cash used in investing activities for the year ended December 31, 2021 was primarily attributable to an increase in property and equipment purchased in connection with the commencement of our new lease. The net cash provided by investing activities for the year ended December 31, 2020 was related to the $3.7 million of cash received in our acquisition of Amplify. These proceeds were offset by the use of $0.8 million of cash to acquire plant and equipment.

Financing Activities

During the year ended December 31, 2021, the net cash provided by financing activities primarily reflects cash proceeds received in connection with the IPO. During the year ended December 31, 2020, the net cash provided by financing activities is related to net proceeds from the issuance of preferred stock of $116.2 million.

Funding Requirements

We expect our expenses to increase 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. 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 and cash equivalents as of December 31, 2021, will enable us to fund our operating expenses and capital expenditure requirements through mid-2024. 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 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.

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 lease payments under this commitment to total $1.8 million in 2022 and increase annually through the lease expiration in 2026. Our total future minimum lease payments for each of the next five years and in total are included in Note 14.

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 do not contain any minimum purchase commitments and are cancelable by us upon prior notice of 30 days. Payments due upon cancelation 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 and our license agreement with AskAt, Inc. 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 accounting principles generally accepted in the United States, or 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.

In December 2021, the Company re-assessed the IK-412 program, which experienced manufacturing delays previously disclosed in 2021. Considering these delays and the timeline of the BMS partnership, the Company made the strategic decision to pause IK-412 development activities for the remainder of the BMS research term once the ongoing committed CMC work has been completed.

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 employee 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.

Determination of Fair Value of Common Stock contractual obligation

Historically, the fair value of the shares of common stock underlying the stock options was determined by the Company's board of directors. Because there was no public market for the Company's common stock prior to the Company's IPO, the board of directors determined fair value of common stock at the time of grant of the option by considering a number of objective and subjective factors including independent third-party valuations of the Company's common stock, sales of convertible preferred stock to unrelated third parties, operating and financial performance, the lack of liquidity of capital stock and the general and industry specific economic outlook, among other factors. Following the Company's IPO, the fair value of the Company's common stock has been determined based on the closing price of the Company's common stock on the Nasdaq Global Select Market.

Emerging Growth Company

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or an EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for new or revised accounting standards during the period in which we remain an emerging growth company; however, we may adopt certain new or revised accounting standards early.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than $1.07 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 initial public offering.

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 exposed to market risk related to changes in interest rates. As of December 31, 2021 and 2020, our cash equivalents consisted of interest-bearing checking accounts and money market funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term nature and the low risk profile of our interest-bearing accounts, an immediate 10% change in interest rates would not have a material effect on the fair market value of our cash and cash equivalents or on our financial position or results of operations.

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates.

Inflation generally affects us by increasing our costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2021 and 2020.

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, 2021.

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 Securities Exchange Act of 1934, as amended, or 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 (both roles assumed by our Chief Executive Officer), has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021, 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

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the company's registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

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 period covered by this Annual Report on Form 10-K that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

Principal Financial Officer

As previously disclosed, Douglas Carlson resigned from his position as our Chief Operating Officer and Executive Vice President of Finance and principal financial and accounting officer in February 2022. Additionally, as previously disclosed, in February 2022, our board of directors appointed Francisco Olivera, our Vice President of Finance and Administration, as our principal accounting officer. On March 15, 2022, our board of directors appointed Mark Manfredi, Ph.D., our current President and Chief Executive Officer and principal executive officer, as our principal financial officer.

2022 Annual Meeting

As of the date of this Annual Report on Form 10-K, we intend to hold our 2022 Annual Meeting of Stockholders (the "2022 Annual Meeting") on or about June 9, 2022 at 8:30 a.m. local time virtually. We are providing the following disclosure in accordance with our Amended and Restated Bylaws (the "Bylaws") and Rule 14a-8 under the Securities Exchange Act of 1934, as amended (the "Exchange Act").

Bylaws Advance Notice Deadline for Submission of Stockholder Proposals and Director Nominations

Pursuant to our Bylaws, since the 2022 Annual Meeting is the first Annual Meeting following our initial public offering, for notice of stockholder proposals submitted outside of Rule 14a-8 of the Exchange Act and director nominations to be timely, they must be so received not later than the later of (A) the close of business on the 90th day before the 2022 Annual Meeting; or (B) the close of business on the 10th day following the day on which public announcement of the date of the 2022 Annual Meeting is first made by us. As this is our first public disclosure of the date of the 2022 Annual Meeting, to be considered timely, stockholder proposals submitted outside of Rule 14a-8 of the Exchange Act and director nominations, in each case intended to be brought before the 2022 Annual Meeting, must be received no later than the close of business on Monday, March 28, 2022. Any such stockholder proposals and director nominations must be directed to our Corporate Secretary at our corporate offices at Ikena Oncology, Inc., 645 Summer Street, Suite 101, Boston, MA 02210. Such stockholder proposals and director nominations must also comply with the advance notice provisions contained in Sections 2 of our Bylaws.

Rule 14a-8 Deadline for the Submission of Stockholder Proposals

As we did not hold an annual meeting in 2021, pursuant to Rule 14a-8(e)(2) under the Exchange Act, the deadline for the receipt of any stockholder proposals submitted pursuant to Rule 14a-8 of the Exchange Act for inclusion in the Company's proxy materials for the 2022 Annual Meeting would be a reasonable time before the company begins to print and send its proxy materials. We have determined that Monday, March 28, 2022 is a reasonable time before we expect to begin to print and distribute its proxy materials for the 2022 Annual Meeting, and that any stockholder proposals must be received on or before the close of business on that day. Such proposals must be directed to our Corporate Secretary at our corporate offices at Ikena Oncology, Inc., 645 Summer Street, Suite 101, Boston, MA 02210. Such proposals must also comply with Rule 14a-8 of the Exchange Act.

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, 2021.

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, 2021.

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, 2021.

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, 2021.

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, 2021.

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).
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).
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
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	Non-Employee Director Compensation Policy (Incorporated by reference to Exhibit 10.4 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).

10.5	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).
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.
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (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.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

IKENA ONCOLOGY, INC.

Date: March 17, 2022

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 and Principal Financial Officer*	March 17, 2022
/s/ Francisco Oliveira **Francisco Oliveira**	Vice President of Finance and Administration *Principal Accounting Officer*	March 17, 2022
/s/ Ron Renaud **Ron Renaud**	Director	March 17, 2022
/s/ David Bonita **David Bonita, M.D.**	Director	March 17, 2022
/s/ Iain D. Dukes **Iain D. Dukes, D.Phil.**	Director	March 17, 2022
/s/ Jean-François Formela **Jean-François Formela, M.D.**	Director	March 17, 2022
/s/ Maria Koehler **Maria Koehler, M.D., Ph.D.**	Director	March 17, 2022
/s/ Otello Stampacchia **Otello Stampacchia, Ph.D.**	Director	March 17, 2022
/s/ Richard Wooster **Richard Wooster, M.D.**	Director	March 17, 2022

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board 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, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2021, 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, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, 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 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 17, 2022

IKENA ONCOLOGY, INC.

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

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 232,217	$ 162,491
Prepaid expenses and other current assets	4,299	3,478
Total current assets	236,516	165,969
Property and equipment, net	2,439	1,393
Right-of-use asset	6,538	170
Deposits and Other assets	2,386	872
Total assets	$ 247,879	$ 168,404
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 2,384	$ 2,122
Accrued expenses and other current liabilities	5,854	5,402
Operating lease liability	1,851	186
Deferred revenue	17,100	20,622
Total current liabilities	27,189	28,332
Long-term portion of lease liabilities	5,135	—
Deferred revenue, net of current portion	7,678	35,141
Total liabilities	40,002	63,473
Commitments and contingencies (Note 15)		
Redeemable convertible preferred stock (Series A, A-1, A-2, and B), $0.001 par value. No shares authorized, issued and outstanding as of December 31, 2021; 169,396,576 shares, authorized, issued and outstanding as of December 31, 2020 (liquidation preference $0 as of December 31, 2021 and $202.2 million as of December 31, 2020)	—	205,979
Stockholders' deficit:		
Preferred Stock, $0.001 par value - 10,000,000 shares authorized as of December 31, 2021 and no shares authorized as of December 31, 2020; No shares issued and outstanding as of December 31, 2021 or December 31, 2020	—	—
Common stock, $0.001 par value, 150,000,000 shares authorized, 35,975,034 issued and outstanding as of December 31, 2021; 230,000,000 shares authorized, 3,096,903 issued and outstanding as of December 31, 2020	36	3
Additional paid-in capital	353,295	10,288
Accumulated other comprehensive (loss) income	—	—
Accumulated deficit	(145,454)	(111,339)
Total stockholders' equity (deficit)	207,877	(101,048)
Total liabilities, redeemable convertible preferred stock and stockholders' equity	$ 247,879	$ 168,404

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,	
	2021	**2020**
Revenue		
Research and development revenue under collaboration agreement	$ 30,985	$ 9,194
Operating expenses		
Research and development	47,108	44,847
General and administrative	18,015	8,866
Total operating expenses	65,123	53,713
Loss from operations	(34,138)	(44,519)
Other income, net	23	263
Net loss and comprehensive loss	$ (34,115)	$ (44,256)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.22)	$ (16.00)
Weighted-average shares of common stock outstanding, basic and diluted	27,983,359	2,765,494

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

IKENA ONCOLOGY, INC.

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

	Redeemable Convertible Preferred Stock		Common Stock				
	Shares	Amount	Shares	Amount	Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance as of December 31, 2019	75,727,268	$ 78,867	2,651,333	$ 3	$ 5,617	$ (67,083)	$ (61,463)
Issuance of preferred stock and common stock in connection with the acquisition of Amplify Medicines, Inc.	7,863,094	10,924	426,159	—	2,804	—	2,804
Issuance of preferred stock in connection with private placement	85,806,214	116,188	—	—	—	—	—
Exercise of stock options	—	—	19,411	—	70	—	70
Stock-based compensation	—	—	—	—	1,797	—	1,797
Net loss and comprehensive loss	—	—	—	—	—	(44,256)	(44,256)
Balance as of December 31, 2020	169,396,576	$ 205,979	3,096,903	$ 3	$ 10,288	$ (111,339)	$ (101,048)
Initial public offering, net of issuance costs of $2.4 million	—	—	8,984,375	9	131,293	—	131,302
Conversion of convertible preferred stock into common stock	(169,396,576)	(205,979)	23,678,568	24	205,955	—	205,979
Exercise of stock options	—	—	215,188	—	582	—	582
Stock-based compensation	—	—	—	—	5,177	—	5,177
Net loss and comprehensive loss	—	—	—	—	—	(34,115)	(34,115)
Balance as of December 31, 2021	—	$ —	35,975,034	$ 36	$ 353,295	$ (145,454)	$ 207,877

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,	
	2021	2020
Cash flows from operating activities		
Net loss	$ (34,115)	$ (44,256)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities		
Depreciation expense	544	300
Stock-based compensation	5,177	1,797
Non-cash research and development expense for in-process research and development acquired in acquisition	—	11,140
Non-cash lease expense	1,174	964
Changes in operating assets and liabilities		
Prepaid expenses and other current assets	(1,452)	297
Accounts payable	361	519
Accrued expenses and other current liabilities	1,298	1,585
Lease liability	(740)	(978)
Deferred revenue	(30,985)	(9,194)
Deposits and other assets	(1,514)	—
Net cash flows used in operating activities	(60,252)	(37,826)
Cash flows from investing activities		
Cash obtained in asset acquisition	—	3,688
Payments to acquire property and equipment	(1,760)	(766)
Net cash flows (used in) provided by investing activities	(1,760)	2,922
Cash flows from financing activities		
Proceeds from issuance of preferred stock, net of offering costs	(146)	116,171
Proceeds from initial public offering, net of offering costs	131,302	(57)
Proceeds from exercise of stock options	582	70
Net cash flows provided by financing activities	131,738	116,184
Net increase in cash and cash equivalents	69,726	81,280
Cash, cash equivalents and restricted cash, beginning of year	163,363	82,083
Cash, cash equivalents and restricted cash, end of year	$ 233,089	$ 163,363
Cash and cash equivalents	$ 232,217	$ 162,491
Restricted cash included in other assets	872	872
Cash, cash equivalents and restricted cash, end of year	$ 233,089	$ 163,363
Supplemental disclosure of non-cash activities		
Assets obtained in asset acquisition	$ —	$ 34
Liabilities assumed in asset acquisition	$ —	$ 970
Fair value of equity instruments issued in connection with asset acquisition	$ —	$ 13,892
Purchases of property and equipment in accounts payable and accrued expenses	$ 13	$ 367
Deferred transaction costs in accounts payable and accrued liabilities	$ —	$ 591
Right-of-use assets recognized upon adoption of ASC 842	$ —	$ 956
Right-of-use assets and lease liabilities recognized upon lease inception	$ 7,541	$ —

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

1. NATURE OF BUSINESS AND ORGANIZATION

We are a targeted oncology company developing precision medicines tailored to biomarker-defined patient groups with specific unmet needs. With our robust biomarker and translational approach we aim to develop targeted treatments and define patient populations who are most likely to respond to treatment. Our current programs are across the Hippo pathway, RAS pathway, and key immune signals in the tumor-microenvironment (TME), with approaches to targeting both cancer-driving targets and mechanisms of resistance to targeted therapies. Our focus on patient-driven development is platform and process agnostic, allowing us to research both known and novel targets , with a shared guiding principle of aiming to address the unmet need of a biomarker-defined patient population. Since we commenced operations in 2016, we have advanced multiple product candidates into clinical development. In addition, we have a robust pipeline of discovery-stage targeted oncology programs.

On March 22, 2021, ahead of the initial public offering, the Company effected a one-for-7.154 reverse stock split of the Company's common stock. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital. Shares of common stock underlying outstanding stock options and other equity instruments were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased in accordance with the terms of the appropriate securities agreements. Shares of common stock reserved for issuance upon the conversion of the Company's convertible preferred stock were proportionately reduced and the respective conversion prices were proportionately increased.

On March 25, 2021, the Company's registration statement on Form S-1 relating to its initial public offering of its common stock was declared effective by the Securities and Exchange Commission ("SEC"). In the IPO, which closed on March 30, 2021, 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.

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"). 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. Significant 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, and intangible assets acquired in an asset acquisition and, for periods prior to the completion of the IPO, stock based compensation expense.

Liquidity: Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities as of December 31, 2021, will be sufficient to enable us to advance our long-term strategic goals for at least the next 12 months from the filing of this annual report on Form 10-K.

In addition, the Company expects that it will seek additional funding through public or private financings, debt financing, collaboration agreements or government grants. The inability to obtain funding, as and when needed, could have a negative impact on the Company's financial condition and ability to pursue its business strategies, which may include amending, delaying, limiting, reducing, or terminating planned activities related to its product candidates.

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 and cash equivalents. As of December 31, 2021, substantially all of the Company's cash and cash equivalents were deposited at two highly rated financial institutions. The Company maintains balances in operating accounts above federally insured limits. The Company has not experienced any losses on such accounts and does not believe it is exposed to any significant credit risk on cash and cash equivalents.

The Company is dependent on third-party manufacturers and clinical research organizations 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. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

Fair Value of Financial Instruments: The amounts reported for cash equivalents, accounts payable and accrued expenses approximate fair value because of their short maturities. Fair value is estimated based on a three-tier fair value hierarchy to prioritize the inputs used in our 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, therefore requiring us to develop our own assumptions. 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. Our cash equivalents are generally composed of commercial paper, corporate notes, U.S. government-sponsored enterprise securities, U.S. treasury securities and money market funds.

Restricted Cash: As of December 31, 2021 and 2020, the Company maintained restricted cash totaling approximately $0.9 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, 2021, the Company had one collaborative agreement with Bristol-Myers Squibb (“BMS”), which the Company entered into in January 2019 (the “BMS Collaboration Agreement”). For a complete discussion of the accounting related to BMS Collaboration Agreement, see Note 7, Collaboration Agreement and Stock Purchase Agreement with BMS.

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. Research and development expense for the year ended December 31, 2020, also includes the write-off of acquired in-process research and development (“IPR&D”) assets with no alternative future use.

Asset Acquisitions: The Company measures and recognizes asset acquisitions that are not deemed to be business combinations based on the cost to acquire the assets, which includes transaction costs, and the consideration is allocated to the items acquired based on a relative fair value methodology. Goodwill is not recognized in asset acquisitions. In an asset acquisition, the cost allocated to acquire IPR&D with no alternative future use is charged to research and development expense at the acquisition date.

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 our 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, which was adopted on January 1, 2020, 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.

Deferred Issuance Costs: Deferred issuance costs consist of legal, accounting and other third-party fees that are directly associated with in-process equity financings and remain deferred issuance costs until such financings are consummated. After consummation of the equity financing, these costs are recorded as a reduction to the proceeds generated as a result of the offering.

On March 30, 2021, the Company completed its IPO. Accordingly, the Company recognized offering costs of approximately $2.4 million as a reduction from the gross proceeds associated with the closing of the IPO through additional paid-in capital in the accompanying consolidated balance sheet. The Company incurred deferred offering costs of $0.5 million as of December 31, 2020 which were included in prepaid expenses and other current assets.

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 our consolidated financial statements and disclosures.

3. FAIR VALUE MEASUREMENTS

The following table presents information about the Company's financial assets measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values (in thousands):

	As of December 31, 2021	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 232,017	$ 232,017	—	—
Total Cash Equivalents	$ 232,017	$ 232,017	$ —	$ —

	As of December 31, 2020	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 162,290	$ 162,290	—	—
Total Cash Equivalents	$ 162,290	$ 162,290	$ —	$ —

For the years ended December 31, 2021 and 2020, there were no transfers between Level 1 and Level 2 financial assets.

4. PREPAID EXPENSES AND OTHER CURRENT ASSETS

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

	As of December 31,	
	2021	2020
Clinical, manufacturing and scientific development	$ 2,820	$ 1,917
Prepaid Insurance	850	23
Other	629	1,538
Total	$ 4,299	$ 3,478

5. PROPERTY AND EQUITPMENT, NET

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

	As of December 31,	
	2021	2020
Property and equipment:		
Lab equipment	$ 1,776	$ 1,071
Leasehold improvements	923	939
Electronic equipment and software	430	71
Furniture and fixtures	384	—
Total property and equipment	3,513	2,081
Less: accumulated depreciation	(1,074)	(688)
Property and equipment, net	$ 2,439	$ 1,393

Depreciation expense for the years ended December 31, 2021 and 2020 was $0.5 million and $0.3 million, respectively. There were no impairments for the years ended December 31, 2021 and 2020.

6. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

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

	As of December 31,	
	2021	2020
Employee compensation	$ 2,809	$ 1,816
Research and development expenses	2,489	2,251
Professional fees	530	955
Other current liabilities	26	380
Total	$ 5,854	$ 5,402

7. COLLABORATION AGREEMENT AND STOCK PURCHASE AGREEMENT WITH BMS

In January 2019, the Company entered into the BMS Collaboration Agreement with Celgene Corporation, which was acquired by BMS 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 BMS Collaboration Agreement, the Company entered into a stock purchase agreement with BMS, 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 BMS 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"). BMS has the option to receive a global-development, manufacture and commercialization license for the product candidate, which expires in January 2024. Subsequent to the delivery of a license, BMS is responsible for the worldwide development, manufacturing and commercialization of these product candidates.

BMS paid the Company a total of $95.0 million in aggregate upfront consideration related to the BMS Collaboration Agreement and Stock Purchase Agreement. The Company is 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. If the Company does not complete a Phase 1b clinical trial by the end of the research term, the Company may provide a data package to BMS to support the decision to exercise the option for an additional $0.25 million. Upon the exercise of the delivery of each license, the Company becomes 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 BMS 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 BMS Collaboration Agreement was allocated to the equity arrangement.

The Company determined that the BMS 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 recognizing revenue related to each of its performance obligations as the research and development services are performed through January 2024. 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 BMS partnership, the Company made the strategic decision to pause IK-412 development activities for the remainder of the BMS research term once the ongoing CMC work has been completed. As a result of the decision to pause, the Company recorded a change in estimate during the three months ended December 31, 2021 and recognized $16.5 million of research and development revenue.

During the year ended December 31, 2021 and 2020, the Company recognized revenue of $31.0 million and $9.2 million, respectively, from the BMS Collaboration Agreement. The consolidated balance sheet as of December 31, 2021 includes deferred revenue of $24.8 million related this agreement, of which $17.1 million and $7.7 million were classified as current and non-current, respectively. This amount is expected to be recognized as performance obligations are satisfied through the completion of the research and development services for IK-175 and IK-412.

8. REDEEMABLE CONVERTIBLE PREFERRED STOCK

In connection with the closing of the Company’s IPO on March 30, 2021, all issued and outstanding Redeemable Convertible Preferred Stock of 169,396,576 were converted to 23,678,568 shares of the Company’s common stock and are no longer issued.

As of December 31, 2020, the authorized capital stock of the Company included 169,396,576 shares of redeemable convertible preferred stock.

As of December 31, 2020, redeemable convertible preferred stock consisted of the following:

	As of December 31, 2020			
	Shares Authorized	Shares Issued and Outstanding	Carrying Value	Aggregate Liquidation Preference
Series A	28,000,000	28,000,000	$ 27,832	$ 28,000
Series A-1	47,727,268	47,727,268	51,035	47,727
Series A-2	7,863,094	7,863,094	10,924	6,500
Series B	85,806,214	85,806,214	116,188	120,000
Total	169,396,576	169,396,576	$ 205,979	$ 202,227

The Preferred Stock had the following characteristics as of December 31, 2020:

(a) Voting

On any matter presented to the stockholders of the Company for their action or consideration at any meeting of stockholders of the Company (or by written consent of stockholders in lieu of meeting), each holder of outstanding shares of Preferred Stock shall be entitled to cast the number of votes equal to the number of whole shares of Common Stock into which the shares of Preferred Stock held by such holder are convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by the other provisions of the Company's Amended and Restated Certificate of Incorporation, holders of Preferred Stock shall vote together with the holders of Common Stock as a single class and have other special voting rights.

The holders of outstanding shares of Preferred Stock shall be entitled to elect three directors of the Company. The investors have agreed that two of the directors are to be named by one investor and the other director is to be named by a separate investor.

(b) Dividends

The holders of Preferred Stock are entitled to an 8% non-cumulative dividend. Dividends are payable only when, as and if declared by the Board. No dividends are payable to the common stockholders unless a dividend is also paid to Preferred Stockholders equal to at least the amount that would be received if the shares of Preferred Stock were converted into common stock.

Through December 31, 2020 and the completion of the IPO, no dividends have been declared or paid by the Company.

(c) Liquidation Preference

In the event of any voluntary or involuntary liquidation, dissolution, or winding up of the Company, or upon the event of certain other deemed liquidation events, holders of shares of Preferred Stock then outstanding shall be entitled to receive the greater of (i) an amount per share equal to the Preferred Stock original issue price, plus any dividends declared but unpaid thereon or (ii) the amount that would be received if the Preferred Stock was converted into common stock just prior to the liquidation event.

(d) Conversion

Each share of Preferred Stock shall be convertible into shares of common stock at the option of the stockholder, at any time, at a rate of one for one and are automatically converted upon a qualified initial public offering or upon written consent of at least 75% of the holders of the outstanding shares of Preferred Stock. The conversion ratio is initially set at one for one, but may be adjusted for certain issuances of additional shares of Common Stock, stock splits, stock combinations, certain dividends and distributions, and mergers and reorganizations.

The conversion ratio was changed to 7.154 for one upon the Company's filing of its amendment to its Amended and Restated Certificate of Incorporation on March 22, 2021.

9. COMMON STOCK

As of December 31, 2021 and 2020, the Company had 150,000,000 and 230,000,000 shares of common stock authorized, respectively, of which 35,975,034 and 3,096,903 were issued and outstanding as of December 31, 2021 and 2020, 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.

10. 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.

On March 19, 2021, the Company's board of directors approved, and on March 20, 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 initial public offering. However, the 2016 Plan will continue to govern outstanding equity awards granted thereunder. The 2021 Plan allows the Company to make equity-based and cash-based incentive awards to officers, employees, directors and consultants.

As of the effective date of the 2021 Plan, no further awards will be made under the 2016 Plan. Any options or awards outstanding under the 2016 Plan remain outstanding and effective and are governed by their existing terms. 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. No more than 3,263,664 shares of the Company's common stock may be granted subject to incentive stock options under the 2021 Plan. In addition, 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.

As of December 31, 2021, 2,250,479 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,	
	2021	2020
Research and development	$ 2,427	$ 790
General and administrative	2,750	1,007
Total share-based compensation expense	$ 5,177	$ 1,797

The weighted-average fair value of the stock options granted during the year ended December 31, 2021 and 2020 was $6.13 and $3.53 per share, respectively. As of December 31, 2021, the total unrecognized stock-based compensation balance for unvested options was $19.1 million which is expected to be recognized over 2.97 years.

The following table summarizes stock option activity under the Plan for the year ended December 31, 2021:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2020	2,650,396	$ 3.45	8.01	$ 5,463
Granted	3,435,687	9.73		
Exercised	(215,188)	2.70		
Cancelled or forfeited	(48,522)	5.21		
Outstanding as of December 31, 2021	5,822,373	$ 7.17	8.27	$ 33,275
Vested or expected to vest as of December 31, 2021	5,822,373	$ 7.17	8.27	$ 33,275
Options exercisable as of December 31, 2021	1,841,894	$ 3.35	6.71	$ 16,928

The intrinsic value of options exercised for the years ended December 31, 2021 and 2020 was $1.9 million and $30 thousand, respectively.

The fair value of each option award granted during the years ended December 31, 2021 and 2020 is estimated on the date of grant using the Black-Scholes option pricing model and the weighted average assumptions noted in the following table:

	Year Ended December 31,	
	2021	2020
Risk-free interest rate	0.68% to 1.33%	0.27% to 0.47%
Expected dividend yield	0%	0%
Expected option term (in years)	6.00 to 6.08	5.00 to 6.08
Expected stock price volatility range	68.58% to 73.30%	73.15% to 74.89%

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, 2021, no shares have been purchased by employees under the ESPP.

11. 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"). During the years ended December 31, 2021 and 2020, the Company did not make any employer contributions to the plan. 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, 2021 and 2020, were immaterial.

12. INCOME TAXES

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,	
	2021	2020
Tax effected at statutory rate	21.0%	21.0%
State taxes	7.4%	5.2%
Stock compensation	(0.7)%	(0.4)%
Non-deductible expenses	(0.5)%	—%
Acquired in-process R&D	—%	(5.1)%
Federal research and development credits	5.0%	3.2%
Change in valuation allowance	(32.2)%	(23.9)%
Total	—%	—%

The Company's total deferred tax assets are as follows (in thousands):

	As of December 31,	
	2021	2020
Deferred tax assets:		
Federal net operating loss carryforward	$ 18,233	$ 5,445
State net operating loss carryforward	5,269	1,593
R&D credit carryforwards	6,385	4,023
Capitalized start-up costs	242	264
Accruals and reserves	629	327
Deferred revenue	6,769	15,234
Stock options	1,026	318
Lease liability	1,908	—
Total deferred tax asset	40,461	27,204
Deferred tax liability:		
Fixed assets	(648)	(170)
Right of use asset	(1,786)	—
Total deferred tax liability	(2,434)	(170)
Valuation Allowance	(38,027)	(27,034)
Net deferred tax assets and liability	$ —	$ —

The Company has had no income tax expense due to operating losses incurred since inception. ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more-likely-than-not that some portion or all of the deferred tax assets will not be realized. The Company has evaluated the positive and negative evidence bearing upon 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 2021, the valuation allowance increased by $11.0 million primarily due to the increase in the Company's book loss reported in the period.

As of December 31, 2021, the Company had approximately $86.8 million and $83.4 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, 2021, the Company also has federal and state research and development tax credit carryforwards of approximately $5.0 million and $1.7 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.

The Company follows the provisions of ASC 740-10, Accounting for Uncertainty in Income Taxes, which specifies how tax benefits for uncertain tax positions are to be recognized, measured, and recorded in financial statements;

requires certain disclosures of uncertain tax matters; specifies how reserves for uncertain tax positions should be classified on the balance sheet; and provides transition and interim period guidance, among other provisions. As of December 31, 2021, and 2020, the Company has not recorded tax reserves associated with any unrecognized tax benefits. The Company's policy is to recognize interest and penalties accrued on any uncertain tax positions as a component of income tax expense, if any, in its statements of income. As of December 31, 2021, and 2020, the Company had no reserves for uncertain tax positions. For the years ended December 31, 2021 and 2020, no estimated interest or penalties were recognized on uncertain tax positions.

The Company has not conducted a study of its research and development credit carryforwards. This study may result in an adjustment to research and development credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheets or statements of operations if an adjustment were required.

The Company's Federal and Massachusetts income tax returns for the years ended December 31, 2018 to December 31, 2021 remain open and are subject to examination by the Internal Revenue Service and state taxing authorities.

13. 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 upon meeting certain development milestones 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 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.

14. LEASE OBLIGATION

In December 2018, the Company entered into an operating lease with Vertex Pharmaceuticals Inc. ("Vertex") to lease approximately 13,170 square feet of office, laboratory and vivarium space at 50 Northern Ave, Boston, Massachusetts, expiring in December 2020. In July 2020, the Company extended the term of the lease through February 2021.

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 lease provides a three-month free rent period, which commenced on the lease commencement date. The base rent at commencement is $145 thousand 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.

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,	
	2021	2020
Operating lease costs	$ 1,693	$ 1,011
Variable lease costs	479	706
Total lease costs	$ 2,172	$ 1,717

Our variable lease cost primarily related to operating expenses, parking, taxes and insurance associated with our operating leases.

Supplemental cash flow information relating to the Company’s leases were as follows (in thousands):

	December 31,	
	2021	2020
Cash paid for amounts included in the measurement of lease liabilities (operating cash flows)	$ 1,259	$ 1,025

The remaining lease terms and discount rates related to our leases were as follows:

	As of December 31,	
	2021	2020
Remaining lease term	4.4 years	0.2 years
Discount Rate	7.7%	8.0%

The future minimum lease payments for the Company’s operating lease as of December 31, 2021, were as follows (in thousands):

Fiscal Year	Operating Leases
2022	$ 1,774
2023	1,827
2024	1,882
2025	1,938
2026	817
Thereafter	—
Total minimum lease payments	8,238
Less amounts representing interest or imputed interest	1,251
Present value of lease liabilities	$ 6,987

15. 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, 2021 or royalties on future sales of specified products that have not yet occurred as of December 31, 2021.

16. RELATED PARTY TRANSACTIONS

The Company entered into several agreements with a director and an entity affiliated with a director:

1. As discussed in Note 11 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, 2021 and 2020 the Company recorded expenses in connection with University license fees and certain patent-related costs incurred on its behalf of $233 thousand and $182 thousand, respectively.
2. Certain entities affiliated with directors purchased shares in the IPO.

17. NET LOSS PER SHARE ATTRIBUTABLE TO COMMON STOCKHOLDERS

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock and potentially dilutive securities outstanding during the period determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share calculation, convertible preferred stock, restricted common stock, restricted stock units and stock options are considered to be potentially dilutive securities, but are excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive and therefore basic and diluted net loss per share were the same for all periods presented.

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,	
	2021	2020
Redeemable Convertible Preferred Stock	—	169,396,576
Options to Purchase Common Stock	5,822,373	2,650,396
Total	5,822,373	172,046,972

Exhibit 4.3

Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934, as amended

The following summary of the general terms and provisions of the registered capital stock Ikena Oncology, Inc. ("Ikena", "we", "our") does not purport to be complete and is subject to, and qualified in its entirety by, reference to our Fifth Amended and Restated Certificate of Incorporation, or certificate of incorporation, our Amended and Restated Bylaws, or bylaws, each of which is incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part, and applicable provisions of the Delaware General Corporation Law, or the DGCL. Our common stock, par value $0.001 per share is registered pursuant to Section 12(b) of the Securities and Exchange Act of 1934 and trades on The Nasdaq Global Market under the symbol IKNA. The summaries below do not purport to be complete statements of the relevant provisions of the certificate of incorporation, the bylaws or the DGCL.

General

Our authorized capital stock consists of 150,000,000 shares of common stock, par value $0.001 per share, or the common stock, including 8,000,000 shares of non-voting common stock, par value $0.001 per share, or the non-voting common stock, and 10,000,000 shares of undesignated preferred stock, par value $0.001 per share, or the preferred stock.

Common stock and non-voting common stock

The holders of our common stock and non-voting common stock have identical rights subject to two exceptions. First, except as otherwise expressly provided in our certificate of incorporation or as required by applicable law, on any matter that is submitted to a vote by our stockholders, holders of our common stock are entitled to one vote per share of common stock, and holders of our non-voting common stock are not entitled to any votes per share of non-voting common stock, including for the election of directors. Second, holders of our common stock have no conversion rights, while holders of our non-voting common stock shall have the right to convert each share of our non-voting common stock into one share of common stock at such holder's election, provided that as a result of such conversion, such holder, together with its affiliates and any members of a Schedule 13(d) group with such holder, would not beneficially own in excess of 9.99% of our common stock immediately prior to and following such conversion, unless otherwise expressly provided for in our certificate of incorporation. However, this ownership limitation may be increased or decreased to any other percentage designated by such holder of non-voting common stock upon 61 days' notice to us.

Holders of our common stock and non-voting common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock and non-voting common stock have no preemptive rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock and non-voting common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock.

Our common stock is listed on The Nasdaq Global Market under the trading symbol "IKNA."

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 250 Royall Street, Canton, Massachusetts 02021, and its telephone number is (800) 962-4284.

Preferred stock

Our board of directors has the authority, from time to time, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action.

Registration rights

Certain holders of our shares of our common stock are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of a fourth investors' rights agreement, or the investors' rights agreement, between us and certain holders of our common stock and holders preferred stock. The investors' rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us. All selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand registration rights

Holders of certain of our shares of common stock are entitled to demand registration rights. Under the terms of the investors' rights agreement, we will be required, upon the written request of a majority of holders of the registrable securities then outstanding that would result in an aggregate offering price of at least $10.0 million, to file a registration statement and to use commercially reasonable efforts to effect the registration of all or a portion of these shares for public resale.

Short-form registration rights

Holders of certain of our shares of common stock are entitled to short-form registration rights. Pursuant to the investors' rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of at least 20% in interest of these holders to sell registrable securities at an aggregate price of at least $3.0 million, we will be required to use commercially reasonable efforts to effect a registration of such shares. We are required to effect only two registrations in any twelve-month period pursuant to this provision of the investor rights agreement.

Piggyback registration rights

Pursuant to the investors' rights agreement, if we register any of our securities either for our own account or for the account of other security holders, certain holders of our common stock are entitled to include their shares in the registration. Subject to certain exceptions contained in the investors' rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our investors' rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of registration rights

The demand registration rights and short form registration rights granted under the investors' rights agreement will terminate fifth anniversary of our IPO.

Anti-takeover effects of our certificate of incorporation and bylaws and Delaware law

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No written consent of stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of stockholders

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to certificate of incorporation and bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, and limitation of liability must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of a majority of the outstanding shares entitled to vote on the amendment, voting together as a single class, except that the amendment of the provisions relating to notice of stockholder business and nominations and special meetings

must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated preferred stock

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Exclusive forum

Our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers and employees to us or our stockholders; (3) any action asserting a claim arising pursuant to the Delaware General Corporation Law or our certificate of incorporation or by-laws (including the interpretation, validity or enforceability thereof) or (4) any action asserting a claim that is governed by the internal affairs doctrine; provided, however, that this provision shall not apply to any causes of action arising under the Securities Act or Exchange Act. In addition, our amended and restated bylaws will provide that, unless we consent in writing to 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 under the Securities Act (the Federal Forum Provision). Any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and consented to these forum provisions. These forum provisions may impose additional costs on stockholders, may limit our stockholders' ability to bring a claim in a forum they find favorable, and the designated courts may reach different judgments or results than other courts. In addition, there is uncertainty as to whether our Federal Forum Provision will be enforced, which may impose additional costs on us and our stockholders

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or

- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-254858) pertaining to the 2016 Stock Incentive Plan, 2021 Stock Option and Incentive Plan, and 2021 Employee Stock Purchase Plan of Ikena Oncology, Inc. of our report dated March 17, 2022, with respect to the consolidated financial statements of Ikena Oncology, Inc., appearing in this Annual Report (Form 10-K) for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 17, 2022

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Exhibit 31.1

CERTIFICATION 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

I, Mark Manfredi, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ikena Oncology, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 17, 2022

By: /s/ Mark Manfredi
Mark Manfredi
Chief Executive Officer
(Principal Executive Officer and Principal Financial Officer)

Exhibit 31.2

CERTIFICATION 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

I, Francisco Oliveira, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ikena Oncology, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 17, 2022

By: /s/ Francisco Oliveira
Francisco Oliveira
Vice President of Finance and Administration
(Principal Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Annual Report on Form 10-K for the period ending December 31, 2021 of Ikena Oncology, Inc. (the "Company") as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 17, 2022

By: /s/ Mark Manfredi
Mark Manfredi, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer and Principal Financial Officer)

By: /s/ Francisco Oliveira
Francisco Oliveira
Vice President of Finance and Administration
(Principal Accounting Officer)