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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2022

OR

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

Commission File Number: 001-39401

iTeos Therapeutics, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**84-3365066**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
321 Arsenal St Watertown, MA	**02472**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (339) 217 0161

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, $0.001 par value per share	ITOS	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 (§232.40a5 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

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

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

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The NASDAQ Stock Market on March 7, 2023 was $609.7 million.

The number of shares of Registrant's Common Stock outstanding as of March 7, 2023 was 35,720,401.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2023 Annual Meeting of Stockholders to be filed pursuant to Regulation 14A within 120 days of the end of the registrant's fiscal year ended December 31, 2022 are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

PCAOB No. 1133 Auditor Name: Deloitte Bedrijfsrevisoren/Réviseurs d'Entreprises BV/SRL Auditor Location: Zaventem, Belgium

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Special note regarding forward-looking statements

This Annual Report on Form 10-K, including the sections entitled “Risk factors,” “Management’s discussion and analysis of financial condition and results of operations,” and “Business,” contains express or implied forward-looking statements. These statements relate to future events or future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to differ materially from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the timing, progress and success of our clinical trials of EOS-448, inupadenant, EOS-984 and any other product candidates, 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;
- whether the results of our trials will be sufficient to support domestic or foreign regulatory filings or approvals for our product candidates;
- regulatory actions with respect to our product candidates or our competitors’ products and product candidates;
- our ability to obtain, including on an expedited basis, and maintain regulatory approval of our product candidates;
- the outcomes of our preclinical studies;
- our ability to enroll patients in our clinical trials at the pace that we project;
- the costs of development of our product candidates or clinical development programs;
- our expectations regarding the anticipated development of our pipeline of candidates;
- the period of time over which our existing capital resources will be sufficient to fund our operating expenses and capital expenditures, and the degree to which such resources will enable us to fund our planned development of our product candidates;
- the potential attributes and clinical benefits of our product candidates;
- our ability to successfully establish or maintain collaborations or strategic relationships for our product candidates;
- the expected benefits of collaborations, including potential milestones and royalty payments from GSK pursuant to the GSK Collaboration Agreement (each as defined herein);
- the rate and degree of market acceptance of our product candidates;
- our ability to obtain orphan drug or Breakthrough Therapy designation or other accelerated approval for any of our product candidates;
- our ability to manufacture our product candidates in conformity with the Food and Drug Administration’s requirements and to scale up manufacturing of our product candidates to commercial scale, if approved;
- our ability to compete with companies currently producing or engaged in the clinical development of treatments for the disease indications that we pursue or treatment modalities that we develop;
- our reliance on third parties to conduct our clinical trials;
- our reliance on third-party contract manufacture organizations (CMOs) to manufacture and supply our product candidates for us;
- our ability to retain and recruit key personnel;

- our ability to obtain and maintain intellectual property protection for our product candidates;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our need for or ability to obtain additional financing;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act, or JOBS Act;
- our future financial performance;
- the effect of the 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 future preclinical and clinical trials;
- the impact of laws and regulations applicable to our industry; and
- developments and projections relating to our competitors or our industry.

In some cases, you can identify forward-looking statements by terminology such as “may,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain such identifying terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect our results and financial condition. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled “Risk factors” and elsewhere in this Annual Report on Form 10-K and in any subsequent filings with the Securities and Exchange Commission (SEC). If one or more of these risks or uncertainties occur, or if underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K and have filed with the SEC as exhibits to this Annual Report on Form 10-K, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements. Statements regarding our cash runway do not indicate when we may access the capital markets.

While we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are conveyed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this Annual Report on Form 10-K, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section titled “Risk factors” and elsewhere in this Annual Report on Form 10-K, and in any subsequent filings with the SEC.

Risk Factor Summary

The risk factors detailed in Item 1A entitled “Risk Factors” in this Annual Report on Form 10-K are the risks that we believe are material to our investors and a reader should carefully consider them. Those risks are not all of the risks we face and other factors not presently known to us or that we currently believe are immaterial may also affect our business if they occur. The following is a summary of the principal risk factors detailed in Item 1A:

- We must complete successful preclinical studies and clinical trials that demonstrate the safety and efficacy of the product candidates before we can begin the commercialization process.
- Challenges enrolling patients in our clinical trials may delay or prevent clinical trials of our product candidates.
- We anticipate that our 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.
- Interim “top-line” and preliminary results from our clinical trials that we announce or publish from time to time may change as more patient data become available, and audit and verification procedures could result in material changes in the final data.
- We may not be able to file investigational new drug (IND) applications or IND amendments to commence additional clinical trials on the timelines indicated, and, even if we are able to file, the Federal Drug Administration, or FDA, or comparable foreign regulatory authorities may not permit us to proceed.
- We face significant competition from other biopharmaceutical and biotechnology companies, academic institutions, government agencies, and other research organizations, which may result in others discovering, developing, or commercializing products more quickly or marketing them more successfully than us. If their product candidates are shown to be safer or more effective than ours, our commercial opportunity may be reduced or eliminated.
- Negative developments in the field of immuno-oncology or in the field of TIGIT (as defined herein) or adenosine pathway therapeutics could damage public perception of our product candidates or negatively affect our business.
- If we are unable to successfully commercialize any product candidate for which we receive regulatory approval, or experience significant delays in doing so, our business will be materially harmed.
- The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we experience delays in obtaining, required regulatory approvals, our ability to generate revenue may be materially impaired.
- We rely on third parties to conduct our clinical trials and perform some of our research and preclinical studies. Failure by these third parties to satisfactorily carry out their contractual duties or to meet expected deadlines may adversely impact our development programs, business and prospects.
- We may not realize the benefits of our collaborations, alliances or licensing arrangements, including our collaboration with GSK (as defined herein) for the global development of EOS-448.
- We rely on third parties to manufacture our product candidates, and we expect to continue to rely on third parties for the clinical as well as any future commercial supply of our product candidates and other future product candidates. The development of our current and future product candidates, and the commercialization of any approved products, could be stopped, delayed or made less profitable if any such third party fails to provide us with sufficient clinical or commercial quantities of such product candidates or products, fails to do so at acceptable quality levels or prices or fails to achieve or maintain satisfactory regulatory compliance.
- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

- We will require additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- If we are unable to obtain and maintain sufficient intellectual property protection for our current product candidates or any future product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to commercialize successfully our products may be adversely affected.
- We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to implement successfully our business strategy.
- The trading price of our common stock has been and may continue to be volatile.

PART I

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company pioneering the discovery and development of a new generation of immuno-oncology therapeutics for people living with cancer. We leverage our deep understanding of tumor immunology and immunosuppressive pathways to design novel product candidates with the aim of restoring the immune response against cancer. Our innovative pipeline includes two clinical-stage programs targeting novel, validated immuno-oncology pathways. Each of our therapies in development has optimized pharmacologic properties designed to improve clinical outcomes.

Our lead antibody product candidate, EOS-448, also known as GSK4428859A, is an antagonist of TIGIT, or T-cell immunoreceptor with Ig and ITIM domains, an immune checkpoint with multiple mechanisms of action. EOS-448 was selected for its affinity for TIGIT, its potency and its potential to engage the Fc gamma receptor, or FcγR, to activate dendritic cells, natural killer cells and macrophages and to promote cytokine release, activation of antigen presenting cells and antibody-dependent cellular cytotoxicity, or ADCC, activity. In 2020, we started an open-label Phase 1/2a clinical trial of EOS-448 in adult cancer patients with advanced solid tumors. In April 2021, we reported preliminary safety, pharmacokinetic, engagement and pharmacodynamic data, indicating target engagement and early evidence of clinical activity as a single agent. In September 2021, we dosed the first patients in a Phase 1/2 clinical trial of EOS-448 in combination with pembrolizumab and in combination with our $A_{2A}R$ antagonist inupadenant in patients with solid tumors.

On June 11, 2021, our wholly owned subsidiary, iTeos Belgium S.A., and GlaxoSmithKline Intellectual Property (No. 4) Limited, or GSK, executed a Collaboration and License Agreement, or the GSK Collaboration Agreement, which became effective on July 26, 2021. Pursuant to the GSK Collaboration Agreement, we granted GSK a license under certain of our intellectual property rights to develop, manufacture, and commercialize products comprised of or containing EOS-448, which license is exclusive in all countries outside of the United States and co-exclusive, with iTeos, in the United States. GSK and iTeos intend to develop EOS-448 in combination, including with other oncology assets of GSK, and iTeos and GSK will jointly own the intellectual property created under the GSK Collaboration Agreement that covers such combinations. In partnership with GSK, we are enrolling patients with first line, non-small cell lung cancer (NSCLC) in a randomized Phase 2 trial assessing the doublet of GSK's anti-PD-1 (Jemperli (dostarlimab-gxly)) with EOS-448. In addition, we are enrolling patients with first-line advanced or metastatic head and neck squamous cell carcinoma (HNSCC) for the Phase 2 expansion part of the trial assessing the doublet of GSK's dostarlimab with EOS-448. We and GSK continue to explore two novel triplets in selected advanced solid tumors both in Phase 1b trials: EOS-448 with dostarlimab and GSK's investigational anti-CD96 antibody, and EOS-448 with dostarlimab and GSK's anti-PVRIG.

Based on favorable preclinical data generated in collaboration with Fred Hutchinson Cancer Research Center, we are also enrolling patients in an open-label dose-escalation/expansion Phase 1/2 trial evaluating the safety, tolerability and preliminary activity of EOS-448 as monotherapy and in combination with Bristol Myers Squibb's iberdomide - a novel, potent oral cereblon E3 ligase modulator (CELMoD®) compound with enhanced tumoricidal and immune-stimulatory effects compared with immunomodulatory (IMiD®) agents - with or without dexamethasone, in adults with relapsed or refractory multiple myeloma.

We are also advancing inupadenant, a next-generation adenosine A_{2A} receptor antagonist tailored to overcome the specific adenosine-mediated immunosuppression found in tumor microenvironment, into proof-of concept trials in several indications following encouraging single-agent activity in Phase 1. We are investigating inupadenant in an open-label multi-arm Phase 1/2a clinical trial in adult cancer patients with advanced solid tumors. The single-agent dose-escalation and expansion portions of our Phase 1/2a clinical trial of inupadenant have demonstrated durable monotherapy antitumor activity in some patients with advanced solid tumors and safety consistent with previously reported results. As part of this monotherapy assessment of inupadenant, we identified a potential predictive biomarker and we have completed enrolling patients in the biomarker cohort of the ongoing Phase 1b/2a trial. We confirmed a partial response using inupadenant in monotherapy in a patient who had the highest level of the biomarker that we have recorded. We are also enrolling patients in the dose ranging part (Part 1) of an ongoing two-part Phase 2 trial in post-IO metastatic non-squamous non-small cell lung cancer (NSCLC) to evaluate the combination of inupadenant with platinum-doublet chemotherapy compared to standard

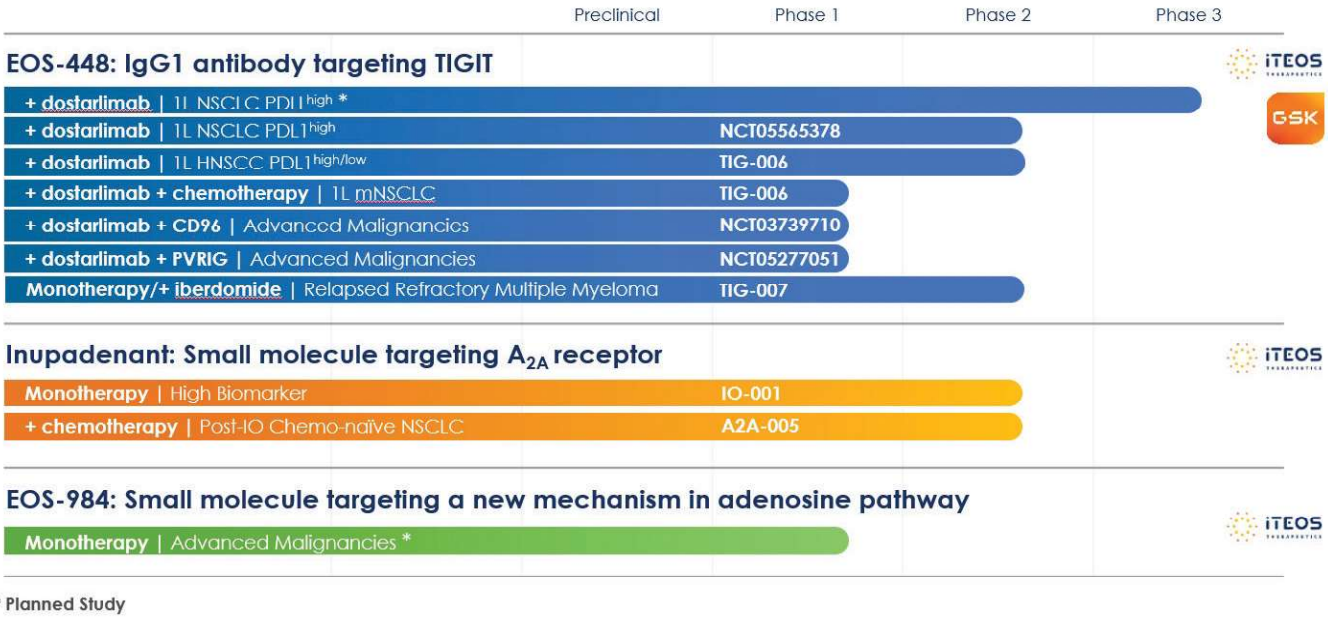
platinum-doublet chemotherapy. We have completed enrollment in the safety evaluation portion of the clinical trial of inupadenant in combination with chemotherapy and with pembrolizumab, as well as the monotherapy expansion cohort in prostate cancer. We have completed enrollment in the Phase 2a trial evaluating inupadenant in combination with pembrolizumab in post-PD-1 melanoma and have decided to prioritize development of inupadenant in our ongoing study in combination with platinum-doublet chemotherapy in patients with chemo-naïve NSCLC as we have determined that the post-PD-1 melanoma setting is not a path to accelerated approval. In addition, we are evaluating a salt form of inupadenant in a Phase 1 study.

In September 2021, we nominated a product candidate, EOS301984, or EOS-984, which targets a new mechanism in the adenosine pathway for Investigational New Drug, or IND, enabling studies. EOS-984 has the potential to fully reverse adenosine immune suppression, as a monotherapy and in combination with inupadenant and other standards of care. We expect to initiate clinical studies for EOS-984 in mid-2023.

We began our research and development activities as a spin-off of Ludwig Cancer Research and have built significant expertise in designing novel cancer immunotherapies. Our internal research and development team has extensive expertise in tumor immunology, characterization of immunosuppressive mechanisms in the tumor microenvironment, pharmacology and translational medicine. We have also built discovery capabilities to develop both small molecules and antibodies with differentiated and optimized product profiles for targets validated by a strong scientific rationale. We continue to progress research programs focused on additional targets that complement our TIGIT and adenosine pathway programs or address additional immunosuppressive pathways. Our expertise also allows us to integrate a biomarker-rich strategy into our clinical programs to measure the activity of a product candidate in patients, seek to optimize combination agents and identify patients we deem most likely to benefit from treatment.

Our pipeline

The following chart summarizes our current and expected development of our pipeline of therapeutic candidates during 2023.



* Planned Study

Objectives and Business Strategy

Our vision is to transform the treatment of people living with cancer by creating a broad portfolio of immuno-oncology therapies targeting major mechanisms of immunosuppression on in the tumor microenvironment. The key pillars of our strategy to achieve our vision include:

- **Advance the development of our clinical candidates toward registration**. In collaboration with GSK, we aim to exploit the broad potential of TIGIT inhibition and advance EOS-448, our FcγR engaging anti-TIGIT antibody, through clinical development and regulatory approval. For the adenosine pathway, our goal is to build upon the differentiated profile of inupadenant and EOS-984 to advance these programs through clinical development and regulatory approval.
- **Leverage our deep understanding of immune pathways and the tumor microenvironment to identify and develop additional novel product candidates.** Since our inception, we have established extensive knowledge in immuno-metabolism, characterization of the immunosuppressive mechanisms in the tumor microenvironment, pharmacology and translational medicine. We will continue to apply our expertise in understanding and targeting immunosuppressive cells and mechanisms of resistance within the tumor microenvironment. Once these new targets are validated, we will use our expertise to develop differentiated clinical candidates to progress in clinical development for the treatment of cancer.
- **Maximize the value of our product candidates and pipeline by selectively entering into strategic collaborations.** We seek to establish collaborative relationships that will provide us with access to capital, opportunities and/or expertise to move our clinical products toward commercialization. In June 2021, we entered into the GSK Collaboration Agreement to co-develop and co-commercialize EOS-448. Under the GSK Collaboration Agreement, GSK made an upfront payment of $625.0 million to us, and we are also eligible to receive up to $1.45 billion in milestone payments, contingent upon the EOS-448 program achieving certain development and commercial milestones. By combining forces with GSK's and their global reach and leading pipeline in the TIGIT/CD226 pathway, this collaboration expands and accelerates our ability to bring EOS-448 to patients globally in multiple indications. In addition, we have and may in the future enter into collaborations that grant us access to certain compounds owned by third parties to enable therapeutic combinations that could enhance the clinical and commercial potential of our product candidates. For example, we entered into a non-exclusive, clinical supply agreement with Merck & Co, or Merck, to evaluate inupadenant in combination with pembrolizumab and with Bristol Myers Squibb to evaluate EOS-448 in combination with iberdomide.
- **Maintain a strong culture of innovation and putting patients first**. We will continue to nurture our culture, which is based on scientific innovation, collaboration, excellence and putting patients first in everything we do. We believe that our presence in the United States and Belgium is a strategic advantage that enhances our ability to attract global talent and remain at the forefront of innovation in the field of immuno-oncology.

The promise of immuno-oncology

In recent years, the treatment of cancer has been reshaped by the promise of immuno-oncology therapies. These therapies work to harness the patients' own immune system to attack their own cancer tissue. The most widely used of these interventions are the immune checkpoint inhibitors, or CPIs, with anti-PD-1 antibodies being the most successful immunotherapies. Immune checkpoints are proteins on certain immune cells that regulate the activation, often functioning as on-off switches, of effector cells. The success of these CPIs has demonstrated the potential of harnessing the immune system to treat cancer and increased understanding of the sophisticated mechanisms by which cancer evades the immune system.

Our drug discovery efforts are dedicated to understanding immune resistance pathways with the specific goal of generating differentiated product candidates that restore the immune response against cancer. We currently have two clinical-stage product candidates, EOS-448 and inupadenant, each targeting a key mechanism which may inhibit an effective antitumor immune response: the novel checkpoint TIGIT/CD226 pathway, and the adenosine pathway, respectively. We believe that both product candidates have the potential to increase patient responses to immunotherapy, including in patients resistant to currently approved CPIs. We are also using our deep understanding of critical immune resistance pathways to identify new targets and generate additional product candidates that have the potential to be complementary to our current cancer therapies.

EOS-448

Highlights of EOS-448

1. **Clinical proof of concept of anti-TIGIT antibodies.** EOS-448 is an antibody specifically designed to target TIGIT, a receptor expressed on immune cells, particularly tumor-infiltrating lymphocytes, or TILs. Its main ligands play both inhibitory and stimulatory roles in regulating immune response and are highly expressed in tumors, where they have been shown to mediate immunosuppression. In the TIGIT field, two recent randomized Phase 2 trials in non-small cell lung cancer of other companies that demonstrated clinical benefit of a-TIGIT treatment and upcoming readouts of other companies uniquely position anti-TIGIT antibodies as a promising next generation cancer immunotherapy.

2. **An anti-TIGIT with strong antagonist potency.** EOS-448 is a recombinant, fully human IgG1 monoclonal antibody directed against human TIGIT that we selected for clinical development based on its favorable characteristics, including affinity, competition with TIGIT ligands CD155 and CD112, cross-reactivity to TIGIT in non-human primates, functionality and suitability for development.

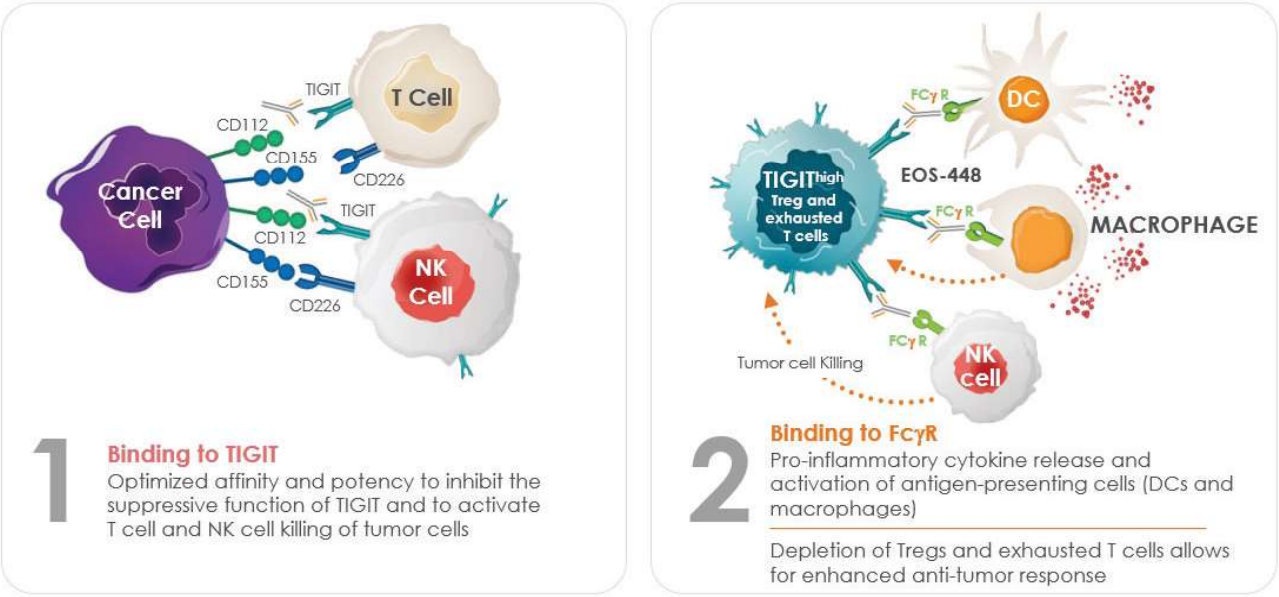
   We produced biosimilar versions of anti-TIGIT antibodies, in development by other companies, based on sequences from the patents of Mereo, Genentech, Bristol-Myers Squibb, Merck and Arcus and compared them to EOS-448 in preclinical assays. As compared to these antibodies, EOS-448 has similar or higher binding affinity for CD8+ T cells and ability to prevent the interaction between TIGIT and CD155 ligand at minimal concentrations of the antibody. EOS-448 also exhibited stronger potency as determined using an IL-2 promoter-dependent functional assay. This is the result of our screening studies, during which we observed that functional activity can be independent of affinity, and selection of a clone that was optimized for both.

   In preclinical models, we also showed that a surrogate anti-TIGIT antibody, sharing similar characteristics as EOS-448 but active in mouse, delayed tumor growth and caused tumor regression both as monotherapy and in combination with other cancer therapies, including anti-PD-1 antibodies.

   We believe these properties could translate into superior clinical benefit of EOS-448 as compared to other anti-TIGIT antibodies in development.

3. **An FcγR-activating anti-TIGIT antibody *to restore anti-tumor activity via multiple mechanisms*.** EOS-448 is designed to restore immune responses through multiple mechanisms. First, EOS-448 is designed to block the binding of the ligands, CD155 and CD112, to TIGIT, which frees these ligands to bind to the stimulatory receptor, CD226, expressed both on NK and T cells, resulting in activation of these immune cells and in immune-mediated killing of tumor cells. Second, as the antibody has been designed as a fully functional IgG1, EOS-448 can engage Fcγ receptors expressed on dendritic cells, natural killers, and macrophages leading to pro-inflammatory signal and enhanced immune activation. Third, these activated macrophages and NK cells can induce antibody-dependent cellular cytotoxicity and directly kill the cells expressing the highest level of TIGIT in the tumor microenvironment, which are the immunosuppressive regulatory T cells (Tregs) and the terminally exhausted T cells that are detrimental to an effective antitumor immune response. With those multiple mechanisms of action, EOS-448 is well suited to improve the balance of effector versus suppressive immune cells and restore the antitumor immune response, particularly in combination with other immunotherapies.

4. **EOS-448 demonstrates strong target engagement and early sign of activity in patients.** EOS-448 is currently under clinical development and early clinical trials have demonstrated strong target engagement in patients treated with different concentration of the drug. Early clinical data suggest that proliferation markers are increased in T cells of treated patients while suppressive regulatory T cells are strongly depleted from the blood and in the tumor after the initial dosing with EOS-448. In addition, multiple patients have experienced prolonged disease stabilization and some regression of tumor size was observed in subjects treated with the drug as single agent. EOS-448 is currently tested in multiple studies and in multiple combinations with the goal of expanding its antitumor potential.



DC = dendritic cell

We believe that EOS-448 has the potential to provide therapeutic benefit to patients across a wide array of tumors. Combination experiments in preclinical models suggest that combining EOS-448 with a number of other immuno-oncology agents and chemotherapy regimens may lead to improved outcomes.

Inupadenant

Inupadenant is an $A_{2A}R$ antagonist that we engineered to specifically inhibit the immunosuppressive activity of adenosine found in the tumor microenvironment. Hypoxia and cell necrosis in the tumor lead to the release of ATP, which is converted to adenosine by adenosine producing enzymes. Adenosine primarily exerts its immunosuppressive effects through the $A_{2A}R$, a receptor found on a broad range of immune cells in the tumor microenvironment. Inupadenant is designed to release adenosine-driven immunosuppression, ultimately allowing T cells to kill their tumor targets. Inupadenant, unlike other $A_{2A}R$ antagonists in IO, has been specifically designed to maintain potency even in the very high concentrations of adenosine found in tumor tissue. We believe that elevated levels of adenosine in the tumor microenvironment may be a modulator of resistance to current cancer therapies, including both CPIs and chemotherapy. High activity of soluble CD73 is associated with poor overall survival and PFS in patients with metastatic melanoma treated with nivolumab, an anti-PD-1 CPI. An association between high adenosine blood concentrations and lack of response to nivolumab has been shown in a clinical trial of renal cell cancer patients conducted by others. In this trial, patients who failed to respond to nivolumab had significantly higher blood adenosine levels than those who responded, both at baseline (158% higher) and at four weeks after initiation of treatment (138% higher). Patients with baseline adenosine levels in the top quartile also had a significantly worse PFS. These data further support our belief that adenosine plays an important role in resistance to CPIs such as nivolumab. Additional data support a potential role in chemotherapy-induced resistance, as chemotherapy has been shown in some cases to increase the production of adenosine in the tumor microenvironment and some chemotherapeutics induce adenosine-mediated immunosuppression that may limit the efficacy of these therapies.

Differentiation of inupadenant

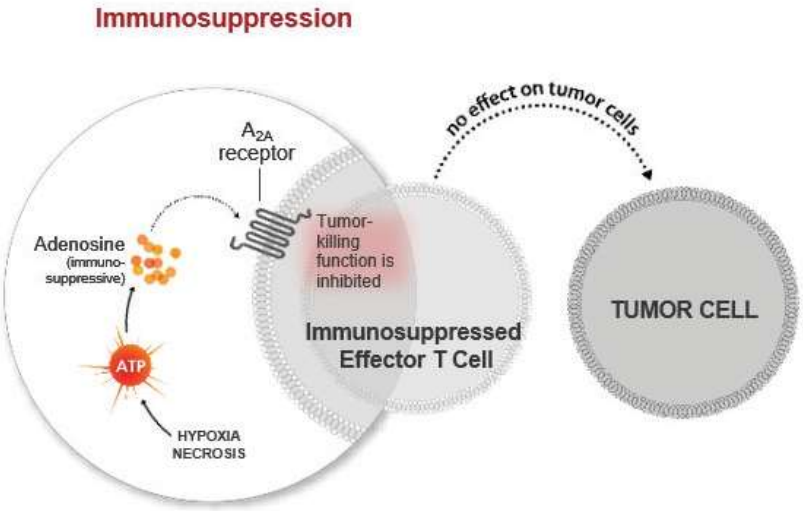
We believe inupadenant has three key characteristics that provide the molecule with a unique profile and potential advantages in clinical settings when compared to other $A_{2A}R$ antagonists currently in development:

1. ***High affinity for $A_{2A}R$ and insurmountable antagonism***. Adenosine is widely accepted as a driver of immunosuppression in cancer tissue. What is less appreciated is the fact that the immunosuppression is driven by very high concentrations of adenosine – concentrations that can be in the high micromolar range. To overcome these very high concentrations we have designed inupadenant to be what is

known as an insurmountable antagonist. This means that the drug is capable of potently blocking the A_{2A} receptor at any concentration of adenosine. Inupadenant achieves this through a combination of affinity and an extended residence time, the length of time the drug remains bound to its receptor. In our *in vitro* studies, we assessed this characteristic in functional T cell assays and compared inupadenant to a range of competitor antagonists. In these assays, we observed that at low adenosine concentrations, inupadenant was the most potent antagonist of the $A_{2A}R$ antagonists we tested, and most notably, when compared to other antagonists developed by competitors, the potency of inupadenant was not reduced at the high adenosine concentrations typically found in the tumor microenvironment.

2. ***Inupadenant has higher selectivity for $A_{2A}R$ than other antagonists in clinical development***. Because $A_{2A}R$ is the primary adenosine receptor on immune cells, we believe that the high specificity of inupadenant will enable it to have potent effects on immune cell function in solid tumors and hematological malignancies, while avoiding potential adverse effects that may be associated with inhibition of other subtypes of adenosine receptors with broader expression profiles. We conducted a study showing the IC_{50} for inhibition of cAMP production in HEK cells overexpressing one of the four adenosine receptors, comparing inupadenant and three other adenosine antagonists currently in development. Inupadenant was the most potent $A_{2A}R$ antagonist among other antagonists as demonstrated by the very low concentrations of drug required to give a 50% response in a functional assay. Higher concentrations were required to give the same effect on other adenosine receptors, further supporting the high selectivity of inupadenant.

3. ***Inupadenant is designed not to cross the blood brain barrier.*** Unlike first generation $A_{2A}R$ antagonists, we designed inupadenant specifically to avoid penetration to the CNS through crossing of the blood-brain barrier. In preclinical models, inupadenant displayed less than 1% blood-brain barrier penetration, and, accordingly, we believe it is designed to minimize the potential for adverse CNS effects.



We are focused on the direct target for adenosine, its receptor, and we chose $A_{2A}R$ as it is the most highly expressed in relevant immune cell populations and one of the receptors with high affinity for the adenosine, rather than targeting upstream enzymes that are involved in production of adenosine. We selected $A_{2A}R$ as the target for inupadenant because we believe it is a key actor that mediates the immunosuppressive effects of adenosine regardless of the source of adenosine production.

Potential broader opportunity for inupadenant

We are evaluating potential predictors of response and potential PD biomarkers in pre- and post-treatment tumor samples. These biomarkers include the expression of $A_{2A}R$ and adenosine-producing enzymes within the tumor, the presence of immune cells within the tumor and several tumor gene signatures, including an immune gene signature. We believe the biomarker findings from our ongoing Phase 1/2a clinical trial provide insight into the mechanism of action of inupadenant, which we anticipate will inform our selection of indications, and may allow us to identify patients more likely to benefit from inupadenant. We will also be guided by our evaluation of the

expression of $A_{2A}R$ and adenosine-producing enzymes, such as CD73, TNAP and PAP in various tumor types. We believe inupadenant has the potential to provide clinical benefit across many indications.

Our Preclinical Novel Adenosine-Pathway Inhibitor Program

We have developed significant expertise in tumor immunology and the tumor microenvironment, which we are exploiting to expand our pipeline. For example, by characterizing the impact of high concentrations of adenosine on immune cells, we have identified a novel mechanism within the adenosine pathway responsible for inhibiting the proliferation of T cells in high adenosine concentrations that can be found in some tumors. In preclinical studies, addition of ATP as a source of adenosine at a concentration of 100μM completely blocked CD8+ T cell proliferation *in vitro.* The addition of an inhibitor to the novel target restored proliferation and could further enhance cytokine secretion in combination with inupadenant.

In September 2021, we nominated a product candidate, EOS-984, targeting a novel mechanism in the adenosine pathway for IND enabling studies. EOS-984 has the potential to fully reverse adenosine immune suppression, as a monotherapy and in combination with inupadenant and other standards of care. We expect to initiate clinical studies for EOS-984 in mid-2023.

Collaborations and Licenses

Collaboration and License Agreement with GSK

On June 11, 2021, our wholly owned subsidiary, iTeos Belgium S.A., and GSK executed the GSK Collaboration Agreement, which became effective on July 26, 2021. Pursuant to the GSK Collaboration Agreement, we agreed to grant GSK a license under certain of our intellectual property rights to develop, manufacture, and commercialize products comprised of or containing EOS-448, referred to as Licensed Products, which license is exclusive in all countries outside of the United States and co-exclusive, with iTeos, in the United States.

Under the GSK Collaboration Agreement, GSK made an upfront payment of $625.0 million to us. Additionally, we are eligible to receive up to $1.45 billion in milestone payments, contingent upon the EOS-448 program achieving certain development and commercial milestones, none of which have been achieved to date. Within the collaboration, GSK and we agreed to share responsibility and costs for the global development of EOS-448 and will jointly commercialize and equally split profits in the United States. Outside of the United States, GSK will receive an exclusive license for commercialization, and we are eligible to receive tiered double digit royalty payments up to 20% during a customary royalty term. We and GSK intend to develop EOS-448 in combination with certain other oncology assets of GSK, and we will jointly own the intellectual property created under the GSK Collaboration Agreement that covers such combinations together with GSK. Subject to certain limited exceptions, other than under the GSK Collaboration Agreement, we and GSK each agreed not to, alone or with or for any Third Party, (i) develop a monospecific, monoclonal antibody that inhibits or is an antagonist of TIGIT through direct physical interaction for a period of time following the first regulatory approval of a Licensed Product in the United States, Germany, France, United Kingdom, Spain, or Italy or (ii) commercialize any such a product during the term of the GSK Collaboration Agreement. Unless terminated earlier in certain specified circumstances, the GSK Collaboration Agreement will continue for so long as we and GSK are commercializing Licensed Products in the United States.

Collaboration with Adimab

In January 2017, we entered into a collaboration agreement with Adimab, LLC, or Adimab. We refer to this agreement, as amended, as the Original Adimab Agreement. On February 22, 2021, we entered into an amendment to the Adimab Agreement (the Amended Adimab Agreement and together with the Original Adimab Agreement, the Adimab Agreement). Adimab has developed an antibody discovery and optimization technology platform. This collaboration enables our research and development efforts on discovery and optimization of new antibodies against immuno-oncology targets we may identify.

Under the terms of the Adimab Agreement, Adimab has granted us a worldwide, non-exclusive research license for a one-year research term period and evaluation period for up to 18 months per research program. We are required to use commercially reasonable efforts to perform our research activities under the Adimab Agreement and, if we exercise our right to obtain a development and commercialization license, we are required to use commercially reasonable efforts to pursue development and commercialization of a product directed to the

applicable target. Under the terms of the Adimab Agreement, we granted Adimab a worldwide, non-exclusive license under all of our patents and know-how that are reasonably necessary or useful for Adimab to perform its research activities under the Adimab Agreement.

Payment terms to Adimab include a one-time upfront technology access fee in the tens of thousands and payments for research support. Adimab is entitled to additional fees of up to a maximum of $0.4 million on a program-by-program basis for the achievement of certain technical milestones, one of which was met, and we paid $0.2 million in April 2017. Upon our exercise of an option for an exclusive development and commercialization license, with respect to a target, we are required to make a low single digit million-dollar payment to Adimab for each exercised option. For example, in August 2018, we paid a $1.0 million nonrefundable fee to exercise an option to acquire certain licenses from Adimab. One of the antibodies licensed under this agreement is what we now refer to as EOS-448. In addition, on a per target basis, we may be required to pay development, regulatory and commercial milestones totaling up to an aggregate of $42.8 million for the first three products and additional milestone payments up to $13.5 million for each additional product. We will pay Adimab low to mid-single-digit royalties on a country-by-country and product-by-product basis, on worldwide net product sales of licensed products. Royalties are payable on a licensed product-by-licensed product and country-by-country basis until the later of (i) expiration of the last valid claim of a licensed patent right that covers such licensed product in such country, and (ii) ten years following the first commercial sale of such licensed product in such country. To date, we have paid a total of $5.4 million to Adimab pursuant to the collaboration agreement.

The Amended Adimab Agreement specifies different milestone payments for new products that are derived from research programs beginning after February 22, 2021 (New Products). For New Products, on a per target basis, we may be required to pay development, regulatory and commercial milestone payments totaling up to an aggregate of $45.8 million for the first three products and additional milestone payments up to $14.5 million for each additional product. Royalty percentages for New Products are slightly different than for original products. There were no other significant changes to the terms in the original Adimab Agreement as a result of the Amended Adimab Agreement.

Adimab controls the filing, prosecution, maintenance and enforcement of the intellectual property that it licenses to us under the Adimab Agreement. We have the right to enforce such licensed intellectual property against infringement if the infringement is competitive with our licensed products and Adimab does not pursue enforcement. We control the filing, prosecution, maintenance and enforcement of the intellectual property we license to Adimab under the Adimab Agreement and all program antibody patents.

The term of the Adimab Agreement will continue until the last to expire royalty term on a product-by-product and country-by-country basis if we exercise our option, or in the event no option is exercised, the conclusion of the last-to-expire evaluation term, unless terminated earlier by either party. Each party has the right to terminate the Adimab Agreement due to the other party's uncured material breach or our abandonment of the product.

WuXi manufacturing agreement

In March 2017, we entered into a biologics master services agreement with WuXi Biologics (Hong Kong) Limited, or WuXi, which we refer to as the WuXi Agreement. The WuXi Agreement provides for IND-enabling CMC development and GMP manufacturing of EOS-448 on a work order basis. Under the WuXi Agreement, we are obligated to pay WuXi a service fee in the amount specified in each work order associated with the agreement for the provision of services. If we manufacture all of our commercial supplies of EOS-448 with a manufacturer other than WuXi, we must pay to WuXi either a low single-digit royalty fee on global net sales or a one-time milestone payment in the low tens of millions.

The WuXi Agreement terminates one year after the date on which the last work order has expired or been terminated, unless terminated earlier. The term of each work order terminates upon completion of the services under such work order, unless terminated earlier.

Competition

Our industry is intensely competitive and subject to rapid and significant technological change. While we believe that our knowledge, experience and scientific resources provide us with competitive advantages, we face substantial competition from major pharmaceutical companies and biotechnology companies, academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and established collaborative arrangements for the research, development, manufacturing and commercialization of cancer therapies. Many of our competitors have significantly greater financial, technical

and human resources. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do.

We face competition with respect to our current product candidates, and will face competition with respect to future product candidates, from segments of the pharmaceutical, biotechnology and other related markets that pursue immune-oncology treatments. For example, there are many other companies that have commercialized and/or are developing immuno-oncology treatments for cancer including large pharmaceutical and biotechnology companies, such as AstraZeneca, Bristol-Myers Squibb, Gilead, Incyte, Merck, Novartis, Pfizer and Roche/Genentech.

For our anti-TIGIT antibody, EOS-448, we are aware of several pharmaceutical companies developing antibodies against this target, including Bristol-Myers Squibb, Merck, Mereo Biopharma Group plc, Roche/Genentech, Beigene, Ltd. (with partner Novartis), Arcus (with partner Gilead), Agenus, Seagen, Innovent (with partner Eli Lilly), Merck KGaA, Junshi and Compugen Ltd. To our knowledge, no anti-TIGIT antibodies have been approved for commercial sale, and the most advanced antibodies are in Phase 3 clinical trials.

For our small molecule antagonist of $A_{2A}R$, inupadenant, we are aware of several other companies that are developing other adenosine receptor antagonists, including AstraZeneca, Corvus Pharmaceuticals, Merck KGaA, Incyte, Arcus (with partner Gilead) and Novartis. To our knowledge, there are no adenosine receptor antagonists approved for the treatment of cancer and the most advanced such selective $A_{2A}R$ antagonists are in Phase 2 clinical trials.

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. Our competitors will also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

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 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 a 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.

The acquisition or licensing of pharmaceutical products is also very competitive. If we seek to acquire or license products, we will face substantial competition from a number of more established companies, some of which have acknowledged strategies to license or acquire products and many of which are bigger than us and have more institutional experience and greater cash flows than we have. These more established companies may have competitive advantages over us, as may other emerging companies taking similar or different approaches to product licenses and/or acquisitions. In addition, a number of established research-based pharmaceutical and biotechnology companies may acquire products in late stages of development to augment their internal product lines, which may provide those companies with an even greater competitive advantage.

Manufacturing and supply

We currently do not own or operate any manufacturing facilities nor have any plans to do so in the foreseeable future. We rely, and expect to continue to rely, on third-party contract development and manufacturing organizations, or CDMOs, or in the case of EOS-448, our collaborator, GSK, to develop a suitable manufacturing

process at scale and produce our small molecule and biologic product candidates for preclinical and clinical testing, as well as for commercial manufacture if our product candidates receive marketing approval. We believe that this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment and personnel while also enabling us to focus our expertise and resources on the development of our product candidates.

To date, we have obtained active pharmaceutical ingredients, or APIs, and drug product for our product candidates from single-source third party CMOs, including WuXi. We are in the process of developing our supply chain for each of our product candidates to ensure continuity of supply.

We maintain agreements with our manufacturers that include confidentiality and intellectual property provisions to protect our proprietary rights related to our product candidates.

We expect to rely on third parties for the manufacture of any companion diagnostics we may develop.

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. 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. With respect to EOS-448, in June of 2021 we entered into a collaboration agreement with GSK in which we agreed to collaborate with GSK on commercialization efforts for EOS-448 and related Licensed Products in the United States, and we have granted GSK a license to develop and commercialize EOS-448 and related Licensed Products outside of the United States.

We also plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. 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.

Intellectual property

As of January 1, 2023, we have two issued United States patents, one issued European patent, and over thirty pending applications in the United States and throughout the world in our TIGIT program portfolio. The patents and pending applications in our TIGIT program portfolio include claims covering EOS-448, its therapeutic use, and manufacture. Not including any potential patent term extension, the issued United States and European patents have a natural expiration date in 2038 and the pending applications in the portfolio, should they grant, have expiration dates ranging from 2038 to 2040.

We also have three issued United States Patents, one issued Australian Patent, one issued European Patent, as well as several other issued patents globally, and over fifty pending applications (including Patent Cooperation Treaty applications) in our $A_{2A}R$ program portfolio both in the United States and throughout the world. The patents and pending applications in our $A_{2A}R$ program portfolio include claims covering inupadenant, such as composition of matter, formulations, methods of treatment, and processes of manufacture. Not including any potential patent term extension, the issued patents have natural expiration dates ranging from 2038 to 2039 and the pending applications in the portfolio, should they grant, have expiration dates ranging from 2038 to 2042.

Government regulation

Government authorities in the United States, at federal, state, and local levels, as well as in foreign countries and jurisdictions, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drugs and biologics such as those we are developing. The process of obtaining regulatory approvals of drugs in the United States and in foreign countries and ensuring subsequent compliance with applicable statutes and regulations and other regulatory authorities requires the expenditure of substantial time and financial resources.

In the United States, where we are initially focusing our product development, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and biologics under the FDCA and the Public Health Service Act, or PHSA, and their implementing regulations. Both drugs and biologics are also subject to other federal, state and local statutes and regulations. Our product candidates are early-stage and have not been approved by the FDA for marketing in the United States.

Our product candidates must be approved for therapeutic indications by the FDA through either a new drug application, or NDA, or a biologics license application, or BLA, process before they may be marketed in the United States. An NDA is a request for approval to market a new drug for one or more specified indications, and a BLA is a request for approval to market a new biologic for one or more specified indications. The process generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with Good Laboratory Practice, or GLP, requirements;
- submission to the FDA of an IND that must become effective before clinical trials may begin and must be updated annually or when significant 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 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 after completion of all pivotal trials;
- payment of user fees for FDA review of the 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 inspections of the manufacturing facility or facilities where the product will be produced to assess compliance with current Good Manufacturing Practice requirements, or cGMPs, to assure that the facilities, methods and controls are adequate to ensure and preserve the drug or biological product's continued safety, purity and potency;
- potential FDA audit of the clinical trial sites that generated the data in support of the NDA or BLA; and
- FDA review and approval of the NDA or BLA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug or biologic in the United States.

The failure to comply with the applicable requirements in the United States at any time during the product development process, including preclinical testing, clinical testing, the approval process, or post-approval, may subject an applicant to delays in the conduct of the study, regulatory review and approval and/or administrative or judicial sanctions.

Preclinical and clinical trials

Before testing any drug or biologic in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of 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 regulations and requirements. The results of the preclinical studies, together with manufacturing information, analytical data, and plans for the proposed clinical trials 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 IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

The FDA may, at any time during the initial 30-day IND review period or while clinical trials are ongoing under the IND, impose a partial or complete clinical hold based on concerns for patient safety and/or noncompliance with regulatory requirements. This order issued by the FDA would delay a proposed clinical study or cause suspension of an ongoing study until all outstanding concerns have been adequately addressed, and the FDA has notified the

company that investigations may proceed. Imposition of a clinical hold could cause significant delays or difficulties in completing planned clinical studies in a timely manner.

A separate submission to an existing IND must be made for each successive clinical trial conducted during product development of a product candidate, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin. The clinical stage of development involves the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, 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 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 either centrally or individually for each institution at which the clinical trial will be conducted. The IRB also approves the informed consent information that must be provided to each clinical trial subject or his or her legal representative and must operate in compliance with FDA regulations. 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 or that the trial is not being conducted in accordance with FDA requirements, including GCP. Some studies also include oversight by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk to subjects or on other grounds, such as lack of efficacy.

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. The FDA may accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements, the foreign data are applicable to the U.S. population and U.S. medical practice, the studies have been performed by clinical investigators of recognized competence, 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 and BLAs 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 into healthy human volunteers or patients with the target disease or condition. These trials are typically designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, evaluate the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.
- Phase 2—Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3—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. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA or BLA.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional data 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 approval of an NDA or BLA.

Information about applicable clinical trials, including clinical trials results, must be submitted within specific timeframes for publication on the www.clinicaltrials.gov website.

IND sponsors must submit annual reports on the progress of investigations under the IND to FDA and submit IND safety reports to FDA when certain serious and unexpected adverse reactions and certain other safety issues occur.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the drug or biological 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 and to identify appropriate storage conditions for the product candidate.

FDA review process

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 requesting approval to market the product for one or more indications. 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 approval of an NDA or BLA must be obtained before a drug or biologic may be marketed in the United States.

In addition, under the Pediatric Research Equity Act, or PREA, certain NDAs and BLAs and certain supplements to an NDA or BLA must contain data to assess the safety and effectiveness of the drug or biological 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 Food and Drug Administration Safety and Innovation Act requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient or clinically active component, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan within 60 days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements, under specified circumstances. PREA does not generally apply to a drug or biological product for an indication for which orphan designation has been granted, PREA requirements are applicable to original applications for a new active ingredient that is intended for the treatment of an adult cancer and is directed at a molecular target that the FDA determines to be substantially relevant to the growth or progression of a pediatric cancer, regardless of whether the drug is for an indication for which orphan designation has been granted.

The FDA has 60 days after submission of an NDA or BLA to conduct an initial review to determine whether it is sufficient to accept for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the application. The FDA reviews an NDA or BLA to determine, among other things, whether the product is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's 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 an original NDA or BLA and respond to the applicant, and six months from the filing date of an original NDA or BLA filed for priority review. A major amendment to an NDA or BLA submitted at any time during the review cycle, including in response to a request from the FDA, may extend the goal date by three months The FDA does not always meet its PDUFA goal dates for standard or priority NDAs or BLAs.

The FDA may refer an application for a 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 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.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, as a condition for approving the NDA or BLA to ensure that the benefits of the product outweigh its risks. The REMS could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk-minimization tools.

After evaluating the application 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. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. 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 will usually describe all of the deficiencies that the FDA has identified in the NDA or BLA, and the FDA may recommend actions that the applicant might take to place the NDA or BLA in condition for approval, including requests for additional information or clarification. Sponsors that receive a complete response letter may submit to the FDA information that represents a complete response to the issues identified by the FDA. The FDA will not approve an application until it determines that the issues identified in the complete response letter have been addressed.

Even if the FDA approves a product, depending on the specific risk(s) to be addressed, the FDA 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 designation and exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation, or ODD, to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with either a patient population of fewer than 200,000 individuals in the United States, or a patient population greater of than 200,000 individuals in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States of that drug or biologic. ODD must be requested before submitting an NDA or BLA. After the FDA grants ODD, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has received ODD and subsequently receives the first FDA approval for that drug for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full NDA or BLA, to market the same drug or biologic for the same indication for seven years from the approval of the NDA or BLA, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of ODD are tax credits for certain research and a waiver of the NDA or BLA application user fee.

Expedited development and review programs

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, and priority review.

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 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, meaning that the FDA may consider for review sections of the NDA or BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA or BLA, the FDA agrees to accept sections of the NDA or BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

In addition, a new drug or biological product 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 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 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 priority review. A product is eligible for priority review if it is intended to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness over available therapies. For original NDAs and BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (compared with ten months under standard review).

Fast Track designation, Breakthrough Therapy designation, and priority review do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval but may expedite the development or review process. Each of the designations may also be rescinded if a product no longer meets the program's criteria.

Accelerated approval pathway

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

The accelerated approval pathway is most often used in settings in which the course of a disease is long, and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

For drugs granted accelerated approval, FDA generally requires sponsors to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. Failure to conduct required post-approval studies with due diligence, failure to confirm a clinical benefit during the post-approval studies, or dissemination of false or misleading promotional materials would allow the FDA to withdraw the product approval on an expedited basis. All promotional materials for product candidates approved under accelerated approval are subject to prior review by the FDA unless FDA informs the applicant otherwise.

FDA approval of companion diagnostics

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and in vitro companion diagnostics. According to the guidance, for novel drugs and biologics, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. Approval or clearance

of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population.

Under the FDCA, in vitro diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution.

The FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval, or PMA, simultaneously with approval of the therapeutic product candidate. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. After a device is placed on the market, it remains subject to significant regulatory and reporting requirements.

U.S. post-approval requirements for drugs and biologics

Drugs and biologics manufactured or distributed pursuant to FDA approvals are subject to pervasive and 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. The FDA and other agencies actively enforce the laws and regulations applicable to drugs and biologics, including those prohibiting the promotion of off-label uses, and a company that is found to have violated FDA regulatory requirements, including improperly promoting off-label uses may be subject to significant liability.

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.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, 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;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- mandated modification of promotional materials and labeling and issuance of corrective information;
- fines, warning letters, or untitled letters;
- holds on 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.

In addition, drug and biologics manufacturers and their subcontractors involved in the manufacture of approved products are required to register their establishments with the FDA and certain state agencies and are subject to

periodic inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented.

U.S. patent term restoration and marketing exclusivity

Depending upon the timing, duration and specifics of FDA approval of our future product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act, which permits a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date and only those patents covering such approved drug product, a method for using it or a method for manufacturing it may be extended. The patent-term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Marketing exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. Examples of applications that may require new clinical investigations essential to approval and receive three-year exclusivity include applications for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

A drug or biological product 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.

Biosimilars and exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Biosimilarity requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

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 full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law. However, since the passage of the BPCIA, many states have passed laws or amendments to laws, including laws governing pharmacy practices, which are state regulated, to regulate the use of biosimilars.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. The ultimate impact, implementation, and regulatory interpretation of the BPCIA remain subject to significant uncertainty.

Other healthcare laws

Our business operations and any current or future arrangements with third-party payors, physicians, other healthcare providers, patients and other individuals and organizations in the health care industry may expose us to healthcare and other 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 may obtain marketing approval. In the United States, federal laws include, without limitation, the following (some of which may be implicated only if we have an approved product).

- The federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing any remuneration, 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 under a federal healthcare program such as Medicare and Medicaid;
- The federal civil and criminal false claims laws, including the civil False Claims Act, or FCA, which 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 a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim 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 FCA;
- The federal civil monetary penalties laws, which 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 need not have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended, and its implementing regulations, which establish privacy and security standards applicable to certain health care providers and other entities and their business associates that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information;
- federal laws, including the Medicaid Drug Rebate Program, which require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;

- the so-called “federal sunshine” law or Open Payments, which requires pharmaceutical and medical device companies to monitor and report certain financial interactions with physicians, certain non-physician practitioners and teaching hospitals to the federal government for re-disclosure to the public; and
- federal consumer protection and unfair competition laws and regulations, which broadly regulate marketplace activities and that potentially harm consumers.

Also, many states have similar laws and regulations, such as anti-kickback and false claims laws that may be broader in scope and may apply to claims reimbursed by private payors as well as government programs regardless of reimbursement. Additionally, we may be subject to state laws that require pharmaceutical companies to comply with the federal government’s and/or pharmaceutical industry’s voluntary compliance guidelines, impose specific restrictions on interactions between pharmaceutical companies and healthcare providers or require pharmaceutical companies to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Other state laws may require pharmaceutical companies to file reports relating to pricing and marketing information and state and local laws that require the registration of pharmaceutical sales representatives. The distribution of drugs and biological products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products. Finally, there are state 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. Many of these laws and regulations also contain ambiguous requirements or require administrative guidance for implementation.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Given the breadth of the laws and regulations, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, governmental authorities may possibly conclude that our business practices may not comply with such laws. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly, time-consuming and may require significant 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.

Coverage and reimbursement

In the United States and markets in other countries, patients and providers generally rely on third-party payors to reimburse all or part of the costs associated with treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. 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 United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. Obtaining coverage and an adequate reimbursement may prove challenging for new products as such products may need to demonstrate their relative cost effectiveness and gain market acceptance.

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, which could further limit a company’s revenue generated from the sale of any approved products. Coverage and reimbursement may vary across payors. 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.

Healthcare reform

The U.S. government and individual states have been aggressively pursuing healthcare reform designed to impact delivery of, and/or payment for, healthcare, which include initiatives intended to reduce the cost of

healthcare. For example, in March 2010, the U.S. Congress enacted the ACA, which, among other things, expanded healthcare coverage through Medicaid expansion and the implementation of the individual health insurance mandate; included changes to the coverage and reimbursement of drug products under government healthcare programs; imposed an annual fee on manufacturers of branded drugs; and expanded government enforcement authority. We face uncertainties because there have been, and may be additional, federal legislative and administrative efforts to repeal, substantially modify or invalidate some or all of the provisions of the ACA. For example, tax reform legislation was enacted at the end of 2017 that eliminated the tax penalty for individuals who do not maintain sufficient health insurance coverage beginning in 2019. The ACA has also been subject to judicial challenge. For example, in June 2021, the Supreme Court rejected a challenge to the constitutionality of the ACA on the grounds that the states and individuals that brought the challenge did not have standing.

Beyond the ACA, there have been ongoing legislative and administrative reform efforts that affect pricing or payment for drug products or the healthcare industry more generally. Drug pricing and payment reform was a focus of the Trump Administration and has been a focus of the Biden Administration. For example, federal legislation enacted in 2021 eliminates a statutory cap on Medicaid drug rebate program rebates effective January 1, 2024. As another example, in 2022, the Inflation Reduction Act (IRA) of 2022 contains various drug pricing and payment provisions. Among other provisions, the IRA imposes a yearly cap ($2,000 in 2025) on out-of-pocket prescription drug costs in Medicare Part D, implements a new Medicare Part D manufacturer discount drug program in 2025; requires manufacturers to pay a rebate to the federal government if prices for single-source drugs and biologicals covered under Medicare Part B and nearly all covered drugs under Part D increase faster than the rate of inflation and, starting in 2026, creates a drug price negotiation program under which the prices for certain high Medicare spend drugs and biologicals without generic or biosimilar competition will be limited by a cap that is defined by reference to, among other things, a specified non-federal average manufacturer price.

Some of the health care reform changes have been and may continue to be subject to legal challenge. For example, revisions to regulations under the federal anti-kickback statute would remove protection for traditional Medicare Part D discounts offered by pharmaceutical manufacturers to pharmacy benefit managers and health plans. Pursuant to court order, the removal was delayed, and the IRA further delayed implementation of the rule until January 1, 2032. Adoption of new healthcare reform legislation at the federal or state level could negatively affect demand for, or pricing of, our products or product candidates if approved for sale.

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 manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, Centers for Medicare & Medicaid Services, or CMS, may develop new payment and delivery models, such as bundled payment models. In addition, in recent years, 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.

In addition, individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

In addition, other legislative changes have been adopted that could have an adverse effect upon, and could prevent, our products' or product candidates' commercial success. For example, the Budget Control Act of 2011, as amended, or the Budget Control Act, includes provisions intended to reduce the federal deficit, including reductions in Medicare payments to providers through 2031 (except May 1, 2020 to March 31, 2022). Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs, or any significant taxes or fees imposed as part of any broader deficit reduction effort or legislative

replacement to the Budget Control Act, or otherwise, could have an adverse impact on our anticipated product revenues.

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 and pricing and reimbursement schemes vary widely from country to country. For example, the domestic laws of various European Union (EU), may restrict the range of products for which their national health insurance systems provide reimbursement and control, both directly and indirectly, the prices of medicinal products for human use. Some EU Member States provide that products may be marketed only after a reimbursement price has been agreed. Some EU Member States may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or standard of care in order to obtain reimbursement or pricing approval. 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. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

Other U.S. environmental, health and safety laws and regulations

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

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. 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 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.

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 record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

European Union drug development

In the EU, our future products also may be subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls. The EU clinical trials regulatory framework is currently in the process of transitioning to an updated regime. Although the old regime, the EU Clinical Trials Directive 2001/20/EC, or the CTD, sought to harmonize the EU clinical trials regulatory framework the EU Member States applied the provisions of the CTD differently. This led to significant variations in the Member State regimes. Under the current regime, before a clinical trial can be initiated it must be authorized in each of the EU Member States where the trial is to be conducted by the National Competent Authority, or NCA, and an Ethics Committee, or EC, in each EU Member State where the trial is to be conducted must have issued a favorable opinion on the trial. Under the old regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the EU Member State where they occurred.

As of January 31, 2022, Regulation (EU) No 536/2014 on clinical trials (the CTR), came into effect, and with it, the launch of the Clinical Trials Information System (CTIS), the centralized EU portal and database for clinical trials.

The CTR is directly applicable in all EU Member States (and so does not require national implementing legislation in each EU Member State). The CTR has simplified the approval process for clinical trials to be carried out in the EU. Rather than applying for a clinical trial authorization in each EU Member State where the trial will be conducted, the CTR provides that one application be submitted centrally, via CTIS, which will then be reviewed by designated NCAs. If successful, the resulting decision arising from the evaluation process would cover all EU Member States concerned by the application. The CTR foresees a transition period: until January 30, 2023, sponsors can choose whether to submit an initial clinical trial authorisation application in line with the CTD or via CTIS; and from January 31, 2023, the submission of initial CTA applications for a new clinical trial via CTIS will become mandatory. By January 31, 2025, all ongoing trials approved under the CTD must comply with the CTR and information relating to such clinical trials must be recorded in CTIS.

We will no longer pursue renewal of the designation as a small and medium-sized enterprise, or SME, with the European Medicines Agency, or EMA, because iTeos SA, an entity based in Belgium for the purpose of the designation, exceeds the thresholds set out in the Commission Recommendation of 6 May 2003 (2003/361/EC). The SME designation was withdrawn in December 2022.

European Union drug marketing

Much like the Anti-Kickback Statue prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to induce or reward improper performance generally is usually governed by the national anti-bribery laws of EU Member States, and the Bribery Act 2010 in the UK. Infringement of these laws could result in substantial fines and imprisonment according to the respective local enforcement regimes. EU Directive 2001/83/EC, which governs medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the United Kingdom, or UK, despite its departure from the EU.

In the EU and UK, the statutory regimes applicable to the advertising of medicinal products are supplemented by codes of practice which are developed by trade organizations. Such codes of practice are only binding on companies which are members of the relevant trade organization. However, since they represent the best practice, many non-members choose to abide by these codes of practices too. Pursuant to these codes of practice, payments made to physicians must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, their competent professional organization and/or the regulatory authorities of the individual EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

European drug review and approval

In the European Economic Area, or EEA, which is comprised of the 27 Member States of the EU together with Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a marketing authorization, or MA. There are two types of marketing authorizations.

- The centralized MA is issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and is valid throughout the entire territory of the EEA. The centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products (i.e.; those which are developed using recombinant DNA technology, controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells, and hybridoma and monoclonal antibody methods), orphan medicinal products, advanced-therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines) and medicinal products containing a new active substance indicated for the treatment of an acquired immune deficiency syndrome (such as HIV or AIDS), cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance for indications not covered by the mandatory centralized procedure, for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the centralized procedure the maximum timeframe for the evaluation of a MA application 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 a MA application considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant an MA, which is ordinarily 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 a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of a MA application under the accelerated assessment procedure is 150 days, excluding stop-clocks, 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 MAs, which are issued by the NCAs of the EEA Member States and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EEA Member State, this national MA can be recognized in another EEA Member States through the mutual recognition procedure. If the product has not received a national MA in any Member State at the time of application, it can be approved simultaneously in various EEA Member States through the decentralized procedure.

Under the above described procedures, before granting the MA, the EMA or the NCAs of the EEA Member States make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety, and efficacy.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized MAs (under the Northern Irish Protocol, centralized MAs will continue to be recognized in Northern Ireland). All medicinal products with a current centralized MA were automatically converted to Great Britain MAs on January 1, 2021, unless the MA holders opted-out of the automatic conversion process. For a period of three years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or 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 MA. A separate application will, however, still be required.

European new active substance exclusivity

In the EEA, innovative medicinal products (including both small molecules and biological medicinal products), sometimes referred to as new active substances, qualify for eight years of data exclusivity upon grant of MA and an additional two years of market exclusivity. The overall ten-year period can be extended to a maximum of 11 years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with currently approved therapies. The equivalent provisions are reflected in domestic law in the UK.

European orphan designation and exclusivity

In the EEA, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions which either affect not more than five in 10,000 persons in the EU, or where it is unlikely that the marketing of the medicine in the EU would generate sufficient return to justify the necessary investment in its development. In each case, there can be no satisfactory method of diagnosis, prevention or treatment of the condition already authorized (or, if such a method exists, the product would be a significant benefit to those affected by the condition).

In the EEA, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers. If orphan status is maintained at the grant of MA, the medicinal product will attract ten years of market exclusivity. This period may be reduced to six years if, at the end of the fifth year, it is established that the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. During the period of market exclusivity, MAs may only be granted "similar medicinal products" for the same therapeutic indication if it can be established that: (i) the new product, although similar to the authorized product, is safer, more effective or otherwise clinically superior; (ii) the MA holder for the authorized product consents to a second orphan medicinal product application; or (iii) the MA holder

for the authorized product cannot supply enough orphan medicinal product. A “similar medicinal product” is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

An equivalent regime is reflected in domestic law in the UK. Under the UK regime, however, orphan designations are not granted and instead a decision is made at the point of MA grant.

European pediatric investigation plan

In the EEA, companies developing a new medicinal product must agree upon a pediatric investigation plan, or PIP, with the EMA’s Pediatric Committee, or PDCO, and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO in circumstances where the medicinal product or the product class is likely to be ineffective or unsafe in part or all of the pediatric population; or the disease or condition occurs only in adult populations or the specific medicinal product does not represent a significant therapeutic benefit over existing treatments in pediatric patients. Products that are granted an MA with the results of the pediatric clinical trials conducted in accordance with the PIP (even where such results are negative) are eligible for six months’ supplementary protection certificate extension. 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.

Brexit and the Regulatory Framework in the United Kingdom

In June 2016, the electorate in the UK voted in favor of leaving the EU (commonly referred to as “Brexit”). The UK formally left the EU on January 31, 2020 and a transition period began on February 1, 2020, during which EU pharmaceutical law remained applicable to the UK, which ended on December 31, 2020. The EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable from 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 the outcomes of GMP inspections and applicants and marketing authorization holders may submit GMP certificates issued by the UK MHRA for sites located outside the EU/EEA as supporting information for EU regulatory submissions. However, the TCA does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. Great Britain has also 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 currently broadly aligns with EU regulations, however it is possible that these regimes may diverge in future. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the UK in the long-term.

European data collection

The collection and use of personal health data in the EEA, is governed by the General Data Protection Regulation, or GDPR, which became effective May 25, 2018. The GDPR applies to any company established in the EEA and to companies established outside the EEA that process personal data in connection with the offering of goods or services to data subjects in the EU or the monitoring of the behavior of data subjects in the European Union. 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, requirements to conduct privacy impact assessments for “high risk” processing, limitations on retention of personal data, special provisions for “sensitive information” including health and genetic information of data subjects, mandatory data breach notification and “privacy by design” requirements, and direct obligations on service providers acting as data 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 U.S. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EEA Member States may result in fines up to 20 million euros or 4% of a company’s global annual revenues for the preceding financial year, whichever is higher. Moreover, the GDPR grants data subjects the right to request deletion of personal

information in certain circumstances, and claim material and non-material damages resulting from infringement of the GDPR. Maintaining compliance with the GDPR will require significant time, resources, and expense, and we may be required to put in place additional mechanisms to ensure compliance with data protection rules. This may be onerous and adversely affect our business, financial condition, results of operations, and prospects.

In addition, as of January 1, 2021, the United Kingdom'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.

Rest of the world regulation

For other countries outside of the European Union and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Human Capital Resources

Our mission to discover, develop and deliver breakthrough immunotherapies to improve and extend the lives of people with cancer is dependent on our ability to attract, develop and retain the industry's best and brightest talent around the world and across all dimensions of diversity. This understanding lies at the forefront of our approach to human capital management.

General Information: As of December 31, 2022, we had 125 full-time employees, 47 of whom have Ph.D. or M.D. degrees. Of these full-time employees, 99 employees are engaged in research and development activities and 26 employees are engaged in finance, legal, human resources, facilities and general management. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages. We consider our relationship with our employees to be good.

Equity, Diversity and Inclusion: At iTeos, we celebrate our differences and value the power of a diverse array of people who bring all of themselves to work. We embrace cultural, racial, gender, cognitive, social and professional diversity because we know that the only way we can make new cures possible is by working together. Among our employees as of December 31, 2022, women represent 58% and men represent 42% of our global workforce. Women represent 43% of the leadership positions at the Director level or above, and our Executive Committee, which represents the most senior leadership positions at the Company, is 43% female.

Compensation and Benefits: We are committed to rewarding, supporting, and developing our employees. To that end, we offer a comprehensive total rewards package that includes market-competitive pay, broad-based equity grants and bonuses, healthcare benefits, pension and retirement savings plans, paid time off and an Employee Assistance Program.

Ongoing Professional Development: We prioritize our employees' career advancement, and actively work across the organization to provide opportunities for our people to grow with the company and assume more senior roles as the company expands.

Safety and Well-Being: Employee health and safety in the workplace is one of our main priorities. We established a Health and Safety Committee, which provides a forum for employees and management to work together to prevent health and safety problems and to develop strategies to ensure a safe and healthy work environment. As a result of the challenges the COVID-19 pandemic brought, we took various steps to support our employees, including transitioning to a hybrid work model and offering flexible schedules.

Corporate Information

We were incorporated in October 2019 under the laws of the State of Delaware. Our principal executive offices are located at 321 Arsenal Street, Watertown, Massachusetts 02472, and our telephone number is (339) 217-0162. We have a subsidiary located in Belgium, iTeos Belgium SA, which was incorporated in August 2011 under the laws of Belgium.

Available Information

Our website address is www.iteostherapeutics.com, and our investor relations website is located at investors.iteostherapeutics.com. The information contained in or accessible from our websites is not incorporated into this Annual Report, and you should not consider it part of this Annual Report. We have included our websites address in this Annual Report solely as an inactive textual reference. We will make available on our website, free of charge, our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The SEC maintains an Internet site (http://www.sec.gov) containing reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC.

Item 1A. Risk Factors.

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see the Section titled "Forward-Looking Statements" of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks related to the development of our product candidates

We must complete successful preclinical studies and clinical trials that demonstrate the safety and efficacy of our product candidates before we can begin the commercialization process.

We are focused on the development of inupadenant and EOS-448. A key part of our strategy, however, is to continue to pursue clinical development of additional product candidates designed to address the main causes of PD-1 or other standard-of-care resistance. Developing, obtaining marketing approval for, and commercializing product candidates requires substantial funding and remains subject to the risks of failure inherent at each stage of product development, including the occurrence of unexpected or unacceptable adverse events or the failure to demonstrate efficacy in clinical trials. Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain.

The results of preclinical studies, preliminary study results, and early clinical trials of our current product candidates and any future product candidates may not be predictive of the results of later-stage clinical trials. Even if early-stage clinical trials are successful, we may need to conduct additional clinical trials of our product candidates in additional patient populations or under different treatment conditions before we are able to seek approvals from the FDA or comparable foreign regulatory authorities. Our product candidates may not perform as we expect, may ultimately have a different or no impact on tumors, may have a different mechanism of action than we expect, and may not ultimately prove to be safe and effective. We may modify development plans, including selecting different combinations or indications or discontinuing clinical activities, or determine to pursue development of different product candidates as we obtain additional clinical and nonclinical data.

Results from preclinical studies and early-stage trials, and trials in compounds that we believe are similar to ours, may not be representative of results that are found in larger, controlled, blinded, and longer-term studies and trials. Product candidates may fail at any stage of preclinical or clinical development. Product candidates may fail to show the desired safety and efficacy traits even if they have progressed through preclinical studies or initial clinical trials. Preclinical studies and clinical trials may also reveal unfavorable product candidate characteristics, including safety concerns. A number of companies in the biopharmaceutical industry have suffered significant setbacks in clinical trials, notwithstanding promising results in earlier preclinical studies or clinical trials or promising mechanisms of action. In some instances, 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. Moreover, flaws in the design of a clinical trial may negatively impact results. We may not discover such a flaw until the clinical trial is at an advanced stage.

Additionally, our clinical trials, to date, have been open-label trials, where both the patient and investigator know whether the patient is receiving the investigational product candidate or an existing approved drug, which may introduce study bias. Most typically, open-label clinical trials test only the investigational product candidate and sometimes do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Positive results observed in open-label trials may not be replicated in later placebo-controlled trials. We may also experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial, conduct a clinical trial at a prospective trial site, or may require that we modify or amend our clinical trial protocols;

- we may experience delays in reaching, or fail to reach, agreement on acceptable terms for clinical trial contracts or clinical trial protocols with prospective trial sites and/or clinical research organizations, or CROs;
- we may be unable to initiate or complete preclinical studies or clinical trials on time or at all due to the ongoing impacts of the COVID-19 pandemic;
- clinical trials may produce negative or inconclusive results, or our studies may fail to reach the necessary level of statistical significance, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials or be lost to follow-up at a higher rate than we anticipate, or participants may elect to participate in alternative clinical trials sponsored by our competitors with product candidates that treat the same indications as our product candidates;
- our third-party contractors may fail to comply with regulatory requirements or the clinical trial protocol, or meet their contractual obligations to us in a timely manner, or at all, or we may be required to engage in additional clinical trial site monitoring;
- we, regulators, or IRBs may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects, or other unexpected characteristics of the product candidate, including where combination dosing of or with our product candidates results in serious adverse events or undesirable side effects, or due to findings of undesirable effects caused by a chemically or mechanistically similar therapeutic or therapeutic candidate;
- marketing approval policies could change during the development period, rendering our data insufficient to obtain marketing approval;
- statutes or regulations or site policies could be amended or new ones could be adopted;
- changes could be adopted in the regulatory review process for submitted product applications;
- the cost of clinical trials may be greater than we anticipate or we may have insufficient funds for a clinical trial;
- the supply or quality of materials necessary to conduct clinical trials may be insufficient or inadequate or may be interrupted or impacted by the COVID-19 pandemic;
- we may decide, or regulators may require us, to conduct or gather, as applicable, additional clinical trials, analyses, reports, data, or preclinical studies, or we may abandon product development programs;
- we may fail to reach an agreement with regulators or IRBs regarding the scope, design, or implementation of our clinical trials, and the FDA or comparable foreign regulatory authorities may require changes to our study designs that make further study impractical or not financially prudent;
- we may have delays in adding new investigators or clinical trial sites, or we may experience a withdrawal of clinical trial sites;
- patients that enroll in our studies may misrepresent their eligibility or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the study or clinical trial, increase the needed enrollment size for the clinical trial or extend its duration;
- there may be regulatory questions or disagreements regarding interpretations of data and results, or new information may emerge regarding our current product candidates and any future product candidates;
- the FDA or comparable foreign regulatory authorities may disagree with our study design, including endpoints, or our interpretation of data from preclinical studies and clinical trials or find that a product candidate’s benefits do not outweigh its safety risks;

- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug or biologic candidate is safe and effective for its proposed indication or a related companion diagnostic is suitable to identify appropriate patient populations;
- the FDA or comparable foreign regulatory authorities may not accept data from studies with clinical trial sites in foreign countries;
- the FDA or comparable foreign regulatory authorities may disagree with our intended indications;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or our manufacturing facilities for clinical and future commercial supplies;
- the data collected from clinical trials of our current product candidates and any future product candidates may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of an BLA or NDA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may take longer than we anticipate to make a decision on our current product candidates and any future product candidates; and
- we may not be able to demonstrate that a product candidate provides an advantage over current standards of care or current or future competitive therapies in development.

Our development costs also will increase if we experience delays in testing or approvals, and we may not have sufficient funding to complete the testing and approval process. We may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization. Significant delays relating to any preclinical or clinical trials also could shorten any periods during which we may have the exclusive right to commercialize our current product candidates and any future product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our current product candidates and any future product candidates and may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays in clinical trials may ultimately lead to the denial of marketing approval of any of our current product candidates and any future product candidates. If any of these occur, our business, financial condition, results of operations, stock price and prospects may be materially harmed.

Challenges enrolling patients in our clinical trials may delay or prevent clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials is critical to our success. The timing of completion of our clinical trials depends in part on the speed at which we can recruit patients to participate in our clinical trials. We may not be able to initiate or continue clinical trials if we are unable to locate and enroll and retain sufficient numbers of eligible patients to participate in these trials. The COVID-19 pandemic may impact our ability to initiate clinical sites and recruit, enroll and retain patients or may divert healthcare resources away from clinical trials.

In addition to the competitive trial environment, the eligibility criteria of our planned clinical trials will further limit the pool of available participants as we will require that participants have specific, measurable characteristics to assure their cancer is severe enough but not too advanced for inclusion in a trial and exclude participants who have conditions that may increase the risk associated with participation in a trial. Additionally, the process of finding patients is costly. If patients are unwilling to participate in our trials, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products will be delayed.

The enrollment of patients further depends on many factors, including:

- the size of the patient population and process for identifying patients;
- the eligibility criteria for the clinical trial in question;
- the availability of an appropriate screening test, as necessary;
- the perceived risks and benefits of the product candidate under study, including as a result of lack of efficacy or adverse events observed in similar or competing product candidates;
- the efforts to facilitate timely enrollment in clinical trials;
- the proximity and availability of clinical trial sites for prospective patients;
- the design of the clinical trial;

- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents;
- reporting of preliminary results of any of our clinical trials, and/or reporting of results of clinical trials of our competitors; and
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion.

Our clinical trials compete with other clinical trials for product candidates that treat the same indications or are in the same therapeutic areas, and this competition may reduce the number and types of eligible patients available to us because some patients who might have opted to enroll in our clinical trials may instead opt to enroll in a competitor's clinical trial. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation of such patients in our clinical trials.

We anticipate that our 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.

Our product candidates have the potential to be administered or co-formulated in combination with checkpoint inhibitor immunotherapies or other standards of care like chemotherapies, targeted therapies or radiotherapy. For example, we are currently conducting a multi-arm Phase 1/2a clinical trial of inupadenant as a single agent and in combination with pembrolizumab. In addition, in collaboration with GSK, we are exploring the development of EOS-448 with multiple combinations, including with dostarlimab. Our ability to develop and ultimately commercialize our product candidates used in combination with pembrolizumab or any other checkpoint inhibitor immunotherapies 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 the commercialized product, if approved. We cannot be certain that commercial relationships, including our collaborations with Merck and GSK, will provide us with a steady supply of such drugs or biologics on commercially reasonable terms or at all.

Failure to maintain or enter into new successful commercial relationships, or the expense of purchasing checkpoint inhibitor immunotherapies or other comparator therapies, may delay our development timelines, increase our costs and jeopardize our ability to develop our product candidates as commercially viable therapies. If any of these occur, our business, financial condition, results of operations, 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. We are currently developing inupadenant and EOS-448 for use in combination with checkpoint inhibitor immunotherapies and with other therapies and may develop inupadenant, EOS-448, or any future product candidates for use with other therapies. The FDA 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. The results of such trials could show that any positive previous trial results are attributable to the combination therapy and not our product candidates. Moreover, following product approval, the FDA or comparable foreign regulatory authorities may require that products used in conjunction with each other be cross labeled for combined use, which may require us to work with a third party to satisfy such a requirement. Additionally, developments related to the other product may impact our clinical trials for the combination as well as our commercial prospects should we receive marketing approval. Such developments may include changes to the other product’s safety or efficacy profile, changes to the availability of the approved product, quality, manufacturing and supply issues, and changes to the standard of care.

In the event that Merck, GSK or any other collaborator or supplier cannot continue to supply their products on commercially reasonable terms, we would need to identify alternatives for accessing such products. Additionally, should the supply of products from Merck, GSK or any other 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, results of operations, stock price and prospects may be materially harmed.

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

Because we have limited financial and managerial resources, we must focus on a limited number of research programs and product candidates and on specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial

potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future discovery and preclinical development programs and product candidates for specific indications may not yield any commercially viable products.

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

From time to time, we may publish interim top-line or preliminary results from our clinical trials. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

We may not be able to file IND applications or IND amendments to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA or comparable foreign regulatory authorities may not permit us to proceed.

The FDA or comparable foreign regulatory authorities may require us to file separate INDs for additional clinical trials we plan to conduct with our current lead product candidates, inupadenant and EOS-448. We may not be able to file any additional INDs on the timelines we expect. For example, we may experience manufacturing delays or other delays with IND-enabling studies, including due to the impact of the COVID-19 pandemic on suppliers, study sites, or third-party contractors and vendors on whom we depend. Moreover, we cannot be sure that submission of an IND or submission of a trial to an IND will result in the FDA or comparable foreign regulatory authorities allowing further clinical trials to begin, or that, once begun, issues will not arise that lead us to suspend or terminate clinical trials. Additionally, even if regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, such regulatory authorities may change their requirements in the future. The FDA or comparable foreign regulatory authorities may require the analysis of data from trials assessing different doses of the product candidate alone or in combination with other therapies to justify the selected dose prior to the initiation of large trials in a specific indication. Any delays or failure to file INDs, initiate clinical trials, or obtain regulatory approvals for our trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all. We are subject to similar risks related to the review and authorization of our protocols and amendments by comparable foreign regulatory authorities.

We are conducting clinical trials for product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We are conducting and in the future may conduct one or more clinical trials outside the United States, including in Europe and in Asia. The acceptance of data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice, or GCP, regulations. In general, the patient population for any clinical trials conducted outside the United States must be representative of the population for whom we intend to label the product candidate in the United States. Additionally, the FDA's clinical trial requirements, including applicable study design, sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA 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, additional trials would be needed, which could be costly and time-consuming, and which may result in our product candidates not receiving approval for commercialization in the applicable jurisdiction.

As an organization, we have never conducted pivotal clinical trials, and we may be unable to do so for any product candidates we may develop.

We will need to successfully complete pivotal clinical trials in order to obtain the approval of the FDA or comparable foreign regulatory authorities to market inupadenant, EOS-448, or any future product candidate. Carrying out pivotal clinical trials is a complicated process. As an organization, we have not previously conducted any later stage or pivotal clinical trials. In order to do so, we will need to continue to expand our clinical

development and regulatory capabilities, and we may be unable to recruit and train qualified personnel. We also expect to continue to rely on third parties to conduct our pivotal clinical trials. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to BLA or NDA submission and approval of inupadenant, EOS-448, or future product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates.

We face significant competition from other biopharmaceutical and biotechnology companies, academic institutions, government agencies, and other research organizations, which may result in others discovering, developing or commercializing products more quickly or marketing them more successfully than us. If their product candidates are shown to be safer or more effective than ours, our commercial opportunity may be reduced or eliminated.

The development and commercialization of cancer immunotherapy products is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary rights. We face competition with respect to our product candidates, from major biopharmaceutical companies, specialty biopharmaceutical companies, and biotechnology companies worldwide. A number of large biopharmaceutical and biotechnology companies currently market and sell products, or are pursuing the development of products, for the treatment of solid and liquid tumors. 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.

While our product candidates are intended to be used in combination with other drugs or biologics with different mechanisms of action, if and when marketed they will compete with a number of drugs and biologics that are currently marketed or in development.

Our commercial opportunities 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 easier to administer, or are less expensive alone or in combination with other therapies than products we may develop alone or in combination with other therapies. Our competitors also may obtain FDA or comparable foreign regulatory authorities' approval for their products more rapidly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected by insurers, government, or other third-party payor coverage decisions.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products. Mergers and acquisitions in the biopharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties 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 developing or acquiring technologies complementary to, or necessary for, our programs. If we are unable to successfully compete with these companies our business, financial condition, results of operations, stock price and prospects may be materially harmed.

The size of the potential market for our product candidates is difficult to estimate and, if our assumptions are inaccurate, the actual market for our product candidates may be smaller than our estimates.

The potential market opportunities for our product candidates are difficult to estimate and depend on the drugs with which our product candidates are co-administered or co-formulated and the success of competing therapies and therapeutic approaches. Our estimates of potential market opportunities are predicated on many assumptions that involve the exercise of significant judgment on the part of our management, are inherently uncertain, and their reasonableness has not been assessed by an independent source. New information may change the estimated incidence or prevalence of indications, and regulatory approvals, if received, may include limitations for use or contraindications that decrease the addressable patient population. If any of the assumptions proves to be inaccurate, the actual markets for our current product candidates and any future product candidates could be smaller than our estimates of the potential market opportunities.

Negative developments in the field of immuno-oncology or in the field of TIGIT or adenosine pathway therapeutics could damage public perception of our product candidates or negatively affect our business.

The commercial success of our product candidates will depend in part on public acceptance of the use of cancer immunotherapies and our mechanisms of action and developments in TIGIT or adenosine pathway programs of other companies. Adverse events or disappointing results in clinical trials of our product candidates, or in clinical

trials of similar products, as well as any other negative developments in the field of immuno-oncology, including in connection with competitor therapies, could reduce expectations regarding the potential success of our programs and potentially have a negative impact on collaborations. These events also could result in the suspension, discontinuation, or clinical hold of or modification to our clinical trials. If public perception is influenced by claims that the use of cancer immunotherapies is unsafe or ineffective, whether related to our therapies or those of our competitors, our product candidates may not be accepted by the general public or the medical community and potential clinical trial subjects may be discouraged from enrolling in our clinical trials or may discontinue their participation in our clinical trials. Negative developments could result in reduced probability of success of clinical trials involving our product candidates, challenges enrolling clinical trials, greater governmental regulation, stricter labeling requirements, and potential regulatory delays in the testing or approvals of our product candidates.

If we are unable to successfully commercialize any product candidate for which we receive regulatory approval, or experience significant delays in doing so, our business will be materially harmed.

If we are successful in obtaining marketing approval from applicable regulatory authorities for our current or future product candidates, our ability to generate revenues from our product candidates will depend on our success in:

- launching commercial sales, whether alone or in collaboration with others;
- receiving an approved label with claims that are necessary or desirable for successful marketing and does not contain limitations that impede our ability to market the product;
- creating market demand through marketing, sales and promotion activities;
- hiring, training, and deploying a sales force or contracting with third parties to commercialize our product candidates in the United States;
- manufacturing the product in sufficient quantities and at acceptable quality and cost to meet commercial demand;
- establishing and maintaining agreements with wholesalers, distributors, and group purchasing organizations on commercially reasonable terms;
- creating partnerships with, or offering licenses to, third parties to promote and sell our product candidates in foreign markets where we receive marketing approval;
- maintaining patent and trade secret protection or regulatory exclusivity;
- achieving market acceptance of our current product candidates or any future product candidates by patients, the medical community, and third-party payors;
- reimbursement decisions;
- effectively competing with other therapies; and
- maintaining a continued acceptable safety profile of our products.

To the extent we are not able to do any of the foregoing, our business, financial condition, results of operations, stock price and prospects will be materially harmed.

Risks related to government regulation

Even if our development efforts are successful, we may not obtain regulatory approval for any product candidates in the United States or other jurisdictions, which would prevent us from commercializing our product candidates. Even if we obtain regulatory approval for our product candidates, any such approval may be subject to limitations, including with respect to the approved indications or patient populations, which may impair our ability to successfully commercialize our product candidates.

We are not permitted to market, promote, or sell our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information for each therapeutic indication. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Even if our product candidates are approved, they may:

- be subject to limitations on the indicated uses or patient populations for which they may be marketed, distribution restrictions, or other conditions of approval;

- contain significant safety warnings, including boxed warnings, contraindications, and precautions;
- not be approved with label statements necessary or desirable for successful commercialization; or
- contain requirements for costly post-market testing and surveillance, or other requirements, including the submission of a REMS to monitor the safety or efficacy of the products.

We have not previously submitted a BLA or NDA to the FDA, or a similar marketing application to comparable foreign regulatory authorities, for any product candidate, and we may not ultimately be successful in obtaining regulatory approval for claims that are necessary or desirable for successful marketing, or at all.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable. If we experience delays in obtaining required regulatory approvals, our ability to generate revenue may be materially impaired.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the discretion of regulatory authorities. 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. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change and may vary among jurisdictions. These regulatory requirements may require us to amend our clinical trial protocols, conduct additional preclinical studies or clinical trials that may require regulatory or IRB approval, or otherwise cause delays in the approval or rejection of an application. Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability to generate revenue from the particular product candidate, which may materially harm our business, financial condition, results of operations, stock price and prospects.

The FDA or a comparable foreign regulatory authority may determine that our product candidates have serious adverse events or undesirable side effects that delay or prevent their regulatory approval or commercialization.

Serious adverse events or undesirable side effects caused by our product candidates could cause us, IRBs, and other reviewing entities or regulatory authorities to interrupt, delay, or halt clinical trials and could result in enrollment challenges, discontinuation of trials, a more restrictive label, or delay or denial of marketing approval. We have identified in the past and may in the future identify serious adverse events suspected to be related to our product candidates. If concerns are raised regarding undesirable side effects or serious adverse events identified during clinical or preclinical testing, including any dose-limiting toxicities, the FDA or comparable foreign regulatory authority may request additional data or information or order us to pause or cease further development, e.g., by issuing a clinical hold on ongoing or planned clinical trials, declining to approve the product candidate, or issuing a letter requesting additional data or information prior to making a final decision regarding whether or not to approve the product candidate. The FDA or comparable foreign regulatory authorities, or IRBs and other reviewing entities, may also require, or we may voluntarily develop, strategies for managing adverse events during clinical development, which could include restrictions on our enrollment criteria, the use of stopping criteria, adjustments to a study's design, reconsent of enrolled patients, or the monitoring of safety data by a data monitoring committee, among other strategies. Requests for additional data or information from the FDA or a comparable foreign regulatory authority also could result in substantial delays in the approval of our product candidates. Additionally, we may evaluate our product candidates in combination with one another, and safety concerns arising during a combination trial could negatively affect the individual development program of each candidate, as the FDA or comparable foreign regulatory authorities may require us to discontinue single-candidate trials until the contribution of each product candidate to any safety issues is better understood.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of a drug or biologic candidate may only be uncovered when a significantly larger number of patients are exposed to the drug or biologic candidate or when patients are exposed for a longer period of time.

Later discovered undesirable side effects may further result in the imposition of a REMS, label revisions, post-approval study requirements, or other testing, and surveillance.

If our product candidates are associated with serious adverse events or undesirable side effects or have properties that are unexpected, we may need to abandon development or limit development of that product candidate to certain 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. The therapeutic-related side effects

could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may materially harm our business, financial condition, results of operations, stock price and prospects.

Regulatory approval by the FDA or comparable foreign regulatory authorities is limited to specific indications and conditions, and we may be subject to substantial fines, criminal penalties, injunctions, or other enforcement actions if we are determined to be promoting the use of our products for unapproved or "off-label" uses, or in a manner inconsistent with the approved labeling, resulting in damage to our reputation and business.

We must comply with requirements concerning advertising and promotion for any product candidates for which we obtain marketing approval. Promotional communications with respect to therapeutics are subject to a variety of legal and regulatory restrictions and continuing review by the FDA and comparable foreign regulatory authorities. When the FDA or comparable foreign regulatory authorities issue regulatory approval for a product candidate, the regulatory approval is limited to those specific uses and indications for which a product is approved. If we are not able to obtain FDA or comparable foreign regulatory authority approval for desired uses or indications for our product candidates, we may not market or promote them for those indications and uses, referred to as off-label uses, and our business, financial condition, results of operations, stock price, prospects and reputation may be materially harmed. We also must sufficiently substantiate any claims that we make for our products, including claims comparing our products to other companies' products, and must abide by the FDA or comparable foreign regulatory authority's strict requirements regarding the content of promotion and advertising.

While physicians may choose to prescribe products for uses that are not described in the product's labeling, we and any third parties engaged on our behalf are prohibited from marketing and promoting the products for indications and uses that are not specifically approved by the FDA or comparable foreign regulatory authorities. If we market our medicines for off-label use, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. A company that is found to have promoted off-label uses may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions. Even if it is later determined that we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions and have to divert significant management resources from other matters.

Even if our current product candidates and any future product candidates receive regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense and limit how we manufacture and market our products.

Any product candidate for which we obtain marketing approval will be subject to extensive and ongoing requirements of and review by the FDA and comparable foreign regulatory authorities, including requirements related to the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, applicable tracking and tracing requirements, export, import, advertising, marketing, and promotional activities. These requirements further include submissions of safety and other post-marketing information, including manufacturing deviations and reports, registration and listing requirements, the payment of annual fees, continued compliance with the FDA's cGMP, requirements relating to manufacturing, quality control, quality assurance, and corresponding maintenance of records and documents, and GCPs for any clinical trials that we conduct post-approval.

We and any of our suppliers or collaborators, including our CMOs, would be subject to periodic inspections by the FDA to monitor and ensure compliance with cGMPs and other FDA regulatory requirements. Application holders must further notify the FDA, and depending on the nature of the change, obtain FDA pre-approval for product and manufacturing changes.

In addition, later discovery of previously unknown adverse events or that the product is less effective than previously thought or other problems with our products, manufacturers, or manufacturing processes, or failure to comply with regulatory requirements either before or after approval, may yield various negative results, including:

- restrictions on manufacturing, distribution, or marketing of such products;
- restrictions on the labeling, including required additional warnings, such as boxed warnings, contraindications, precautions, and restrictions on the approved indication or use;
- modifications to promotional pieces;
- issuance of corrective information;

- requirements to conduct post-marketing studies or other clinical trials;
- clinical holds or termination of clinical trials;
- requirements to establish or modify a REMS or similar strategy;
- changes to the way the product candidate is administered;
- liability for harm caused to patients or subjects;
- reputational harm;
- the product becoming less competitive;
- warning or untitled letters;
- suspension of marketing or withdrawal of the products from the market;
- regulatory authority issuance of safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the product candidate;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recalls of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure or detention;
- FDA or comparable foreign regulatory authority debarment, suspension and debarment from government contracts, and refusal of orders under existing government contracts, exclusion from federal healthcare programs, consent decrees, or corporate integrity agreements; or
- injunctions or the imposition of civil or criminal penalties, including imprisonment.

We may in the future seek orphan drug status for our product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.

We may seek orphan drug designation for some or all of our product candidates in orphan indications in which there is a medically plausible basis for the use of these products. Even if we obtain orphan drug designation, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan designated indication and 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 quantities of the product to meet the needs of patients with the rare disease or condition. In addition, the FDA has expressed concerns regarding the regulatory considerations for orphan drug designation as applied to tissue agnostic therapies, and the FDA may interpret the federal Food, Drug and Cosmetic Act, as amended, or the FD&C Act, and regulations promulgated thereunder in a way that limits or blocks our ability to obtain orphan drug designation or orphan drug exclusivity, if our current product candidates and any future product candidates are approved, for our targeted indications.

The FDA may reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

We may pursue Fast Track or Breakthrough Therapy designation by FDA. These designations may not actually lead to a faster development or regulatory review or approval process, and they do not assure FDA approval of any product candidates we may develop.

FDA's Fast Track and Breakthrough Therapy designations programs are intended to expedite the development of certain qualifying products intended for the treatment of serious diseases and conditions. While we may seek Fast Track or Breakthrough Therapy designation, there is no guarantee that we will be successful in obtaining any such designation. Even if we do obtain such designation, we may not experience a faster development process, review, or approval compared to conventional FDA procedures. Fast Track or Breakthrough Designation alone do

not guarantee qualification for the FDA's priority review procedures. A Fast Track or Breakthrough Therapy designation does not ensure that the product candidate will receive marketing approval or that approval will be granted within any particular timeframe. In addition, the FDA may withdraw Fast Track or Breakthrough Therapy designation if it believes that the designation is no longer supported by data from our clinical development program.

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 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 product candidates. 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, likely will require the conduct of clinical trials to demonstrate the safety and effectiveness of any diagnostics we or our collaborators may develop, which we expect will require separate regulatory clearance or approval prior to commercialization.

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 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 marketing approval, and we may not realize the full commercial potential of any of these therapeutics that obtain marketing approval. As a result, our business, results of operations and financial condition could be materially harmed.

Inadequate funding for the FDA, the SEC, and other government agencies 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 or comparable foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. 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.

The FDA generally is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals. However, FDA may not be able to continue its current pace and review timelines could be extended. In addition, where a pre-approval inspection or an inspection of clinical sites is required and due to the COVID-19 pandemic and travel restrictions FDA is unable to complete such required inspections during the review period, action on such applications may be delayed or prevented. Similarly, regulatory authorities outside the United States may experience delays in their regulatory activities.

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

The regulations that govern regulatory approvals, pricing and reimbursement for new drugs and biologics vary widely from country to country. Some countries require approval of the sale price of a drug or biologic before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some

foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product candidate, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product candidate in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more of our product candidates, even if our product candidates obtain marketing approval.

In the United States, the availability and adequacy of coverage and reimbursement by third-party payors, including governmental healthcare programs such as Medicare and Medicaid, as well as private health insurance, will likely be essential for most patients to be able to afford our product candidates, assuming regulatory approval. There is significant uncertainty related to third party payor coverage and reimbursement of newly-approved products. No uniform policy for coverage and reimbursement for products exists among third-party payors. Coverage and reimbursement for products can differ significantly from payor to payor and coverage and reimbursement by one payor does not guarantee coverage and reimbursement by another payor. Third-party payors increasingly are limiting coverage and utilization of pharmaceutical products and challenging prices charged for pharmaceutical products and services. Assuming we obtain coverage for a product by a third-party payor, the third-party payor may implement utilization management controls, such as requiring pre-approval before our product will be covered for a particular patient, which may limit access to our product. In addition, the reimbursement rates may not be adequate or may require co-payments that patients find unacceptably high. Net prices for our products may be reduced by mandatory discounts or rebates that we are required to provide to certain government healthcare programs or private payors or by discounts we negotiate with third party payors. If coverage is limited, access to our products is subject to utilization management controls or reimbursement is inadequate, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates.

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

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell a product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, numerous legislative and regulatory initiatives have been proposed to contain healthcare costs, some of which have been implemented. We expect that federal and state 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 product candidates or additional pricing pressures. See “Government Regulation – Healthcare Reform”.

Limitations in coverage or reduction in reimbursement from Medicare or other government programs may result in similar actions from private payors, which may adversely affect our future profitability.

Our relationships with healthcare providers, customers, and third-party payors will be subject to applicable fraud and abuse, privacy and price reporting and payment and other healthcare laws and regulations, which could expose us to significant administrative, civil, and criminal penalties, damages, fines, disgorgement, imprisonment, exclusion from government healthcare programs, contractual damages, reputational harm, and diminished profits and future earnings.

Our arrangements with healthcare providers, third-party payors, customers, and others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that constrain the business or financial arrangements and relationships through which we research, market, sell, and distribute our product candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;

- the federal civil and federal false claims laws and civil monetary penalty laws, including the False Claims Act which can be enforced through civil whistleblower or qui tam actions, impose criminal and civil penalties 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. 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 or fraudulent claim for purposes of the False Claims Act;
- HIPAA imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended, and its implementing regulations which also establish privacy and security standards applicable to certain health care providers and other entities and their business associates that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information;
- federal laws, including the Medicaid Drug Rebate Program, which require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;
- the so-called “federal sunshine” law, which requires pharmaceutical and medical device companies to monitor and report certain financial interactions with physicians, certain non-physician practitioners and teaching hospitals to the federal government for re-disclosure to the public; and
- federal consumer protection and unfair competition laws and regulations, which broadly regulate marketplace activities and that potentially harm consumers.

Also, many states have similar laws and regulations, such as anti-kickback and false claims laws that may be broader in scope and may apply to claims reimbursed by private payors as well as government programs regardless of reimbursement. Additionally, we may be subject to state laws that require pharmaceutical companies to comply with the federal government’s and/or pharmaceutical industry’s voluntary compliance guidelines, impose specific restrictions on interactions between pharmaceutical companies and healthcare providers or require pharmaceutical companies to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Other state laws may require pharmaceutical companies to file reports relating to pricing and marketing information and state and local laws that require the registration of pharmaceutical sales representatives. The distribution of drugs and biological products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products. Finally, there are state 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. Many of these laws and regulations also contain ambiguous requirements or require administrative guidance for implementation.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. We have entered into certain advisory board and consulting agreements with physicians, including some who are compensated in the form of stock or stock options, who may influence the ordering or use of our product candidates, if approved. Given the breadth of the laws and regulations, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, governmental authorities may possibly conclude that our business practices may not comply with such laws and regulations. If our operations were to be found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations.

Failure to comply with environmental, health, and safety laws and regulations, may subject us to fines or penalties, or 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.

Our business activities will be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery and anti-corruption laws.

Expanding our business activities outside of the United States, including our clinical trial efforts, subjects us to the FCPA and similar anti-bribery or anti-corruption laws, regulations, or rules of other countries. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-United States government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-United States governments. Additionally, in many other countries, the healthcare providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers will be subject to regulation under the FCPA. Our employees, agents, suppliers, manufacturers, contractors, or collaborators, or those of our affiliates, may fail to comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of facilities, including those of our suppliers and manufacturers, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries as well as difficulties in manufacturing or continuing to develop our products, and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

Risks related to reliance on third parties

We rely on third parties to conduct our clinical trials and perform some of our research and preclinical studies. Failure by these third parties to satisfactorily carry out their contractual duties or to meet expected deadlines may delay and increase the costs of our development programs, adversely impacting our business and prospects.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are, and expect to remain, dependent on third parties to conduct our ongoing preclinical and clinical trials and any future preclinical and clinical trials of our product candidates. The timing of the initiation and completion of these trials, therefore, is partially controlled by such third parties and may result in delays to our development programs. Specifically, we expect CROs, clinical investigators, and consultants to play a significant role in the conduct of these trials and the subsequent collection and analysis of data. We are not able to control all aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with

product produced under cGMP regulations. Our failure to comply with these regulations may require us to stop and/or repeat clinical trials, which would delay or prevent marketing.

CROs, clinical trial investigators or other third parties on which we rely may fail to devote adequate time and resources to our development activities or perform as contractually required. The performance of our CROs may also be interrupted by the COVID-19 pandemic, including due to travel or quarantine policies, heightened exposure of CRO staff to COVID-19, prioritization of resources toward the pandemic or high turnover rate, including as a result of the "great resignation". If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise performs in a substandard manner, or terminates its engagement with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in such clinical trials unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible. In addition, clinical trial investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or comparable foreign regulatory authorities concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any marketing application we submit by the FDA or any comparable foreign regulatory authority. Any such delay or rejection could prevent us from commercializing our product candidates.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our current product candidates or any future product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our products.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired development timelines. Though we endeavor to carefully manage our relationships with our CROs and other third parties, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We may not realize the benefits of our collaborations, alliances or licensing arrangements, including our collaboration with GSK for the global development of EOS-448.

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

Currently we are party to the GSK Collaboration Agreement, pursuant to which we share with GSK responsibility and costs for the global development of EOS-448. Under the GSK Collaboration Agreement, in the United States we and GSK will jointly commercialize and equally split profits while outside of the United States GSK will receive an exclusive license for commercialization. We are also eligible to receive tiered double digit royalty payments up to 20% during a customary royalty term. Our collaboration with GSK is not without risks, which include the following:

- Our control over the development and commercialization activities of EOS-448 may be limited;
- GSK’s commercialization activities outside the United States may adversely impact our own efforts in the United States;
- Relying on GSK to commercialize any products containing or comprising EOS-448 that obtain regulatory approval, may cause us to receive less revenues than if we commercialized these products ourselves, which could materially harm our prospects;
- GSK may compete with us, or collaborate with our competitors;

- GSK may not properly maintain or defend our intellectual property rights or may improperly use our intellectual property or proprietary information;
- GSK may fail to meet its obligations under the GSK Collaboration Agreement, to apply sufficient efforts at developing and commercializing EOS-448, or to comply with applicable legal or regulatory requirements;
- GSK may terminate the GSK Collaboration Agreement, which could damage perception of our product candidates, slow down our execution and timelines, and negatively affect the clinical development or commercialization of EOS-448; and
- disputes may arise between us and GSK that cause the delay or termination of the development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management attention and resources.

The occurrence of any of the risks detailed above may materially adversely affect our business and our results of operations. Future collaborations will likely be subject to similar risks as outlined above. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex.

We may not realize the benefits of collaborations related to companion diagnostic tests for our therapeutic product candidates.

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 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. 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 candidates.

We rely on third parties to manufacture our product candidates, and we expect to continue to rely on third parties for the clinical as well as any future commercial supply of our product candidates. The development of our product candidates, and the commercialization of any approved products, could be stopped, delayed or made less profitable if any such third party fails to provide us with sufficient clinical or commercial quantities of such product candidates or products, fails to do so at acceptable quality levels or prices or fails to achieve or maintain satisfactory regulatory compliance.

We do not currently have, and we do not plan to build, the infrastructure or capability internally to manufacture product candidates for use in the conduct of our clinical trials or, if approved, for commercial supply. We rely on, and expect to continue to rely on, contract manufacturing organizations, or CMOs. Reliance on third-party providers may expose us to more risk than if we were to manufacture our product candidates ourselves. We do not control the manufacturing processes of the CMOs we contract with and are dependent on those third parties for the production of our product candidates in accordance with relevant applicable regulations such as cGMP, which includes, among other things, quality control, quality assurance and the maintenance of records and documentation.

In complying with the manufacturing regulations of the FDA and comparable foreign regulatory authorities, we and our third-party suppliers must spend significant time, money, and effort in the areas of design and development, testing, production, record-keeping and quality control to assure that the products meet applicable specifications and other regulatory requirements. The failure to comply with these requirements could result in an enforcement action against us, including the seizure of products and shutting down of production. We and any of these third-party suppliers also may be subject to inspections by the FDA or comparable foreign regulatory authorities. If any of our third-party suppliers fails to comply with cGMP or other applicable manufacturing regulations, our ability to develop and commercialize our product candidates could suffer significant interruptions.

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 drugs, operating

restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Any disruption, such as a fire, natural hazards or vandalism at our CMOs, or any impacts on our CMOs due to the COVID-19 pandemic, could significantly interrupt our manufacturing capability. We currently do not have alternative production plans in place or disaster-recovery facilities available. In case of a disruption, we will have to establish alternative manufacturing sources. This would require substantial capital on our part, which we may not be able to obtain on commercially acceptable terms or at all. Additionally, we would likely experience months of manufacturing delays as we build facilities or locate alternative suppliers and seek and obtain necessary regulatory approvals. If this occurs, we will be unable to satisfy manufacturing needs on a timely basis, if at all. If changes to CMOs occur, then there also may be changes to manufacturing processes inherent in the setup of new operations for our product candidates and any products that may obtain approval in the future. Any such changes could require the conduct of bridging studies before we can use any materials produced at new facilities or under new processes in clinical trials or, for any products reaching approval, in our commercial supply. Further, business interruption insurance may not adequately compensate us for any losses that may occur and we would have to bear the additional cost of any disruption. For these reasons, a significant disruptive event of any CMOs could have drastic consequences, including placing our financial stability at risk.

Our product candidates and any drugs that we may develop may compete with other product candidates and drugs for access to manufacturing facilities. We may not be able to enter into similar commercial arrangements with other 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 marketing approval.

If we were to experience an unexpected loss of supply of or if any supplier were unable to meet our clinical or commercial demand for any of our product candidates, we could experience delays in our planned clinical studies or commercialization. For example, the COVID-19 pandemic may impact our ability to procure sufficient supplies for the development of our current and future product candidates, and the extent of such impacts will depend on the severity and duration of the spread of the virus and the actions undertaken to contain COVID-19 or treat its effects. We could be unable to find alternative suppliers of acceptable quality and experience that can produce and supply appropriate volumes at an acceptable cost or on favorable terms. Moreover, our suppliers are subject to strict manufacturing requirements and rigorous testing requirements, which could limit or delay production. The long transition periods necessary to switch manufacturers and suppliers, if necessary, would significantly delay our clinical trials and, for any product candidates that reach approval, the commercialization of our products, which would materially adversely affect our business, financial condition and results of operation.

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 our product candidates for clinical trials or our 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. Changes to the manufacturing process often require preclinical and clinical data showing the comparable identity, strength, quality, purity, or potency of the products before and after such changes. Microbial, viral or other contaminations may require closure of facilities for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. The use of biologically derived ingredients also can lead to allegations of harm, including infections or allergic reactions, or closure of product facilities due to possible contamination.

In addition, risks associated with large scale manufacturing for clinical trials or commercial scale include, 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 marketing approval for any of our product candidates, our manufacturers may not 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.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility of competitor discovery, misappropriation, or disclosure.

Because we rely on third parties to research and develop and to manufacture our product candidates, we must share trade secrets. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements, or other similar agreements with our advisors, employees, third-party contractors, and consultants. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. However, our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with often expect to be granted rights to publish data arising out of such collaboration, and any joint research and development programs may require us to share trade secrets under the terms of our research and development or similar agreements. Sharing trade secrets and other confidential information increases the risk that such information becomes known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors, and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's independent discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets.

Risks related to our limited operating history, financial position and capital requirements

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage immuno-oncology company with a limited operating history. We have not yet demonstrated our ability to successfully conduct or complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing, and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

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

Investment in biopharmaceutical product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. We are still in the early stages of development of our product candidates. Inupadenant and EOS-448 are each in ongoing Phase 2 clinical trials. We have no products licensed for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations.

Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates.

We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if and as we:

- conduct preclinical studies and clinical trials for our current and future product candidates;
- continue our research and development efforts and submit INDs for future product candidates;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- build commercial infrastructure to support sales and marketing for any approved product candidates;

- scale up external manufacturing and distribution capabilities for clinical and, if approved, commercial supply of our product candidates;
- expand, maintain and protect our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel and scale up such capabilities; and
- operate as a public company.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop, seek approval for, and market additional product candidates. We may never succeed in these activities and, even if we succeed in commercializing one or more of our product candidates, we may never generate revenues that are significant or large enough to achieve profitability. In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on stockholders' equity.

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

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from any product sales. We have no products approved for commercial sale, and do not anticipate generating any revenue from product sales until after we have received marketing approval for the commercial sale of a product candidate, if ever. Our ability to generate revenue and achieve profitability depends significantly on our success in achieving a number of goals, including:

- initiating and completing research regarding, and preclinical and clinical development of, inupadenant, EOS-448, and any other product candidates;
- obtaining marketing approvals for inupadenant, EOS-448, and any other product candidates for which we complete clinical trials;
- developing a sustainable and scalable manufacturing process for inupadenant, EOS-448, and any other product candidates, including establishing and maintaining commercially viable supply and manufacturing relationships with third parties;
- launching and commercializing inupadenant, EOS-448, and any other product candidates for which we obtain marketing approvals, either directly or with a collaborator or distributor;
- obtaining market acceptance of inupadenant, EOS-448, and any other product candidates as viable treatment options;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and developing new product candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter; obtaining, maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

We will require additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce, or terminate our product development or commercialization efforts.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to continue the clinical development of our product candidates, including our ongoing clinical trials for inupadenant and EOS-448 and our ongoing and planned IND-enabling studies for our other product candidates. If approved, we will require significant additional amounts in order to launch and commercialize our product candidates.

Changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. Accordingly, we will need to raise substantial additional capital in connection with our continuing operations.

Our future capital requirements depend on many factors, including:

- the scope, progress, results, and costs of researching and developing inupadenant, EOS-448, and any other product candidates, and conducting preclinical studies and clinical trials;
- the timing of, and the costs involved in, obtaining marketing approvals for inupadenant, EOS-448, and any other product candidates if clinical trials are successful;
- the extent to which we develop, in-license or acquire other product candidates and technologies;
- the number and development requirements of other product candidates we may pursue;
- the success of the GSK collaboration and any other collaborations;
- the cost of commercialization activities for any approved product, including marketing, sales and distribution costs;
- the cost of manufacturing inupadenant, EOS-448, and any other product candidates for clinical trials in preparation for marketing approval and commercialization;
- our ability to establish and maintain strategic licensing or other arrangements and the financial terms of such agreements;
- the costs involved in preparing, filing, prosecuting, maintaining, expanding, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the timing, receipt, and amount of sales of, or royalties on, future approved products, if any; and
- the emergence of competing cancer therapies and other adverse market developments.

Until we can generate sufficient product revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing and grant arrangements and other marketing or distribution arrangements. We cannot be certain that additional funding will be available on acceptable terms, or at all. Further, our ability to raise additional capital and maintain liquidity may be adversely impacted by potential worsening global economic conditions and the ongoing disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the COVID-19 pandemic and inflationary pressures among other macroeconomic concerns. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue our research and development initiatives. We could be required to seek additional collaborators for our product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to our product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

Any of the above events could significantly harm our business, prospects, financial condition, and results of operations and cause the price of our common stock to decline.

Risks related to intellectual property

If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates and research programs. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel discoveries and technologies that are important to our business, however, we cannot predict:

- if and when patents may issue based on our patent applications;
- the scope of protection of any patent issuing based on our patent applications;

- whether the claims of any patent issuing based on our patent applications will protect our current product candidates or any future product candidates and their intended uses or prevent others from commercializing competitive technologies or products;
- whether or not third parties will find ways to invalidate or circumvent our patent rights;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications; and/or
- whether we will need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose.

Obtaining and enforcing patents is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications, or maintain and/or enforce patents that may issue based on our patent applications, at a reasonable cost or in a timely manner. Additionally, we may fail to identify patentable aspects of our research and development results before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, CMOs, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

We also cannot be certain that the claims in our pending patent applications directed to our product candidates and/or technologies will be considered patentable by the United States Patent and Trademark Office, or the USPTO, or by patent offices in foreign countries. One aspect of the determination of patentability of our inventions depends on the scope and content of the "prior art," information that was or is deemed available to a person of skill in the relevant art prior to the priority date of the claimed invention. There may be prior art of which we are not aware that may affect the patentability of our patent claims or, if issued, affect the validity or enforceability of a patent claim. Even if the patents do issue based on our patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, patents in our portfolio may not adequately exclude third parties from practicing relevant technology or prevent others from designing around our claims. If the breadth or strength of our intellectual property position with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop and threaten our ability to commercialize our product candidates. In the event of litigation or administrative proceedings, we cannot be certain that the claims in any of our issued patents will be considered valid by courts in the United States or foreign countries.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope, or expiration of a third-party patent which might adversely affect our ability to develop and market our products.

We cannot guarantee that any of our 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 application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction.

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. We must correctly interpret the relevance or the scope of a patent or a pending application, determine whether our products are covered by a third-party patent, predict whether a third party's pending application will issue with claims of relevant scope, and determine the expiration date of any patent in the United States or abroad that we consider relevant. Failure to do so may negatively impact our ability to develop and market our products.

We may need to obtain additional licenses of third-party technology that may not be available to us or are available only on commercially unreasonable terms, which may cause us to operate our business in a more costly or otherwise adverse manner that was not anticipated.

From time to time we may be required to license technology from additional third parties to further develop or commercialize our current product candidates or any future product candidates. Should we be required to obtain licenses to any third-party technology, including any such patents required to manufacture, use or sell our current product candidates or any future product candidates, such licenses may not be available to us on commercially reasonable terms, or at all. The inability to obtain any third-party license required to develop or commercialize any

of our current product candidates or any future product candidates could cause us to abandon any related efforts, which could seriously harm our business and operations.

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

Patents are of national or regional effect, and filing, prosecuting and defending patents on all of our current product candidates or any future product candidates throughout the world would be prohibitively expensive. As such, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Further, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals or biologics, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. In addition, certain developing countries, including China and India, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Changes in patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our current product candidates or any future product candidates.

Our success is heavily dependent on intellectual property, particularly patents. However, the patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and in recent years has been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, that have increased uncertainties as to the ability to obtain and enforce patent rights in the future. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries could increase the uncertainties and costs. For example, in September 2011 the Leahy-Smith America Invents Act, or the America Invents Act, was signed into law and included a number of significant changes to United States patent law as then existed. 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. Such avenues include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. After March 2013, under the America Invents Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. The America Invents Act and its implementation could 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 have a material adverse effect on our business, financial condition, results of operations and prospects.

The United States 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. Depending on future actions by the United States Congress, the United States 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 and future patents.

We may rely on trade secret and proprietary know-how which can be difficult to trace and enforce and, if we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and current product candidates or any future product candidates, we may also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Elements of our current product candidates or any future product candidates, including processes for their preparation and manufacture, may involve proprietary know-how, information, or technology that is not covered by patents, and thus for these aspects we may consider trade secrets and know-how to be our primary intellectual property. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third

parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

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

Patent rights are of limited duration. 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. Even if patents covering our current product candidates or any future product candidates are obtained, once the patent life has expired for a product, we may be open to competition from biosimilar or generic products. A patent term extension based on regulatory delay may be available in the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the patent term extension does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

We may become involved in lawsuits alleging that we have infringed the intellectual property rights of third parties or to protect or enforce our patents or other intellectual property, which litigation could be expensive, time consuming and adversely affect our ability to develop or commercialize our product candidates.

The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our product candidates. Third parties may assert infringement claims against us based on existing or future intellectual property rights. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, which may not be able to do. Proving invalidity may be difficult. For example, in the United States, proving invalidity in court requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business.

In addition, we may find that competitors are infringing our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may

determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks. Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties.

We could be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors.

While we may litigate to defend ourselves against these claims, even if we are successful, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our product candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition.

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

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our current product candidates or any future product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Risks related to our business operations, employee matters, taxes, litigation, and managing growth

The current public health pandemic related to COVID-19 may adversely impact our operations, business and financial results.

The COVID-19 pandemic has presented a substantial public health and economic challenge around the world. To date, the COVID-19 pandemic has caused widespread disruptions to the United States and global economy and has contributed to significant volatility and negative pressure in financial markets.

The continued spread of COVID-19 and identification of new strains of the virus could adversely impact our clinical trials, manufacturing and other operations, including:

- **Clinical trials**: The COVID-19 pandemic may cause delays in some of our clinical trials. Responses to COVID-19 by healthcare providers and regulatory agencies or staffing issues related to the COVID-19 response or the "great resignation" could impact the ability of clinical trial sites to participate in new clinical trials and could delay the commencement of trials, site initiation, compliance in the trials, the completion of trials, slow down enrollment, and make the ongoing collection of data for patients enrolled in studies more difficult or intermittent. Missing data could undermine data integrity and probability of success. In addition, due to COVID-19, some participants and clinical investigators may be unable or unwilling to comply with clinical trial protocols. Any negative impact COVID-19 has on study start-up, patient enrollment, retention or treatment, or data collection and validation could delay our clinical trial timelines and adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, particularly on our current projected timelines, increase our operating expenses and have a material adverse effect on our business and financial results.

- Manufacturing: The COVID-19 pandemic may negatively affect the operations of our third-party manufacturers, which could result in delays or disruptions in the supply of our product candidates for our clinical trials. Demand for vaccines and treatments for COVID-19 may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in clinical trials.
- **Operations**: As a result of the challenges the COVID-19 pandemic brought, we took various steps to support our employees, including transitioning to a hybrid work model and offering flexible schedules. We will continue to monitor and make adjustments in response to the public health environment, together with local, state and federal guidance regarding workplace protective measures. These measures entail risk. For instance, remote work may delay our preclinical programs development, disrupt our operations, and increase the risk of a cybersecurity incident. If there is an increase in COVID-19 infection rates or new outbreaks, our business may be adversely impacted, the extent of which will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as new variants, the duration of outbreaks, the severity of COVID-19 or the effectiveness of actions to contain and treat COVID-19, particularly in the geographies where we, our third party manufacturers, CROs or current and planned clinical trial sites operate.
- **Stock Price**: COVID-19 has also caused volatility in the global financial markets and threatened a slowdown in the global economy, which may negatively affect our ability to raise additional capital on attractive terms or at all.

In addition, to the extent the COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this “Risk factors” section.

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

As we advance our research and development programs and as we continue to operate as a public company, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of management and operations, clinical development, quality, regulatory affairs and, if any of our product candidates receive marketing approval, sales, marketing, and distribution. To manage our anticipated future growth, we must:

- identify, recruit, integrate, retain, and motivate additional qualified personnel;
- manage our development efforts effectively, including the initiation and conduct of clinical trials for our current product candidates or any future product candidates, both as monotherapy and in combination with other intra-portfolio product candidates; and
- improve our operational, financial, and management controls, reporting systems and procedures.

Our future financial performance and our ability to develop, manufacture, and commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert financial and other resources, and a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time, to managing these growth activities. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel.

We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

We are highly dependent on the services of our founder, Michel Detheux, Ph.D., who serves as our Chief Executive Officer and President, and on our other executives. Although we have entered into employment agreements with each of our executives, such agreements are not for a specific term and each executive may terminate their employment with us at any time. We are not aware of any present intention of any of these key personnel to leave us. We do not maintain “key person” insurance for any of our executives or employees. We believe that any of our executives would be difficult to replace.

Our industry has experienced a high rate of turnover in recent years. Our ability to compete in the highly competitive biopharmaceuticals industry depends upon our ability to attract, retain and motivate highly skilled and

experienced personnel with scientific, medical, regulatory, manufacturing and management skills and experience. Although we conduct our research and development in Belgium, our headquarters with management is located in Massachusetts, and we plan on expanding our clinical development activities in the Boston area, a region that is home to many other biopharmaceutical companies as well as many academic and research institutions, resulting in fierce competition for qualified personnel. We may not be able to attract or retain qualified personnel in the future due to the intense competition for a limited number of qualified personnel among biopharmaceutical companies. Many of our competitors have greater financial and other resources, different risk profiles and a longer history in the industry than we do, and may provide higher compensation, more diverse opportunities and/or better opportunities for career advancement. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our 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. Any or all of these factors may limit our ability to continue to attract and retain high quality personnel, which could negatively affect our ability to successfully develop and commercialize our current product candidates or any future product candidates and to grow our business and operations as currently contemplated.

Cyberattacks on our information systems risk disclosure of confidential or proprietary information, including personal data, and could 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. Successful cyberattacks 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. Successful cyberattacks cause serious negative consequences, 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. Information security breaches can result in business, legal, financial, or reputational harm, or 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.*, GDPR) and may cause a material adverse impact to our reputation, affect our ability to conduct new studies and potentially disrupt our business.

If we are unable to prevent or mitigate the impact of security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business. If we or third-party CMOs, CROs or other contractors or consultants fail to comply with United States and international 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.

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

Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, including any potential effects from the current global spread of COVID-19, political instability and military or other conflicts, including Russia's invasion of Ukraine and the potential for a wider European or global conflict, power shortage, telecommunication failure or other natural or man-made accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our third-party CMOs, may negatively impact our supply chain, manufacturing costs or productivity, the economies in geographies in which we operate, or our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the

development of our product candidates or interruption of our business operations. It may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. We maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, our insurance may not be sufficient to satisfy any damages and losses. If our facilities or the manufacturing facilities of our third-party CMOs are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material and adverse effect on our business, financial condition, results of operations and prospects. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets and global trade. We conduct, and we expect to continue to conduct, portions of our clinical trials outside the United States, and unfavorable economic conditions resulting in the weakening of the United States dollar would make those clinical trials more costly to operate. Furthermore, the most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn could result in a variety of risks to our business, such as a reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy, including supply chain disruptions, labor shortages and persistent inflation, could also strain our suppliers, possibly resulting in supply disruption, and could negatively impact our access to liquidity and banking relationships. 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.

A portion of our manufacturing of our lead product candidates takes place in China through third-party manufacturers. A significant disruption in the operation of those manufacturers, a trade war or political unrest in China could materially adversely affect our business, financial condition and results of operations.

We currently and expect to continue to contract manufacturing operations to third parties, and clinical quantities of our lead product candidates inupadenant and EOS-448 are manufactured by these third parties outside the United States, including in China. Any disruption in production or inability of our manufacturers in China to produce adequate quantities to meet our needs, whether as a result of a natural disaster, the COVID-19 pandemic or other causes, could impair our ability to operate our business on a day-to-day basis and to continue our development of our product candidates. Furthermore, since these manufacturers are located in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the United States or Chinese governments, political unrest or unstable economic conditions in China. For example, a trade war could lead to tariffs on the chemical intermediates we use that are manufactured in China and in 2017, the United States proposed tariffs of 25% on raw ingredients for pharmaceuticals, such as the active pharmaceutical ingredients for our proposed product candidates. Any of these matters could materially and adversely affect our business and results of operations. Any recall of the manufacturing lots or similar action regarding our product candidates used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings. In addition, manufacturing interruptions or failure to comply with regulatory requirements by any of these manufacturers could significantly delay clinical development of potential products and reduce third-party or clinical researcher interest and support of proposed trials. These interruptions or failures could also impede commercialization of our product candidates and impair our competitive position. Further, we may be exposed to fluctuations in the value of the local currency in China. Future appreciation of the local currency could increase our costs. In addition, our labor costs could continue to rise as wage rates increase due to increased demand for skilled laborers and the availability of skilled labor declines in China.

We may be exposed to significant foreign exchange risk.

We incur portions of our expenses, and may in the future derive revenues, in a variety of currencies. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. Fluctuations in currency exchange rates have had, and will continue to have, an impact on our results as expressed in United States dollars. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the euro. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows.

Our operations subject us to potentially adverse tax consequences.

We are required to file income tax returns in the U.S. and Belgium, which requires us to interpret the applicable tax laws and regulations in effect in such jurisdictions. Furthermore, significant judgment is required in evaluating our tax positions, including our provision for income taxes, our deferred tax assets and liabilities and any valuation allowance recorded against our net deferred tax assets. Our interpretation or application of accounting policies may be questioned by the relevant tax authorities, and the relevant tax laws and regulations, or the interpretation thereof, including through tax rulings, by the relevant tax authorities, may be subject to change. Any adverse outcome of such a review or change, including any adverse resolution of one or more uncertain tax positions, may lead to adjustments in the amounts recorded in our financial statements, and could have a materially adverse effect on our operating results and financial condition.

United States federal income tax reform or unanticipated changes in Belgian tax laws and regulations could adversely affect our business and financial condition.

We are subject to taxes in the U.S. and Belgium, as well as laws and regulations regarding taxes, levies, and other charges in different countries. These tax rules, which are subject to change, affect tax liabilities imposed in respect of our assets, income, and operations, including transactions with third parties, affiliates and employees. Dealings and other intercompany transactions between current group companies and former group companies as well as additional companies that may form part of our group in the future are subject to transfer pricing regulations imposed by jurisdictions in which such companies are resident and can affect the income tax liability of each company.

Our effective tax rates and liability for tax in Belgium, the United States, and other jurisdictions could be adversely affected by changes in tax laws, treaties and regulations, both internationally and domestically, or the interpretation thereof by the relevant tax authorities, including changes to the innovation income deduction, possible changes to the corporate income tax base, wage withholding tax incentive for qualified research and development personnel in Belgium and other tax incentives and the implementation of new tax incentives.

Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

If we are unable to use Belgian tax loss carryforwards to reduce future taxable income or benefit from the favorable Belgian tax legislation, our business, results of operations and financial condition may be adversely affected.

At December 31, 2022, we had an estimated cumulative carry forward tax losses of $44.4 million in Belgium. Under the current legislation these are available to carry forward and offset against future taxable income for an indefinite period in Belgium. If we are unable to use tax loss carryforwards to reduce future taxable income, our business, results of operations and financial condition may be adversely affected. As a company active in research and development in Belgium we have benefited from the availability of the Belgian research and development tax credit, which can offset the Belgian corporate income tax due or it can be refunded if not used. We also expect to benefit from the innovation income deduction, or IID, in Belgium, which allows net profits attributable to revenue from patented products (or products for which the parent application is pending), among other things, be taxed at a lower rate than other revenues. The tax authorities may challenge our eligibility for, or our calculation of, certain tax reductions and/or deductions in respect of our research and development activities and, should the Belgian tax authorities be successful, we may be liable for additional corporate income tax, and penalties and interest related thereto, which could have a significant impact on our results of operations and future cash flows.

We are subject to certain covenants as a result of certain non-dilutive financial support we have received to date.

We have been awarded grants from the Walloon Region, a federal region of Belgium, or the Walloon Region, and the European Union to fund research and development activities. Several of the grants include no obligation to repay the amount received under the grants. We own the intellectual property rights that result from the research programs or with regard to a patent covered by these grants. Subject to certain exceptions, however, we cannot grant to third parties, by way of license, transfer or otherwise, any right to use the patents or research results without the prior consent of the Walloon Region. In addition, certain grants require that we exploit the patent in the countries where the protection was granted and to make an industrial use of the underlying invention. In case of bankruptcy, liquidation or dissolution, the rights to the patents covered by the patent grants will be assumed by

the Walloon Region by operation of law unless the grants are reimbursed. Furthermore, we would lose our qualification as a small or medium-sized enterprise, the grants subsidies would terminate and no additional expenses would be covered by such patent grants.

Two of the grants, which are referred to as recoverable cash advance grants, or RCAs, include a potential obligation to repay the amount received under the grants. Under the RCAs, the Walloon Region will provide us with up to €23.2 million for our research and development programs for EOS-448 and inupadenant. During the year ended December 31, 2022, we received €1.6 million under the EOS-448 grant and €2.1 million under the inupadenant grant.

We must repay 30% of the amount received under the grants unless we decide not to pursue commercial development or out licensing of the drug candidate, inform the Walloon Region of our decision and justify our decision based upon the failure of the program, and transfer the intellectual property to the Walloon Region. This is referred to as the fixed repayment. In addition, in the event that we receive revenue from products or services related to the results of the program, we will have to pay to the Walloon Region a 0.33% royalty on revenue resulting from the first RCA grant and a 0.15% royalty on revenue resulting from the second RCA grant (increased from 0.12% effective December 2021). The maximum amount payable to the Walloon Region under each grant, including the fixed repayment, the royalty on revenue, and the interest thereon, is twice the amount of funding received.

Subject to certain exceptions, we cannot grant to third parties, by way of license or otherwise, any right to use the results without the prior consent of the Walloon Region. We also need the consent of the Walloon Region to transfer an intellectual property right resulting from the research programs or a transfer or license of a prototype or installation. Obtaining such consent from the Walloon Region could give rise to their review of the applicable financial terms. The RCAs also contain provisions prohibiting us from conducting research within the scope of the RCAs for any third parties. This prohibition is applicable beyond the research phase and decision phase and could restrict our ability to enter into research-related collaboration or partnership agreements with respect to those programs.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in:

- delay or termination of clinical trials;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial subjects;
- initiation of investigations by regulators;
- significant costs to defend the related litigation and diversion of management's time and our resources;
- substantial monetary awards to study subjects or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We may be at an increased risk of securities class action litigation.

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

Risks related to ownership of our common stock

The trading price of our common stock has been volatile.

The trading price of our common stock has been highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this “Risk factors” section, these factors include:

- the results of our ongoing, planned or future preclinical studies, clinical trials or clinical development programs;
- the commencement, enrollment, or results of clinical trials of our product candidates or any future clinical trials we may conduct, or changes in the development status of our product candidates;
- adverse results or delays in preclinical studies and clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial, or to terminate an existing clinical trial;
- any delay in our regulatory filings or any adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- changes in laws or regulations applicable to our products, including but not limited to clinical trial requirements for approvals;
- adverse developments concerning our manufacturers or our manufacturing plans;
- our inability to obtain adequate product supply for any licensed product or inability to do so at acceptable prices;
- our inability to establish collaborations if needed;
- our failure to commercialize our product candidates;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our product candidates;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- changes in the structure of healthcare payment systems;
- our ability to effectively manage our growth;
- the size and growth of our initial cancer target markets;
- our ability to successfully treat additional types of cancers or at different stages;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or immunotherapy in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

- significant lawsuits, including intellectual property or stockholder litigation;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Raising additional capital and future issuances of our common stock or rights to purchase common stock could result in additional dilution of the percentage ownership of our stockholders, restrict our operations, or require us to relinquish rights to our technologies or product candidates, and could cause our stock price to fall.

We expect that significant additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, expanded research and development activities, and costs associated with operating as a public company. To raise capital, we may sell common stock, convertible securities, or other equity securities in one or more transactions, including through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements, at prices and in a manner we determine from time to time. If we sell common stock, convertible securities, or other equity securities, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences, and privileges senior to the holders of our common stock.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholder's ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

We do not intend to pay dividends on our common stock, so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, we may enter into agreements that prohibit us from paying cash dividends without prior written consent from our contracting parties, or which other terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock, which may never occur.

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

Our executive officers, directors, and 5% stockholders beneficially owned approximately 62.4% of our outstanding voting stock as of December 31, 2022. These stockholders have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that our stockholders may feel are in their best interest.

We are an emerging growth company, and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be

an emerging growth company for up to five years following 2020, the year in which we completed our IPO, although circumstances could cause us to lose that status earlier. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of our IPO, (b) in which we have total annual gross revenue of at least $1.235 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption from complying with new or revised accounting standards and, therefore, will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

As of December 31, 2022, we no longer qualified as a smaller reporting company; however, we are allowed to continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies through our annual report for the year ended December 31, 2022. 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.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay, defer 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 stockholders be called only by a majority of the members of our board of directors then in office;
- 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 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 two-thirds of all outstanding shares of our voting stock and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class to amend specific provisions of our certificate of incorporation;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, 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 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 stockholders to elect directors of their choosing or cause

us to take other corporate actions they 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 amended and restated bylaws designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claim for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein, or 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 bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the United States District Court for the District of Massachusetts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision, as our principle office is located in Cambridge, Massachusetts. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

We recognize that the Delaware Forum Provision and the Federal Forum Provision in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage 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 were "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 United States District Court for the District of Massachusetts 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.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal control over financial reporting in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. In connection with our IPO, we began the process of documenting, reviewing, and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act, which will require annual management assessment of the effectiveness of our internal control over financial reporting. We have begun recruiting additional finance and accounting personnel with certain skill sets that we will need as a public company. If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not,

however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and make it more difficult for us to effectively market and sell our service to new and existing customers.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease 9,068 square feet of office space located at 321 Arsenal Street, Watertown, Massachusetts 02472 for our principal office. The lease terminates in February 2027.

For our Belgian subsidiary, we lease a facility containing approximately 1,577 square meters for laboratory and office space, which is located at 29 Rue des Frères Wright, 6041 Charleroi, Belgium. In January 2021, the Company entered into an agreement to extend its office lease in Belgium effective February 1, 2021 through January 2030 and include 201 square meters of additional space. In October 2021, the Company entered into an agreement to lease an additional 453 square meters of space.

We believe that our current facilities are adequate for our current needs and that suitable additional or substitute space at commercially reasonable terms will be available as needed to accommodate any future expansion of our operations.

Item 3. Legal Proceedings.

From time to time, we may be a party to litigation or subject to claims incident to the ordinary course of business. We are not currently a party to any material legal proceedings, and our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations or financial condition.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market information

Our common stock is publicly traded on the Nasdaq Global Select Market under the symbol "ITOS".

Holders of Record

As of March 7, 2023, there were approximately 234 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

We have not declared or paid any cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends to holders of common stock in the foreseeable future. Any future determination to declare cash dividends will be made at the discretion of our board of directors, subject to applicable laws, will depend on a number of factors, including our financial condition, results of operations, capital requirements, contractual restrictions, general business conditions, and other factors that our board of directors may deem relevant.

Securities authorized for issuance under equity compensation plans

The information required by Item 5 of Form 10-K regarding equity compensation plans will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Issuer purchases of equity securities

None

Item 6. Reserved

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 related notes and other financial information appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes 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 the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company pioneering the discovery and development of a new generation of immuno-oncology therapeutics for people living with cancer. We leverage our deep understanding of tumor immunology and immunosuppressive pathways to design novel product candidates with the aim of restoring the immune response against cancer. Our innovative pipeline includes two clinical-stage programs targeting novel, validated immuno-oncology pathways. Each of our therapies in development has optimized pharmacologic properties designed to improve clinical outcomes.

Our lead antibody product candidate, EOS-448, is an antagonist of TIGIT, or T-cell immunoreceptor with Ig and ITIM domains, an immune checkpoint with multiple mechanisms of action. EOS-448 was selected for its affinity for TIGIT, its potency and its potential to engage the FcγR to activate dendritic cells, natural killer cells and macrophages and to promote cytokine release, activation of antigen presenting cells and ADCC activity. In 2020, we started an open-label Phase 1/2a clinical trial of EOS-448 in adult cancer patients with advanced solid tumors. In April 2021, we reported preliminary safety, pharmacokinetic, engagement and pharmacodynamic data, indicating target engagement and early evidence of clinical activity as a single agent. In September 2021, we dosed the first patients in a Phase 1/2 clinical trial of EOS-448 in combination with pembrolizumab and in combination with our $A_{2A}R$ antagonist inupadenant in patients with solid tumors.

On June 11, 2021, our wholly owned subsidiary, iTeos Belgium S.A., and GSK executed the GSK Collaboration Agreement, which became effective on July 26, 2021. Pursuant to the GSK Collaboration Agreement, we granted GSK a license under certain of our intellectual property rights to develop, manufacture, and commercialize products comprised of or containing EOS-448, which license is exclusive in all countries outside of the United States and co-exclusive, with iTeos, in the United States. GSK and iTeos intend to develop EOS-448 in combination, including with other oncology assets of GSK, and iTeos and GSK will jointly own the intellectual property created under the GSK Collaboration Agreement that covers such combinations. In partnership with GSK, we are enrolling patients with first line NSCLC in a randomized Phase 2 trial assessing the doublet of GSK's anti-PD-1 (Jemperli (dostarlimab-gxly)) with EOS-448. In addition, we are enrolling patients with first-line advanced or metastatic head and HNSCC for the Phase 2 expansion part of the trial assessing the doublet of GSK's dostarlimab with EOS-448. We and GSK continue to explore two novel triplets in selected advanced solid tumors both in Phase 1b trials: EOS-448 with dostarlimab and GSK's investigational anti-CD96 antibody, and EOS-448 with dostarlimab and GSK's anti-PVRIG.

Based on favorable preclinical data generated in collaboration with Fred Hutchinson Cancer Research Center, we are also enrolling patients in an open-label dose-escalation/expansion Phase 1/2 trial evaluating the safety, tolerability and preliminary activity of EOS-448 as monotherapy and in combination with Bristol Myers Squibb's iberdomide - a novel, potent oral cereblon E3 ligase modulator (CELMoD®) compound with enhanced tumoricidal and immune-stimulatory effects compared with immunomodulatory (IMiD®) agents - with or without dexamethasone, in adults with relapsed or refractory multiple myeloma.

We are also advancing inupadenant, a next-generation adenosine A2A receptor antagonist tailored to overcome the specific adenosine-mediated immunosuppression found in tumor microenvironment, into proof-of concept trials in several indications following encouraging single-agent activity in Phase 1. We are investigating inupadenant in an open-label multi-arm Phase 1/2a clinical trial in adult cancer patients with advanced solid tumors. The single-agent dose-escalation and expansion portions of our Phase 1/2a clinical trial of inupadenant have demonstrated durable monotherapy antitumor activity in some patients with advanced solid tumors and safety consistent with previously reported results. As part of this monotherapy assessment of inupadenant, we identified a potential predictive biomarker and we have completed enrolling patients in the biomarker cohort of the ongoing Phase 1b/2a trial. We confirmed a partial response using inupadenant in monotherapy in a patient who

had the highest level of the biomarker that we have recorded. We are also enrolling patients in the dose ranging part (Part 1) of an ongoing two-part Phase 2 trial in post-IO metastatic non-squamous non-small cell lung cancer (NSCLC) to evaluate the combination of inupadenant with platinum-doublet chemotherapy compared to standard platinum-doublet chemotherapy. We have completed enrollment in the safety evaluation portion of the clinical trial of inupadenant in combination with chemotherapy and with pembrolizumab, as well as the monotherapy expansion cohort in prostate cancer. We have completed enrollment in the Phase 2a trial evaluating inupadenant in combination with pembrolizumab in post-PD-1 melanoma and have decided to prioritize development of inupadenant in our ongoing study in combination with platinum-doublet chemotherapy in patients with chemo-naïve NSCLC as we have determined that the post-PD-1 melanoma setting is not a path to accelerated approval. In addition, we are evaluating a salt form of inupadenant in a Phase 1 study.

In September 2021, we nominated a product candidate, EOS-984, which targets a new mechanism in the adenosine pathway for IND enabling studies. EOS-984 has the potential to fully reverse adenosine immune suppression, as a monotherapy and in combination with inupadenant and other standards of care. We expect to initiate clinical studies for EOS-984 in mid-2023.

Since our inception in August 2011, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential product candidates, undertaking preclinical studies and clinical trials and establishing arrangements with third parties for the manufacture of initial quantities of our product candidates and component materials. To date, we have financed our operations primarily through license and collaboration revenue generated through the GSK Collaboration Agreement and through our Initial Public Offering, or IPO. Through December 31, 2022, we had raised an aggregate of $210.6 million of net proceeds from the IPO and $177.1 million from the sale of preferred stock and received an up-front payment of $625.0 million with respect to the GSK Collaboration Agreement. As of December 31, 2022, our principal sources of liquidity were cash and cash equivalents, which totaled $284.8 million and available-for-sale securities, which totaled $446.6 million.

We expect to continue to incur significant expenses in connection with ongoing development activities, particularly if and as we:

- continue preclinical studies and clinical trials and initiate new clinical trials for our product candidates;
- pursue regulatory approvals for our product candidates;
- advance the development of our product candidate pipeline;
- continue research activities as we seek to discover and develop additional product candidates;
- obtain, maintain, expand and protect our intellectual property portfolio;
- hire additional research and development, clinical and commercial personnel;
- scale up our clinical and regulatory capabilities; 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.

We are also party to other collaboration and license agreements in addition to the GSK Collaboration Agreement pursuant to which we may be required to make future royalty and milestone payments. In January 2017, we entered into a collaboration agreement with Adimab, LLC, or Adimab, pursuant to which we paid $1.0 million in 2018 to exercise an option to acquire certain licenses from Adimab. One of the antibodies licensed under this agreement is what we now refer to as EOS-448. In February 2021, we entered into an amendment to this agreement (the Amended Adimab Agreement). The Amended Adimab Agreement specifies different milestone payments for new products that are derived from research programs beginning after February 22, 2021 (the New Products). For New Products, on a per target basis, we may be required to pay development, regulatory and commercial milestone payments totaling up to an aggregate of $45.8 million for the first three products and additional milestone payments up to $14.5 million for each additional product. In 2022, the Company made a payment of $2.0 million due to reaching an additional milestone (dosing of first patient for Phase 2 clinical trial). As of the date of this Annual Report on Form 10-K, we have not pursued any additional targets under the Amended Adimab Agreement that could potentially result in such milestone payments. We will also pay Adimab low to mid single-digit percentage royalties on a country-by-country and product-by-product basis on worldwide net sales of licensed products. Through December 31, 2022, we have paid a total of $5.4 million to Adimab relating to milestones, option and other fees pursuant the Adimab Agreement.

We are also party to a biologics master services agreement with WuXi Biologics Hong Kong Limited, or WuXi, pursuant to which we will pay WuXi, at our election, either a low single-digit percentage royalty on global net sales of manufactured products or a one-time milestone payment in the low tens of millions.

On December 10, 2019, we entered into a Clinical Trial Collaboration and Supply Agreement (the MSD Agreement) with MSD International GmbH (MSD), a subsidiary of Merck & Co., Inc. Under the MSD Agreement, we sponsor a clinical trial in which both our compound and MSD's compound are dosed in combination. We conduct the research at our own cost and MSD contributes its compound towards the study at no cost to us. We will equally own the clinical data and inventions from the study, with the exception of inventions relating solely to each party's compound class. The MSD Agreement will expire upon the delivery of a written report on the results of the study, unless earlier terminated or agreed by the parties. We began receiving compounds from MSD on April 1, 2020 and we began the research study in the third quarter of 2020.

Impact of COVID-19

The COVID-19 pandemic has presented a substantial public health and economic challenge around the world. While the COVID-19 pandemic has not significantly impacted our business or results of operations, the future impact of the COVID-19 pandemic on our industry, the healthcare system, our development timelines for EOS-448 and inupadenant, our preclinical research and development, and our current and future operations and financial condition will depend on future developments, which are highly uncertain and cannot be predicted with confidence. Disruptions to the global economy, disruption of global healthcare systems, and other significant impacts of the COVID-19 pandemic could have a material adverse effect on our business, financial condition, results of operations and growth prospects. See "Risk factors" for a discussion of the potential adverse impact of COVID-19 on our business, results of operations and financial condition.

Components of our results of operations

Revenue

To date, our revenues have been derived from the upfront payment associated with the GSK Collaboration Agreement.

For all collaboration agreements, no development or commercial milestones were included in the transaction price at inception, as all milestone amounts were fully constrained. As part of our evaluation of the constraint, we considered numerous factors, including that receipt of the milestones is outside our control and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to GSK and therefore have also been excluded from the transaction price. We are applying the royalty exception for sales-based royalties and will not recognize revenue until the subsequent sale of product occurs.

Research and development expenses

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- costs to obtain licenses to intellectual property and related future payments should certain success, development and regulatory milestones be achieved;
- employee-related expenses, including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, or CROs, contract manufacturing organizations, or CMOs, and independent contractors that conduct research and development, preclinical and clinical activities on our behalf;
- costs of purchasing lab supplies and non-capital equipment used in our preclinical activities and in manufacturing clinical study materials through CMOs;
- consulting and professional fees related to research and development activities; and
- facility costs, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supplies.

We expense research and development costs as incurred. We recognize costs for certain development activities, such as preclinical studies and clinical trials, based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors, such as patient enrollment or clinical site activations for services received and efforts expended.

Research and development activities are central to our business model. We expect research and development costs to increase significantly for the foreseeable future as our current development programs progress and new programs are added.

Because of the numerous risks and uncertainties associated with product development, we cannot determine with certainty the duration and completion costs of the current or future preclinical studies and clinical trials or if, when, or to what extent we will generate revenues from the commercialization and sale of any product candidates that receive regulatory approval. We may never succeed in achieving regulatory approval for our product candidates. The duration, costs and timing of preclinical studies and clinical trials and development of our product candidates will depend on a variety of factors, which could all be impacted by the COVID-19 pandemic, including, but not limited to:

- successful enrollment in, and completion of, clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- successful completion of preclinical studies and IND-enabling studies;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity;
- launching commercial sales of the product, if and when approved, whether alone or in collaboration with others;
- acceptance of a product, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- achieving desirable medicinal properties for the intended indications.

A change in the outcome of any of these factors could mean a significant change in the costs and timing associated with the development of our current and future preclinical and clinical product candidates. For example, if the FDA or comparable foreign regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development, or if we experience significant delays in execution of or enrollment in any of our preclinical studies or clinical trials, we could be required to expend significant additional financial resources and time on the completion of preclinical and clinical development.

The following table summarizes our principal product development programs, including direct research and development expenses allocated to each clinical product candidate:

	Year ended December 31,	
(in thousands)	**2022**	**2021**
Direct research and development expenses by program:		
EOS-448	$ 36,256	$ 14,641
Inupadenant	23,841	18,714
Other non-clinical programs	12,001	8,450
Indirect research and development expenses(1)	25,261	17,564
Total research and development expense	$ 97,359	$ 59,369

(1) The substantial majority of these costs relate to the EOS-448 and inupadenant programs. The majority of these costs are payroll and related costs for our employees performing in-house research and development activities and the remainder represents other research and development costs.

General and administrative expenses

General and administrative expenses consist primarily of employee-related expenses, including salaries, benefits and stock-based compensation, for personnel in executive, finance, business development, facility operations and administrative functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters and fees for accounting, tax and consulting services.

Grant income

We have agreements with granting agencies whereby we receive funding under grants that partially or fully reimburse us for eligible research and development expenditures. Certain grant agreements require us to repay the funding depending on whether we decide to pursue commercial development or out-licensing of any drug candidate that is produced from the research program. The repayment provision includes a portion that is fixed (corresponding to 30% of the grant), payable in annual installments, which is effective unless we decide not to pursue commercial development or out licensing of the drug candidate. The repayment provision also includes a potential obligation to pay a royalty that is contingent upon achieving sales of a product developed through the program. The maximum amount payable to the granting agency under each grant, including the fixed repayments, the royalty on revenue and the interest thereon, is twice the amount of funding received.

Research and development tax credits

Our wholly owned subsidiary iTeos Belgium S.A., as a Belgian biotechnology company, qualifies for a cash-based tax credit on research and development expenses. The credit is calculated based on a percentage of eligible research and development expenses defined by the Belgian government for each fiscal year (13.5% for 2022 and 2021) and then applying the effective tax rate to that result. The research and development tax credits are refundable to us if we are unable to use the credits to offset income taxes for the five subsequent tax years. We record a receivable and other income as the qualified expenses are incurred, as we are reasonably assured that the credit will be received, based upon our history of filing for the tax credits. Research and development tax credits receivable where we expect to receive refunds more than one year after the balance sheet date are classified as noncurrent in the consolidated balance sheet.

Interest income

Interest income consists of interest earned on our available-for-sale securities, money market funds, and bank sweep accounts.

Other income, net

Other income, net includes income and expenses that do not fall within other categories of the statement of operations and comprehensive income. Items included are bank fees and gain or loss on foreign currency transactions.

Income taxes

We are subject to income taxes in the U.S. and Belgium. Belgium has a statutory tax rate different from the U.S. Accordingly, our effective tax rates will vary depending on the relative proportion of foreign to U.S. income, the utilization of foreign tax credits and changes in tax laws. Deferred tax assets are reduced through the establishment of a valuation allowance, if, based upon available evidence, it is determined that it is more likely than not that the deferred tax assets will not be realized. Income tax expense results from foreign minimum income tax and profit on a legal entity basis. For the first time since inception, we recognized income in 2021. Due to the revenue earned, we recognized income tax expense in 2021. As of December 31, 2022, we had foreign net operating loss carryforwards of $44.4 million with no expiration. As of December 31, 2022, we have fully utilized the U.S. net operating loss carryforwards and have $38.4 million of state net operating loss carryforwards. These net operating losses, along with temporary differences related primarily to capitalized research and development, or R&D expenses for tax purposes in Belgium and stock-based compensation in the U.S., resulted in a net deferred tax asset of $45.4 million. We have concluded that it is more likely than not that we will not realize the benefits of the deferred tax asset, and accordingly, established a full valuation allowance as

of December 31, 2022. In addition, the Company recorded a $39.2 million liability as of December 31, 2022, related to an uncertain tax position regarding the Company's allocation of revenue between Belgium and the U.S.

Results of operations

Comparison of the years ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021, together with the dollar change in those items:

(in thousands)	Year ended December 31, 2022	2021	Period to period change
Revenue:			
License and collaboration revenue	$ 267,630	$ 344,775	$ (77,145)
Total Revenue	267,630	344,775	(77,145)
Operating expenses:			
Research and development expenses	97,359	59,369	37,990
General and administrative expenses	43,947	40,505	3,442
Total operating expenses	141,306	99,874	41,432
Income from operations	126,324	244,901	(118,577)
Other income:			
Grant income	2,091	10,181	(8,090)
Research and development tax credits	1,172	—	1,172
Interest income	11,361	78	11,283
Other income, net	7,788	1,304	6,484
Income before income taxes	148,736	256,464	(107,728)
Income tax expense	52,084	41,943	10,141
Net income	$ 96,652	$ 214,521	$ (117,869)

License and collaboration revenue

License and collaboration revenue equaled $267.6 million for the year ended December 31, 2022, resulting from a portion of the GSK upfront payment that was recognized during the year, compared to $344.8 million recognized for the year ended December 31, 2021. The decrease was due to more than half of the revenue relating to the GSK upfront payment having been recognized in 2021.

Research and development expenses

Research and development expenses increased by $38.0 million to $97.4 million for the year ended December 31, 2022, from $59.4 million for the year ended December 31, 2021. This increase was primarily related to an increase of $3.5 million of payroll and related costs, a $29.4 million increase CRO/CMO fees and internal laboratory expenses, a $2.2 million increase in stock-based compensation, an increase of $0.7 million in professional fees and an increase of $1.7 million in collaboration milestones paid. The overall increase was due to an increase in activities related to EOS-448 and inupadenant clinical trials. In addition, there was an increase in spending related to our preclinical programs during the year ended December 31, 2022.

General and administrative expenses

General and administrative expenses increased by $3.4 million to $43.9 million for the year ended December 31, 2022 from $40.5 million for the year ended December 31, 2021. The increase was primarily attributable to an increase of $2.7 million of payroll and related costs resulting from additional executives and finance and administrative employees added to enable us to operate as a public company, a $5.5 million increase in stock-based compensation, an increase of $0.6 million in recruiting fees, and an increase of $0.4 million related to facilities. In addition, there was also a $0.8 million increase related to various other general and administrative expenses. These increases were partially offset by a $6.6 million decrease in professional fees primarily due to $6.3 million in one-time advisor and legal fees incurred by us in connection with the GSK Collaboration Agreement in 2021.

Grant income

Grant income decreased by $8.1 million to $2.1 million for the year ended December 31, 2022 from $10.2 million for the year ended December 31, 2021. The overall decrease in grant income, driven by spending on qualified research and development activities, was primarily attributable to certain grant programs reaching their maturity. For the year ending December 31, 2022, grant income relating to the EOS-448 and inupadenant programs decreased by $4.6 million and grant income relating to preclinical activities decreased by $3.5 million.

Research and development tax credits

Research and development tax credits increased by $1.2 million as no research and development tax credits were recognized as income for the year ended December 31, 2021, as the research and development tax credits were utilized in the income tax return to reduce the 2021 taxes due in Belgium. In 2022, a portion of the research and development tax credits are expected to be utilized in the income tax return to reduce the 2022 taxes due in Belgium.

Interest income

Interest income increased by $11.3 million due to rising interest rates in 2022 and due to the significant purchases and holdings of available-for-sale securities in the fourth quarter of 2022.

Other income, net

The $6.4 million increase in other income, net was primarily due to foreign currency exchange gains driven by the decrease in the euro to dollar exchange rate between December 31, 2021 and 2022.

Income tax expense

	Year ended December 31,	
(in thousands)	2022	2021
Income before income taxes	$ 148,736	$ 256,464
Income tax expense	52,084	41,943
Effective tax rate	35.0%	16.4%

Our effective tax rate increased from 16.4% to 35.0% in the year ended December 31, 2022 as compared to the year ended December 31, 2021, primarily due to the impact of capitalized research and development expenses under Section 174 of the Internal Revenue Code. Section 174 of the Internal Revenue Code was amended on January 1, 2022, in connection with certain provisions of the 2017 Tax Cuts and Jobs Act, Public Law 115-97- Dec. 22, 2017 becoming effective. As a result of the amendment, research and development expenses must now be capitalized and amortized for tax purposes over either five years for work performed in the U.S. and fifteen years for work performed outside of the U.S. Previously, research and development expenses were available to offset taxable income for tax purposes in the year incurred. Although this represents a temporary difference, the related deferred tax asset is fully reserved for under the valuation allowance as of December 31, 2022. In addition, there was a further increase in the liability related to uncertain tax positions in 2022. The Company recorded an additional $22.2 million liability during the year ended December 31, 2022 relating to an uncertain tax position regarding the Company's allocation of revenue from the GSK Collaboration Agreement between Belgium and the U.S. These factors also caused the 2022 effective tax rate to be higher than the federal and foreign statutory rates of 21% and 25%, respectively. The 2021 effective tax rate was lower than the federal and foreign statutory rates of 21% and 25%, respectively, primarily due to the mix of income between the U.S. and Belgium, the Innovation Income Deduction in Belgium, which excludes 85% of the net revenue generated from qualifying intellectual property from taxation and the taxation in the U.S. from the inclusion of foreign earnings under the Global Intangible Low-Taxed Income ("GILTI") regime. The liability balance was $39.2 million and $17.0 million as of December 31, 2022 and December 31, 2021, respectively.

See Note 9, *Income Taxes*, to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for further details.

Liquidity and capital resources

In June, 2021, the Company's wholly owned subsidiary, iTeos Belgium S.A., and GSK executed the GSK Collaboration Agreement, pursuant to which we agreed to grant GSK a license under certain of our intellectual

property rights to develop, manufacture, and commercialize products comprised of or containing our antibody product, EOS-448. Under the GSK Collaboration Agreement, GSK made an upfront payment of $625.0 million on August 5, 2021.

To date, we have funded our operations primarily with proceeds from the IPO, the sales of preferred stock, grants and licenses and the upfront payment from the GSK Collaboration Agreement. As of December 31, 2022, we had $284.8 million in cash and cash equivalents and $446.6 million in available-for-sale securities. To date we have not generated any revenue from product sales and do not expect to generate revenue from the sales of products for the foreseeable future.

In addition, in the event that we receive revenue from products or services related to the intellectual property developed arising from the programs, we must pay to the Walloon Region a 0.33% royalty on revenue related to the inupadenant grant and a 0.15% royalty on revenue on the EOS-448 grant (increased from 0.12% effectively December 2021). The maximum amount payable to the Walloon Region under each grant, including the fixed annual repayments, the royalty on revenue, and the interest thereon, is twice the amount of grant received. The Company recorded a royalty accrual of $0.8 million as of December 31, 2022, due to the upfront payment received pursuant to the GSK Collaboration Agreement.

The following is a summary of our contractual obligations as of December 31, 2022:

Contractual Obligation	Total	Less than 1 year	More than 1 year and less than 3	More than 3 years and less than 5	More than 5 years
(In thousands)					
Operating lease obligation (1)	$ 5,349	$ 1,059	$ 2,051	$ 1,469	$ 770
Grants repayable (2)	7,486	449	765	1,190	5,082
Totals	$ 12,835	$ 1,508	$ 2,816	$ 2,659	$ 5,852

(1) During the year ended December 31, 2021, we entered into two amendments to extend the Belgium lease and increase the office and lab space, effective February 2021 and October 2021, both with a termination date of January 2030. The February 2021 amendment increased the office and laboratory space by 201 square meters and the November 2021 amendment increased the office and laboratory space by 453 square meters. In November 2021, we entered into a new lease for 9,068 square feet of office space in Watertown, Massachusetts, which terminates in February 2027.

(2) We have entered into two arrangements with the Walloon Region of Belgium, whereby the Walloon Region would provide us with up to $24.7 million for our EOS-448 ($4.6 million) and inupadenant ($20.1 million) research and development programs. As of December 31, 2022, we have received $4.6 million under the EOS-448 grant and $20.1 million under the inupadenant grant. We must repay 30% of the amount received under the grants in annual installments from 2023 to 2042 unless we decide not to pursue development and commercialization of the intellectual property developed arising from the program, apply for a waiver from the Walloon Region justifying our decision based upon the failure of the program, and return the intellectual property to the Walloon Region.

The table above does not include potential milestone and success fees, sublicense fees, royalty fees, licensing maintenance fees and reimbursement of patent maintenance costs that we may be required to pay under agreements we have entered into with certain institutions to license intellectual property. Our agreements to license intellectual property include potential milestone payments that are dependent upon the development of products using the intellectual property licensed under the agreements and contingent upon the achievement of development or regulatory approval milestones, as well as commercial and success payment milestones. We have not included such potential obligations in the table above because they are contingent upon the occurrence of future events and the timing, likelihood and amount of such potential obligations are not known with certainty.

The table above does not include any required expenditures part of the GSK Collaboration Agreement as part of the Global Development Plan, the Company and GSK agree to spend an aggregate amount of at least $900 million. GSK is responsible for 60% of the cost, while the Company is responsible for the remaining 40% of the cost related to the Global Development Plan. We have not included such potential expenditures, as the timing of the obligations are not known with certainty.

We enter into contracts in the normal course of business with CROs and clinical sites for the conduct of clinical trials, professional consultants for expert advice and other vendors for clinical supply manufacturing or other services. These contracts are not included in the table above as they provide for termination on notice, and therefore are cancelable contracts and do not include any minimum purchase commitments.

Cash flows

The following table provides information regarding our cash flows for the years ended December 31, 2022 and 2021:

	Year ended December 31,	
(in thousands)	**2022**	**2021**
Net cash (used in) provided by:		
Operating activities	$ (111,193)	$ 513,140
Investing activities	(446,062)	(1,242)
Financing activities	1,984	3,659
Effects of exchange rate changes on cash, cash equivalents and restricted cash	(8,526)	(3,176)
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (563,797)	$ 512,381

Net cash (used in) provided by operating activities

Net cash used in operating activities was $111.2 million during the year ended December 31, 2022. The increase in cash used in comparison to the cash inflow during the prior year was primarily due to the $625.0 million upfront payment from GSK which was received in 2021.

Net cash used in investing activities

Net cash used in investing activities was $446.1 million for the year ended December 31, 2022 compared to $1.2 million for year ended December 31, 2021. The increase in cash used in investing activities was primarily due to the purchase of $445.0 million of available-for-sale securities during the year ended December 31, 2022.

Net cash provided by financing activities

Net cash provided by financing activities was $2.0 million during the year ended December 31, 2022. This was due to the proceeds received from the exercise of stock options, equaling $0.9 million, during the year. We also received proceeds of $1.1 million from grants received from the Walloon region for which a portion is repayable. Net cash provided by financing activities was $3.7 million during the year ended December 31, 2021, primarily driven by $3.0 million in proceeds received from the exercise of stock options. Additionally, the Company received $0.7 million in proceeds from grant programs with a potential obligation for repayment.

Effects of exchange rate changes on cash, cash equivalents and restricted cash

The $8.5 million in the effects of exchange rate changes on cash, cash equivalents and restricted cash for the year ended December 31, 2022 was primarily caused by the decrease in the euro to dollar exchange rate between December 31, 2021 and 2022. The $3.2 million increase for the year ended December 31, 2021 was also primarily related to a decrease in the euro to dollar exchange rate between December 31, 2020 and December 31, 2021.

Funding requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue our Phase 1/2 trials for both EOS-448 and inupadenant and move to larger randomized and registration-directed trials for both programs, advance the development of pipeline programs, initiate new research and preclinical development efforts and seek marketing approval for any product candidates that we successfully develop. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant

commercialization expenses related to establishing sales, marketing, distribution and other commercial infrastructure to commercialize such products.

In June, 2021, the Company's wholly owned subsidiary, iTeos Belgium S.A., and GSK executed the GSK Collaboration Agreement, pursuant to which we agreed to grant GSK a license under certain of our intellectual property rights to develop, manufacture, and commercialize products comprised of or containing our antibody product, EOS-448. Under the GSK Collaboration Agreement, GSK made an upfront payment of $625.0 million on August 5, 2021. Additionally, we are eligible to receive up to $1.45 billion in milestone payments, contingent upon the EOS-448 program achieving certain development and commercial milestones.

As of December 31, 2022, we had cash and cash equivalents of $284.8 million and available-for-sale securities of $446.6 million. We believe our existing cash and cash equivalents and available-for-sale securities will enable us to fund our operating expenses and capital expenditure requirements into 2026.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with the development and commercialization of EOS-448 and inupadenant, and the research, development and commercialization of other potential product candidates, we are unable to estimate the exact amount of our operating capital requirements. Our future capital requirements will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of product candidates;
- research and preclinical development efforts for any future product candidates that we may develop;
- our ability to enter into and the terms and timing of any collaborations, licensing agreements or other arrangements;
- the number of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of our current and future product candidates;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims;
- the costs of operating as a public company; and
- the emergence of competing therapies and other adverse market developments.

Critical accounting policies and significant judgments and estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. We believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as critical because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we make the estimate, and different estimates—which also would have been reasonable—could have been used. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be 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. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

We generate revenue from our GSK Collaboration Agreement. We recognize revenue in accordance with ASC 606, which applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, 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) the entity satisfies a performance obligation.

We only apply the five-step model to contracts when it is probable that the entity will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations, and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. We do not include a financing component in our estimated transaction price at contract inception unless we estimate that certain performance obligations will not be satisfied within one year. Additionally, we recognize the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that we otherwise would have recognized is one year or less.

Research and development expenses

As part of the process of preparing our 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 personnel to identify services that have been performed for us and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time, which we periodically confirm with the service providers and make adjustments if necessary. Examples of accrued research and development expenses include fees paid to:

- CROs in connection with clinical trials;
- CMOs with respect to clinical materials, intermediates, drug substance and drug product;
- vendors in connection with research and preclinical development activities; and
- vendors related to manufacturing, development and distribution of clinical supplies.

We must develop assumptions that require judgment to determine whether the individual promises should be accounted for as separate performance obligations or as a combined performance obligation, and to determine the stand-alone selling price for each performance obligation identified in the contract. Since the upfront license was bundled with other promises, we utilized judgment to assess the nature of the combined performance obligation and determined that the combined performance obligation is satisfied over time. Revenue is recognized using a percent complete method based on costs incurred compared with the total expected costs to be incurred (cost to cost measure of progress). There are no outputs from the performance obligation. As a result, an input method was appropriate. A cost to cost measure of progress provides a faithful depiction of the transfer of services to the customer since the predominant inputs to the performance obligation are labor costs, research

and development supplies and manufacturing supplies related to the Phase 1 Study, clinical manufacturing and know-how transfer.

The preceding estimates and judgments materially affect our recognition of revenue. Changes in our estimates of forecasted development costs could impact percentage complete and could have a material effect on revenue recorded in the period in which we determine that change occurs.

Stock-based compensation expense

The fair value of stock options and Employee Stock Purchase Plan awards we grant is estimated using the Black Scholes option pricing model. This option pricing model based on certain subjective assumptions, including (i) the expected stock price volatility, (ii) the expected term of the award, (iii) the risk-free rate of interest, and (iv) expected dividends. The fair value of our common stock utilized in the model is determined based on the quoted market price of our common stock.

There were no significant changes to assumptions used to value options using the Black Scholes option pricing model in 2022, with the exception of the stock and exercise prices.

The fair value of restricted stock units we grant is based on the quoted market price of our common stock on the date of grant.

Government grant funding and potential repayment commitments under recoverable cash advance grants (RCAs)

We have agreements with granting agencies whereby we receive funding under grants, which partially or fully reimburse us for eligible research and development expenditures. Certain grant agreements require us to repay the funding wherein the repayment provision of the grants are predicated on whether we decide to pursue commercial development or out licensing of the drug candidate that is produced from the results of the research program. The repayment provision includes a portion that is fixed (corresponding to 30% of the grant) which is effective after we decide to pursue commercial development or out licensing of the drug candidate. The repayment provision also includes a potential obligation to pay a royalty that is contingent upon achieving sales of a product developed through the program. The maximum amount payable to the granting agency under each grant, including the fixed repayments, the royalty on revenue, and the interest thereon, is twice the amount of funding received.

Grant funding for research and development received under grant agreements where there is a repayment provision is recognized as other income to the extent there is no potential obligation to repay this funding. We record the present value of the liability as a grant repayable in the accompanying consolidated balance sheets. The grant repayable is subsequently recorded at amortized cost. There were no significant changes to assumptions in 2022.

Income taxes

We are subject to taxes in the U.S. and Belgium. Significant judgment is required in determining our provision for income taxes, our deferred tax assets and liabilities and any valuation allowance recorded against our net deferred tax assets. We make these estimates and judgments about our future taxable income that are based on assumptions that are consistent with our future plans. Tax laws, regulations and administrative practices may be subject to change due to economic or political conditions including fundamental changes to the tax laws applicable to corporate multinationals. The U.S. and many countries in the European Union are actively considering changes in this regard. As of December 31, 2022 and 2021, we had recorded a full valuation allowance on our net deferred tax assets because we expect that it is more likely than not that our deferred tax assets will not be realized. Should the actual amounts differ from our estimates, the amount of our valuation allowance could be materially impacted.

Furthermore, significant judgment is required in evaluating our tax positions. In the ordinary course of business, there are many transactions and calculations for which the ultimate tax settlement is uncertain. As a result, we recognize the effect of this uncertainty on our tax attributes or taxes payable based on our estimates of the eventual outcome. These effects are recognized when, despite our belief that our tax return positions are supportable, we believe that it is more likely than not that some of those positions may not be fully sustained upon review by tax authorities. We are required to file income tax returns in the U.S. and Belgium, which requires us to interpret the applicable tax laws and regulations in effect in such jurisdictions. Such returns are subject to audit by the various federal, state and foreign taxing authorities, who may disagree with respect to our tax positions. We believe that our consideration is adequate for all open audit years based on our assessment of many factors, including past experience and interpretations of tax law. We review and update our estimates in light of changing

facts and circumstances, such as the closing of a tax audit, the lapse of a statute of limitations or a change in estimate. To the extent that the final tax outcome of these matters differs from our expectations, such differences may impact income tax expense in the period in which such determination is made. The eventual impact on our income tax expense depends in part on if we still have a valuation allowance recorded against our deferred tax assets in the period that such determination is made.

Recent accounting pronouncements

Refer to Note 2, “Summary of Significant Accounting Policies,” in the accompanying notes to the consolidated financial statements for a discussion of recent accounting pronouncements.

Emerging growth company and smaller reporting company status

The Jumpstart Our Business Startups Act of 2012 permits an “emerging growth company” such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected not to “opt out” of this provision and, as a result, we will adopt new or revised accounting standards at the time private companies adopt the new or revised accounting standard and will do so until such time that we either (i) irrevocably elect to “opt out” of such extended transition period or (ii) no longer qualify as an emerging growth company. We have, however, elected to early-adopt certain new or revised accounting standards as of dates that may or may not coincide with the effective dates of private companies.

As of December 31, 2022, we no longer qualified as a “smaller reporting company”; however, we are allowed to continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies through our Annual Report on Form 10-K for the year ended December 31, 2022.

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, 2022 and December 31, 2021, we had cash and cash equivalents of $284.8 million and $848.5 million, respectively. We had available-for-sale fixed income securities of $446.6 million as of December 31, 2022. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of interest rates in the United States and Belgium. As of December 31, 2022, our cash and cash equivalents is held primarily in savings, money market accounts and money market funds. Our fixed income securities were held primarily in U.S. treasury obligations and U.S. government agency obligations. The majority of the fixed income securities will mature within one year from December 31, 2022. There are no securities that will mature in a period greater than two years from December 31, 2022. Because of the short-term nature of the instruments in our portfolio, an immediate 10% change in the interest rate would not have a material impact on the fair market value of our investment portfolio or on our financial position or results of operations.

We are subject to the risk of fluctuations in foreign currency exchange rates, specifically with respect to the euro. Our functional currency is the U.S. dollar and the functional currency of our wholly owned subsidiary, iTeos Belgium SA, is the euro. An immediate 5% change in the Euro exchange rate would not have any material effect on our results of operations.

Assets and liabilities of iTeos Belgium SA are translated into U.S. dollars at the exchange rate in effect on the balance sheet date. Income items and expenses are translated at the average exchange rate in effect during the period. Unrealized translation gains and losses are recorded as a cumulative translation adjustment, which is included in the condensed consolidated statements of stockholders' equity as a component of accumulated other comprehensive income (loss). Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the local currency are included in other income and expenses, net in the condensed consolidated statements of operations and comprehensive income as incurred.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15, Exhibits and Financial Statement Schedules, of this Annual/ Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022, the end of the period covered by this Annual Report on Form 10-K. The term "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, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving our objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

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

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP, and that receipts and expenditures are being made only in accordance with the authorizations of management and directors; and
- provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use or disposition of assets that could have a material effect on our financial statements.

Under the supervision and with the participation of our management, including our principal executive officer and our principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework provided in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework). Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2022. This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies".

Changes in Internal Control over Financial Reporting

The Company has adopted a hybrid work model for all employees. For when employees are working in the office, the Company has implemented safety measures designed to comply with applicable federal, state and local guidelines instituted in response to the COVID-19 pandemic. The Company has also maintained efficient communication with the Company's partners and clinical sites as the COVID-19 situation has progressed. The Company has taken these precautionary steps while maintaining business continuity so that it can continue to progress with its programs. These changes did not materially impact our internal control over financial reporting.

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting except for the items listed below.

Item 9B. Other Information.

None

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item 10 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics, or Code, that applies to all of our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the Code is available on the investor section of our website at investors.iteostherapeutics.com. The information contained in or accessible from our website is not incorporated into this Annual Report, and you should not consider it part of this Annual Report. We have included our website address in this Annual Report solely as an inactive textual reference. We intend to disclose on our website any amendments to, or waivers from, our Code that are required to be disclosed pursuant to SEC rules.

Item 11. Executive Compensation

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference. All financial statements;

(2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

(3) Exhibits

Exhibit Number	Description
3.1	Second Amended and Restated Certificate of Incorporation of the Registrant (Incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-39401) filed with the Securities and Exchange Commission on July 28, 2020).
3.2	Amended and Restated Bylaws of the Registrant (Incorporated by reference to Exhibit 3.3 to the Registrant's Current Report on Form 8-K (File No. 001-39401) filed with the Securities and Exchange Commission on July 28, 2020).
4.1	Amended and Restated Stockholders' Agreement, dated as of March 24, 2020 (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
4.2	Form of Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
4.3	Description of Securities (incorporated by reference to Exhibit 4.3 of the Registrant's Annual Report on Form 10-K(File No. 001-39401) filed on March 24, 2021).
10.1+	2019 Stock Option and Grant Plan, and forms of award agreements thereunder (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
10.2+	2020 Stock Option and Incentive Plan, and forms of award agreements thereunder (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
10.3>	Third Amended and Restated Collaboration Agreement between iTeos Belgium SA and Adimab, LLC, dated February 22,2021 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-39401) filed on May 13, 2021).
10.4>	Master Services Agreement between iTeos Belgium and WuXi Biologics (Hong Kong) Limited, dated March 21, 2017 (incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
10.5+	2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
10.6+	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
10.7	Form of Officer Indemnification Agreement (incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
10.8	Form of Director Indemnification Agreement (incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).

10.9+	Employment Agreement between the Registrant and Michel Detheux, Ph.D. (incorporated by reference to Exhibit 10.9 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
10.10+	Employment Agreement between the Registrant and Matthew Call (incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
10.11+	Employment Agreement between the Registrant and Joanne Jenkins Lager, M.D (incorporated by reference to Exhibit 10.11 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
10.12+	Employment Agreement between the Registrant and Matthew Gall (incorporated by reference to Exhibit 10.12 of the Registrant's Registration Statement on Form S-1/A (File No. 333-239415) filed on July 20, 2020).
10.13>	Collaboration and License Agreement between iTeos Belgium S.A and GlaxoSmithKline Intellectual Property (No. 4) Limited dated June 11, 2021 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-39401) filed on August 11, 2021).
10.14*>	Amendment No. 1 to Collaboration and License Agreement between iTeos Belgium S.A and GlaxoSmithKline Intellectual Property (No. 4) Limited dated January 24, 2022
10.15*>	Amendment No. 2 to Collaboration and License Agreement between iTeos Belgium S.A and GlaxoSmithKline Intellectual Property (No. 4) Limited dated September 30, 2022
10.16	Lease Agreement between ARE-MA Region No. 75, LLC and iTeos Therapeutics, Inc. dated November 8, 2021 (incorporated by reference to Exhibit 10.14 of the Registrant's Annual Report on Form 10-K (File No. 001-39401) filed on March 23, 2022).
10.17+	Employment Contract between iTeos Belgium S.A. and Yvonne McGrath effective as of May 18, 2020 (incorporated by reference to Exhibit 10.15 of the Registrant's Annual Report on Form 10-K (File No. 001-39401) filed on March 23, 2022).
10.18*+	Addendum to Employment Contract between iTeos Belgium S.A. and Yvonne McGrath dated September 23, 2020
10.19*+	Letter Agreement between iTeos Therapeutics, Inc. and Yvonne McGrath dated November 23, 2022
10.20+	Amended and Restated 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-39401) filed with the Securities and Exchange Commission on June 13, 2022).
10.21+	First Amendment to the iTeos Therapeutics, Inc. 2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-39401) filed on November 10, 2022).
10.22*+	Consultancy Letter Agreement between iTeos Therapeutics, Inc. and Matthew Roden effective as of January 31, 2023
21.1*	Subsidiaries of the Registrant
23.1*	Consent of Deloitte Bedrijfsrevisoren / Réviseurs d'Entreprises BV/SRL
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 Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)

* Filed herewith.

> Identified information has been excluded from this exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

+ Management contract or compensatory plan or arrangement.

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.

iTeos Therapeutics, Inc.

Date: March 15, 2023 By: /s/ Michel Detheux

Michel Detheux

Title: President, Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose individual signature appears below hereby authorizes and appoints Michel Detheux and Matthew Gall, and each of them, with full power of substitution and re-substitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

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/ Michel Detheux **Michel Detheux**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 15, 2023
/s/ David L. Hallal **David L. Hallal**	Director and Chairman of the Board of Directors	March 15, 2023
/s/ Matthew Gall **Matthew Gall**	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 15, 2023
/s/ Detlev Biniszkiewicz **Detlev Biniszkiewicz**	Director	March 15, 2023
/s/ Aaron Davis **Aaron Davis**	Director	March 15, 2023
/s/ Derek DiRocco **Derek DiRocco**	Director	March 15, 2023
/s/ Tim Van Hauwermeiren **Tim Van Hauwermeiren**	Director	March 15, 2023
/s/ Tony Ho **Tony Ho**	Director	March 15, 2023
/s/ Robert Iannone **Robert Iannone**	Director	March 15, 2023
/s/ Ann D. Rhoads **Ann D. Rhoads**	Director	March 15, 2023

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

To the stockholders and the board of directors of iTeos Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of iTeos Therapeutics, Inc. and subsidiaries (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive income, stockholders' equity, and cash flows for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

/s/ Deloitte Bedrijfsrevisoren/Réviseurs d'Entreprises BV/SRL

Zaventem, Belgium

March 15, 2023

We have served as the Company's auditor since 2017.

iTeos Therapeutics, Inc. and Subsidiaries
Consolidated Balance Sheets

(in thousands, except share amounts)	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 284,803	$ 848,537
Short-term investments (amortized cost of $328,405)	328,359	—
Grants receivable	1,001	4,022
Research and development tax credits receivable	—	524
Refundable income taxes	1,434	7,544
Prepaid expenses and other current assets	12,701	14,086
Total current assets	628,298	874,713
Property and equipment, net	2,121	2,072
Long-term investments (amortized cost of $118,330)	118,225	—
Research and development tax credits receivable, net of current portion	1,128	2,004
Restricted cash	235	298
Right of use assets	4,652	5,329
Other assets	332	296
Total assets	754,991	884,712
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	7,662	5,145
Accrued expenses and other current liabilities	19,727	17,157
Deferred income	1,180	827
Deferred revenue	12,595	280,225
Lease liabilities	836	770
Total current liabilities	42,000	304,124
Grants repayable	6,622	6,164
Lease liabilities, net of current portion	3,837	4,571
Unrecognized tax benefits	39,200	17,000
Other noncurrent liabilities	—	33
Total liabilities	91,659	331,892
Commitments and contingencies (Note 10)		
Stockholders' equity:		
Common stock, $0.001 par value, 150,000,000 shares authorized at December 31, 2022 and 2021, respectively; 35,611,219 and 35,466,001 shares issued and outstanding at December 31, 2022 and 2021, respectively	36	35
Additional paid-in capital	435,665	413,180
Accumulated other comprehensive loss	(9,644)	(1,018)
Retained earnings	237,275	140,623
Total stockholders' equity	663,332	552,820
Total liabilities and stockholders' equity	$ 754,991	$ 884,712

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

iTeos Therapeutics, Inc. and Subsidiaries
Consolidated Statements of Operations and Comprehensive Income

(in thousands, except share and per share amounts)	Year ended December 31, 2022	2021
Revenue:		
License and collaboration revenue	$ 267,630	$ 344,775
Total revenue	267,630	344,775
Operating expenses:		
Research and development expenses	97,359	59,369
General and administrative expenses	43,947	40,505
Total operating expenses	141,306	99,874
Income from operations	126,324	244,901
Other income:		
Grant income	2,091	10,181
Research and development tax credits	1,172	—
Interest income	11,361	78
Other income, net	7,788	1,304
Income before income tax expense	148,736	256,464
Income tax expense	52,084	41,943
Net income	96,652	214,521
Net income attributable to common stockholders	$ 96,652	$ 214,521
Basic net income per common share	2.72	$ 6.10
Diluted net income per common share	$ 2.56	$ 5.68
Weighted-average common shares outstanding—basic	35,552,025	35,181,383
Weighted-average common shares outstanding—diluted	37,766,507	37,774,790
Net income	$ 96,652	$ 214,521
Foreign currency translation adjustments	(8,478)	(1,635)
Unrealized loss related to available-for-sale debt securities	$ (148)	$ —
Comprehensive income	88,026	212,886

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

iTeos Therapeutics, Inc. and Subsidiaries
Consolidated Statements of Stockholders' Equity

(in thousands except share amounts)	Common Stock Shares	Common Stock Amount	Additional Paid- In Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings (Accumulated Deficit)	Total Stockholders' Equity
Balance at December 31, 2020	35,044,758	35.00	$ 396,443	$ 617	$ (73,898)	$ 323,197
Stock-based compensation			13,794			13,794
Common stock issued upon exercises of options	421,243	—	2,943	—	—	2,943
Currency translation adjustment	—	—	—	(1,635)	—	(1,635)
Net income	—	—	—	—	214,521	214,521
Balance at December 31, 2021	35,466,001	35	$ 413,180	$ (1,018)	$ 140,623	$ 552,820
Stock-based compensation			21,561			21,561
Common stock issued upon exercises of options and ESPP purchases	145,218	1	924	—	—	925
Currency translation adjustment	—	—	—	(8,478)	—	(8,478)
Unrealized loss on available-for-sale securities	—	—	—	(148)	—	(148)
Net income	—	—	—	—	96,652	96,652
Balance at December 31, 2022	35,611,219	36	$ 435,665	$ (9,644)	$ 237,275	$ 663,332

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

iTeos Therapeutics, Inc. and Subsidiaries
Consolidated Statements of Cash Flows

(in thousands)	Year Ended December 31, 2022	2021
Cash flows from operating activities		
Net income	$ 96,652	$ 214,521
Adjustments to reconcile net income to net cash (used in) provided by operating activities:		
Depreciation and amortization	803	603
Stock-based compensation	21,561	13,794
Amortization/accretion of available-for-sale debt securities	(1,728)	-
Change in operating lease right-of-use assets	10	12
Changes in operating assets and liabilities:		
Grants receivable	2,751	(4,071)
Research and development tax credits receivable	1,237	727
Refundable income taxes	6,107	(7,544)
Prepaid expenses and other current assets	590	(11,789)
Accounts payable	2,761	2,280
Accrued expenses and other liabilities	3,096	9,959
Deferred income	397	(3,480)
Deferred revenue	(267,630)	281,128
Unrecognized tax benefits	22,200	17,000
Net cash (used in) provided by operating activities	(111,193)	513,140
Cash flows from investing activities		
Purchases of investments	(445,004)	-
Purchase of property and equipment	(938)	(1,181)
Purchase of other assets	(120)	(61)
Net cash used in investing activities	(446,062)	(1,242)
Cash flows from financing activities		
Proceeds from issuance of common stock upon exercise of options and ESPP purchase	925	2,943
Proceeds from grants repayable	1,059	716
Net cash provided by financing activities	1,984	3,659
Effects of exchange rate changes on cash, cash equivalents and restricted cash	(8,526)	(3,176)
Net (decrease) increase in cash, cash equivalents and restricted cash	(563,797)	512,381
Cash, cash equivalents and restricted cash at beginning of year	848,835	336,454
Cash, cash equivalents and restricted cash at end of year	$ 285,038	$ 848,835
Non-cash investing and financing activities		
Capital expenditure included in accounts payable	$ 94	$ 175
Operating lease liabilities arising from obtaining right-of-use assets	$ 350	$ 5,877
Unrealized loss on available-for-sale securities	$ 148	$ —
Supplemental disclosure of cash flows		
Cash paid for taxes	$ 22,816	$ 32,019

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

iTeos Therapeutics, Inc.
Notes to Consolidated Financial Statements

Note 1. Nature of Business and Basis of Presentation

Organization

iTeos Therapeutics, Inc. (iTeos Inc. or the Company), a Delaware corporation headquartered in Watertown, Massachusetts (incorporated on October 4, 2019), is the successor to iTeos Belgium SA (iTeos Belgium) a company organized under the laws of Belgium in 2011 and headquartered in Charleroi, Belgium. The Company is a clinical-stage biopharmaceutical company pioneering the discovery and development of a new generation of immuno-oncology therapeutics for people living with cancer. The Company leverages its deep understanding of the tumor immunology and immunosuppressive pathways to design novel product candidates with the aim of restoring the immune response against cancer. The Company's innovative pipeline includes two clinical-stage programs targeting novel, validated immuno-oncology pathways. Each of the Company's therapies in development has optimized pharmacologic properties designed to improve clinical outcomes.

The Company's lead antibody product candidate, EOS-448, also known as GSK4428859A, is an antagonist of TIGIT, or T-cell immunoreceptor with lg and ITIM domains, an immune checkpoint with multiple mechanisms of action. EOS-448 was selected for its affinity for TIGIT, its potency and its potential to engage the Fc gamma receptor, or FcγR, to activate dendritic cells, natural killer cells, and macrophages and to promote cytokine release, activation of antigen presenting cells, and antibody-dependent cellular cytotoxicity, or ADCC, activity. In 2020, the Company started an open-label Phase 1/2a clinical trial of EOS-448 in adult cancer patients with advanced solid tumors. In April 2021, the Company reported preliminary safety, pharmacokinetic, engagement and pharmacodynamic data, indicating target engagement and early evidence of clinical activity as a single agent. In September 2021, the Company dosed the first patients in a Phase 1/2 clinical trial of EOS-448 in combination with pembrolizumab and in combination with the Company's $A_{2A}R$ antagonist inupadenant in patients with solid tumors.

On June 11, 2021, the Company's wholly owned subsidiary, iTeos Belgium S.A., and GlaxoSmithKline Intellectual Property (No. 4) Limited, or GSK, executed a Collaboration and License Agreement, or the GSK Collaboration Agreement, which became effective on July 26, 2021. Pursuant to the GSK Collaboration Agreement, the Company agreed to grant GSK a license under certain of its intellectual property rights to develop, manufacture, and commercialize products comprised of or containing EOS-448, which license is exclusive in all countries outside of the United States and co-exclusive, with iTeos, in the United States. GSK and iTeos intend to develop EOS-448 in combination, including with other oncology assets of GSK, and iTeos and GSK will jointly own the intellectual property created under the GSK Collaboration Agreement that covers such combinations. In partnership with GSK, the Company began enrolling patients with first line NSCLC in a randomized Phase 2 trial assessing the doublet of GSK's anti-PD-1 (Jemperli (dostarlimab-gxly)) with EOS-448. In addition, the Company is enrolling patients with first-line advanced or metastatic head and HNSCC for the Phase 2 expansion part of the trial assessing the doublet of GSK's dostarlimab with EOS-448. The Company and GSK continue to explore the Phase 1b trial evaluating the novel triplet of EOS-448 with dostarlimab and GSK's investigational anti-CD96 antibody.

Based on favorable preclinical data generated in collaboration with Fred Hutchinson Cancer Research Center, the Company is also advancing an open-label dose-escalation/expansion Phase 1/2 trial evaluating the safety, tolerability and preliminary activity of EOS-448 as monotherapy and in combination with Bristol Myers Squibb's iberdomide - a novel, potent oral cereblon E3 ligase modulator (CELMoD®) compound with enhanced tumoricidal and immune-stimulatory effects compared with im984melamunomodulatory (IMiD®) agents - with or without dexamethasone, in adults with relapsed or refractory multiple myeloma.

The Company is also advancing inupadenant, a next-generation adenosine A2AR antagonist tailored to overcome the specific adenosine-mediated immunosuppression found in tumor microenvironment, into proof-of concept trials in several indications following encouraging single-agent activity in Phase 1. The Company is investigating inupadenant in an open-label multi-arm Phase 1/2a clinical trial in adult cancer patients with advanced solid tumors. The single-agent dose-escalation and expansion portions of the Company's Phase 1/2a clinical trial of inupadenant have demonstrated durable monotherapy antitumor activity in some patients with advanced solid tumors and safety consistent with previously reported results. As part of this monotherapy assessment of inupadenant, the Company identified a potential predictive biomarker and the Company is enrolling patients in the

biomarker cohort of the ongoing Phase 1b/2a trial. The Company is also enrolling patients in a Phase 2 trial in post-IO metastatic NSCLC to evaluate the combination of inupadenant with platinum-doublet chemotherapy compared to standard platinum-doublet chemotherapy. The Company has completed enrollment in the safety evaluation portion of the clinical trial of inupadenant in combination with chemotherapy and with pembrolizumab, as well as the monotherapy expansion cohort in prostate cancer. The Company has completed enrollment in the Phase 2a trial evaluating inupadenant in combination with pembrolizumab in post-PD-1 melanoma and has decided to prioritize development of inupadenant in our ongoing study in combination with platinum-doublet chemotherapy in patients with chemo-naïve NSCLC as the Company has determined that the post-PD-1 melanoma setting is not a path to accelerated approval. In addition, the Company is evaluating a salt form of inupadenant in a Phase 1 study.

The Company began its research and development activities as a spin-off of Ludwig Cancer Research and have built significant expertise in designing novel cancer immunotherapies. The Company's internal research and development team has extensive expertise in tumor immunology, characterization of immunosuppressive mechanisms in the tumor microenvironment, pharmacology and translational medicine. The Company has also built discovery capabilities to develop both small molecules and antibodies with differentiated and optimized product profiles for targets validated by a strong scientific rationale. The Company continues to progress research programs focused on additional targets that complement its TIGIT and $A_{2A}R$ programs or address additional immunosuppressive pathways. In September 2021, the Company nominated a product candidate, EOS-984, targeting a novel mechanism in the adenosine pathway for Investigational New Drug, or IND, enabling studies. The Company's expertise also allows it to integrate a biomarker-rich strategy into its clinical programs to measure the activity of a product candidate in patients, seek to optimize combination agents and identify patients it deems most likely to benefit from treatment.

On December 2, 2020, iTeos Securities Corporation (iTeos SC) was incorporated as a Massachusetts Security Corporation. It is a wholly-owned subsidiary of iTeos Inc. On July 27, 2021, iTeos BE, LLC (iTeos LLC) was incorporated as a Delaware Limited Liability Company. It is a wholly-owned subsidiary of iTeos Belgium.

Liquidity and capital resources

Since inception, the Company’s activities have consisted primarily of performing research and development to advance its product candidates. For the first time since inception, the Company earned income during the year ended December 31, 2021, which equaled net income of $214.5 million. For the year ended December 31, 2022, the Company had net income of $96.7 million and retained earnings of $237.3 million. As of March 15, 2023, the issuance date of the consolidated financial statements for the year ended December 31, 2022, the Company expects that its cash and cash equivalents would be sufficient to fund its operating expenses, capital expenditure requirements and debt service payments through at least 12 months from the issuance date of the consolidated financial statements.

The Company may seek additional funding in order to reach its development and commercialization objectives. The Company may not be able to obtain funding on acceptable terms, or at all, and the Company may not be able to enter into collaborations or other arrangements. The terms of any funding may adversely affect the holdings or the rights of the Company’s stockholders. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects.

The Company’s future results of operations involve a number of risks and uncertainties. Factors that could affect the Company’s future operating results and cause actual results to vary materially from expectations include, but are not limited to, uncertainty regarding results of clinical trials and reaching milestones, uncertainty of regulatory approval of the Company’s current or future product candidates, uncertainty of market acceptance of the Company’s product candidates, if approved, competition from substitute products and larger companies, securing and protecting proprietary technology, strategic relationships and dependence on key individuals and sole source suppliers. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities and may not ultimately lead to a marketing approval and commercialization of a product.

The Company’s product candidates require approvals from the U.S. Food and Drug Administration (FDA) and comparable foreign regulatory agencies prior to commercial sales in their respective jurisdictions. There can be no assurance that any product candidates will receive the necessary approvals. If the Company was denied approval, approval was delayed or the Company was unable to maintain approval for any product candidate, it could have a materially adverse impact on the Company. Even if the Company’s product development efforts are

successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales. The Company will need to generate significant revenue to achieve sustained profitability, and it may never do so.

COVID-19

The COVID-19 pandemic has presented a substantial public health and economic challenge around the world. While the COVID-19 pandemic has not significantly impacted the Company's business or results of operations, the future impact of the COVID-19 pandemic on the biotechnology industry, the healthcare system, the Company's development timelines for EOS-448 and inupadenant, the Company's preclinical research and development, and the Company's current and future operations and financial condition will depend on future developments, which are highly uncertain and cannot be predicted with confidence. Disruptions to the global economy, disruption of global healthcare systems, and other significant impacts of the COVID-19 pandemic could have a material adverse effect on the Company's business, financial condition, results of operations and growth prospects.

Basis of presentation

The consolidated financial statements and accompanying notes have been prepared in accordance with generally accepted accounting principles in the United States of America (U.S. GAAP).

Note 2. Summary of significant accounting policies

Principles of consolidation

The consolidated financial statements include the Company’s accounts and those of its wholly owned subsidiaries. All intercompany accounts, transactions and balances have been eliminated.

Use of estimates

The preparation of the Company’s consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, and expenses, as well as the related disclosures of contingent assets and liabilities. The Company bases its estimates and assumptions on historical experiences, when available, and on various factors that it believes to be reasonable under the circumstances. The Company evaluates its estimates and assumptions on an ongoing basis. Actual results could differ materially from these estimates.

The full extent to which the COVID-19 pandemic will directly or indirectly impact the Company’s business, results of operations and financial condition, including expenses, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19 and the actions taken to contain or treat COVID-19, as well as the economic impact on local, regional, national and international markets. The Company has considered the impact of COVID-19 on estimates within its financial statements and there may be changes to those estimates in future periods. As of the date of issuance of these consolidated financial statements, the Company has not experienced material business disruptions or incurred impairment losses in the carrying value of its assets as a result of the pandemic and is not aware of any specific related event or circumstance that would require it to update its estimates.

Cash, cash equivalents and restricted cash

Cash and cash equivalents consist of standard checking accounts, money market accounts, and a sweep account that consists of money market funds with highly liquid investments with maturities of three months or less. Restricted cash represents collateral provided for letters of credit issued as security deposits in connection with the Company’s leases of its corporate facilities.

Short-term and long-term investments

Short-term investments consist of fixed income securities with maturities more than three months but less than twelve months from the date of purchase. Long-term investments consist of fixed income securities with maturities greater than twelve months from the date of purchase. The Company intends to dispose of securities within its

portfolio if the need for additional liquidity arises. As such, the Company classifies its securities as available-for-sale.

Foreign currency, currency translation and comprehensive income

The reporting currency of the consolidated financial statements is the U.S. dollar (USD). The functional currency for iTeos Belgium is the euro and the functional currency for iTeos Inc., iTeos SC, and iTeos LLC is the USD.

Income items and expenses are translated at the average exchange rate in effect during the period. Unrealized translation gains and losses are recorded as a cumulative translation adjustment, which is included in the Consolidated Statements of Stockholders' Equity as a component of accumulated other comprehensive income. Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the local currency are included in Other income, net in the Consolidated Statements of Operations and Comprehensive Income as settled.

Comprehensive income is defined as a change in equity of a business enterprise during a period, resulting from transactions from non-owner sources. The Company had unrealized gains from foreign currency translation of iTeos Belgium during the years ended December 31, 2022 and 2021, which meets the criteria as other comprehensive income and, therefore, the Company has reported comprehensive income and net income.

Fair value measurements

Fair value accounting is applied for all financial assets and liabilities. The carrying amount of the Company's financial instruments, including grants receivable, R&D credits receivable—current, accounts payable, accrued expenses and other current liabilities approximate fair value due to the short-term duration of those instruments. The carrying amounts of long-term R&D credits receivable and grants repayable approximate fair value due to low local market interest rates.

FASB ASC Topic 820, *Fair Value Measurement and Disclosures* (ASC 820), established a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the financial instrument based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the financial instrument and are developed based on the best information available in the circumstances.

The accounting standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value, which are the following:

- Level 1—Quoted prices in active markets that are accessible at the market date for identical unrestricted assets or liabilities.
- Level 2—Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs for which all significant inputs are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Financial instruments measured at fair value on a recurring basis include cash equivalents (money market funds) and fixed income securities. Fixed income securities include U.S. treasury securities, U.S. government agency backed securities, and investment grade corporate securities.

The fair value of cash equivalents and U.S. treasury securities was determined based on Level 1 inputs as described in Note 3. The fair value of U.S. government agency backed securities and corporate securities was

determined based on Level 2 inputs as described in Note 3. An entity may elect to measure many financial instruments and certain other items at fair value at specified election dates. The Company did not elect to measure any additional financial instruments or other items at fair value.

There have been no changes to the valuation methods utilized by the Company during the years ended December 31, 2022 or 2021. The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of financial instruments between levels during the years ended December 31, 2022 or 2021.

Concentration of credit risk

As of December 31, 2022 and 2021, the Company's cash and cash equivalents consisted primarily of cash balances held in U.S. dollars in money market funds and money market accounts and euro in accounts with European banks in excess of publicly insured limits. The Company does not believe it is subject to unusual credit risk associated with commercial banking relationships.

As of December 31, 2022, the Company's fixed income securities consisted of investment grade U.S. treasury, U.S. government agency, and corporate securities. There are no securities in the Company's portfolio with a credit rating below "A-". Approximately 99% of the Company's fixed income holdings as of December 31, 2022 consisted of U.S. treasury and U.S. government agency securities. The Company does not believe it is subject to unusual credit risk associated with its investment portfolio.

Research and development tax credits

iTeos Belgium is considered a biotech company in Belgium and therefore qualifies for a cash-based tax credit on research and development (R&D) expenses. The R&D tax credit is calculated based on a percentage of eligible R&D expenses defined by the Belgian government for each fiscal year (13.5% for 2022 and 2021) and then applying the effective tax rate to that result. Under current tax laws, the R&D tax credits are refundable if the Company is unable to use the credits to offset income taxes for the five subsequent tax years. The Company records a receivable and other income as the eligible R&D expenses are incurred, as it is reasonably assured that the R&D tax credit will be received, based upon its history of filing for the tax credits. R&D tax credits receivable where cash is expected to be received by the Company more than one year after the balance sheet date are classified as noncurrent in the consolidated balance sheets.

Property and equipment

Property and equipment, including leasehold improvements, are stated at cost and depreciated when placed into service using the straight-line method over the estimated useful lives as follows:

Asset	Estimated Useful Life
Computer equipment and software	3 years
Furniture, fixtures and other	5 years
Scientific equipment	5 – 6 years
Leasehold improvements	Shorter of useful life or term of lease

Upon retirement or sale, the cost and related accumulated depreciation are removed from the consolidated balance sheets and the resulting gain or loss is reflected in the consolidated statements of operations and comprehensive income.

Impairment of long-lived assets

The Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. An impairment charge would be recorded when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. Impairment, if any, is assessed using discounted cash flows or other appropriate measures of fair value. As there were no indicators of impairment, the Company did not recognize any impairment charges for the years ended December 31, 2022 or 2021.

Revenue recognition

The Company analyzes its collaboration arrangements to assess whether they are within the scope of Accounting Standards Codification ASC Topic 808, *Collaborative Arrangements (*ASC 808). If the Company concludes that some or all aspects of the arrangement are within the scope of ASC 808 and do not represent a transaction with a customer, the Company recognizes its allocation of the shared costs incurred with respect to the jointly conducted activities pursuant to ASC 730, *Research and Development*. As such, the Company will expense costs as incurred, including any reimbursements made, and recognize reimbursements received as a reduction of research and development expense. If the Company concludes that some or all aspects of the arrangement represent a transaction with a customer, the Company accounts for those aspects of the arrangement within the scope of ASC 606, *Revenue from Contracts with Customers* (ASC 606).

At inception, the Company determines whether contracts are within the scope of ASC 606 or other topics. For contracts that are determined to be within the scope of ASC 606, revenue is recognized when a customer obtains control of promised goods or services. The amount of revenue recognized reflects the consideration to which the Company expects to be entitled to receive in exchange for these goods and services. To achieve this core principle, the Company applies the following five steps (i) identify the contract with the 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 performance obligation is satisfied. The Company only applies the five-step model to contracts when it determines that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct and are distinct in the context of the contract. To the extent a contract includes multiple promised goods and services, the Company applies judgment to determine whether promised goods and services are both capable of being distinct and distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method, depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in management's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes. Determining the transaction price requires significant judgment.

For arrangements that include sales-based royalties, including milestone payments based on levels of sales, if the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its agreements.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis unless the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation.

The Company satisfies performance obligations either over time or at a point in time. Revenue is recognized over time if either (i) the customer simultaneously receives and consumes the benefits provided by the entity's performance, (ii) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or (iii) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer.

For licenses of intellectual property (IP), if the license to the Company's IP is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from consideration allocated to the license when the license is transferred to the customer and the customer can use

and benefit from the licenses. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

At the inception of each arrangement that includes development or regulatory milestone payments, the Company evaluates the probability of reaching the milestones and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur in the future, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's, such as regulatory approvals, are not considered probable of being achieved until those approvals are received and therefore revenue is constrained as management is unable to assert that a reversal of revenue would not be possible. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. To date, the Company has not recognized any milestone revenue resulting from any of its agreements.

Deferred revenue arises from amounts received in advance of the transfer of control and is recognized as revenue in future periods as performance obligations are satisfied. Deferred revenue expected to be recognized within the next twelve months is classified as a current liability. Upfront payment contract liabilities resulting from the Company's license agreements do not represent a financing component as the payment is not financing the transfer of goods or services, and the technology underlying the licenses granted reflects research and development expenses already incurred by the Company.

Contract costs

The Company recognizes as an asset the incremental costs of obtaining a contract with a customer if the costs are expected to be recovered. The Company has elected the practical expedient in ASC 340, *Other Assets and Deferred Costs*, wherein it recognizes the incremental costs of obtaining a contract as an expense when incurred if, at inception, the expected amortization period of the asset that the Company otherwise would have recognized is one year or less.

Collaborative Arrangements

The Company analyzes its collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and are, therefore within the scope of ASC Topic 808, *Collaborative Arrangements*. This assessment is performed throughout the life of the arrangement and takes into consideration changes in the responsibilities of all parties to the arrangement. Collaboration agreements may include reimbursements from and payments to parties due to the activities performed by either party. Any reimbursement from parties involved in a collaboration agreement are recorded as a reduction to research and development expense. Payments made to parties involved in a collaboration agreement are recorded as research and development expense.

Research and development expenses

Research and development costs are expensed as incurred. Research and development expenses consist of personnel costs for the Company's research and product development employees, as well as non-personnel costs such as facilities and overhead costs attributable to research and development, and professional fees payable to third parties for preclinical and clinical studies and research services, clinical trial costs, laboratory supplies and equipment maintenance, and other consulting costs.

The Company estimates preclinical and clinical study and research expenses based on the services performed, pursuant to contracts with research institutions that conduct and manage preclinical and clinical studies and research services on its behalf. The Company estimates these expenses based on discussions with internal management personnel and external service providers as to the progress or stage of completion of services and the contracted fees to be paid for such services. If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the accrual accordingly. When third-party service providers' billing terms do not coincide with the Company's period-end, the Company is required to make estimates of its obligations to those third parties, including clinical trial and pharmaceutical development costs, contractual services costs and costs for supply of its drug candidates, incurred in a given accounting period and record accruals at the end of the period. The Company bases its estimates on its knowledge of the research and

development programs, services performed for the period, history for related activities and the expected duration of the third-party service contract, where applicable. Payments associated with licensing agreements to acquire exclusive licenses to develop, use, manufacture and commercialize products that have not reached technological feasibility and do not have alternate commercial use are expensed as incurred. Payments made to third parties under these arrangements in advance of the performance of the related services by the third parties are recorded as prepaid expenses until the services are rendered.

Government grant funding and potential repayment commitments under recoverable cash advance grants (RCAs)

The Company has agreements with granting agencies whereby the Company receives funding under grants which partially or fully reimburse the Company for qualifying research and development expenditures. Certain grant agreements require the Company to repay the funding depending on whether the Company decides to pursue commercial development or out licensing of any drug candidate that is produced from the research program. The repayment provision includes a portion that is repayable in fixed annual installments (corresponding to 30% of the grant), which is effective unless the Company decides not to pursue commercial development or out licensing of the drug candidate. The repayment provision also includes a potential obligation to pay a royalty that is contingent upon achieving sales of a product developed through the program. The maximum amount repayable to the granting agency under each grant, including the fixed repayments, the royalty on revenue, and the interest thereon, is twice the amount of funding received.

Grant funding for research and development received under grant agreements where there is no obligation to repay is recognized as grant income in the period during which the related qualifying expenses are incurred, based on the applicable reimbursement percentage, provided that the grants are fully approved by the granting agencies and the conditions under which the grants were provided have been met.

Grant funding for research and development received under grant agreements where there is a repayment provision is recognized as grant income to the extent there is no potential obligation to repay this funding. The Company records the present value of the liability of the portion of funding relating to fixed repayment upon receipt in the consolidated balance sheets. The grant repayable is subsequently recorded at amortized cost.

The Company assesses whether there is an obligation to make a royalty payment based on the probability of successful completion of the research and development and future sales and commercial success of the drug candidate.

Grant funding that has been received by the Company in advance of incurring qualifying expenses is recorded as deferred income. Grant income recognized upon incurring qualifying expenses in advance of receipt of grant funding is recorded in the consolidated balance sheets as grants receivable.

Leases

On January 1, 2021, the Company adopted Accounting Standard Update, or ASU No. 2016-02 (Topic 842), Leases, or ASC 842. Under the standard, the Company accounts for leases using a right-of-use, or ROU, model, which recognizes that, at the date of commencement, a lessee has a financial obligation to make lease payments to the lessor for the right to use the underlying asset during the lease term. On the date of adoption, the Company recognized $0.9 million of right-to-use assets and lease liabilities in the consolidated balance sheet.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as ROU assets and short-term and long-term lease liabilities, as applicable. The Company typically only includes an initial lease term deemed reasonable certain to occur. It also considers termination options and factors those into the determination of lease payments. Options to renew a lease are not included in the assessment unless there is reasonable certainty that the Company will renew.

Operating lease liabilities and their corresponding ROU assets are recorded based on the present value of lease payments over the expected remaining lease term. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate, which reflects the fixed rate at which it could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Lease expense for lease payments is recognized on a straight-line basis over the lease term. The Company is required to pay fees for operating expenses in addition to monthly

base rent for certain operating leases (non-lease components). The Company will elect the practical expedient, which allows non-lease components to be combined with lease components on an asset-by-asset class basis. For real estate asset class, the Company has not elected the practical expedient. Variable non-lease components are not included within the lease right-of-use asset and lease liability on the consolidated balance sheet, and instead are reflected as expense in the period they are paid.

Stock-based compensation

The Company accounts for stock-based compensation arrangements with employees in accordance with ASC 718, *Stock Compensation.* Stock-based awards granted are in the form of stock options, Employee Stock Purchase Plan (ESPP) awards, and a limited amount of restricted stock units. ASC 718 requires the recognition of stock-based compensation expense, using a fair value-based method, for costs related to all stock awards granted. The Company's determination of the fair value of stock options and ESPP awards with time-based vesting on the date of grant utilizes the Black-Scholes option-pricing model, and is impacted by the estimated fair value of its common stock as well as other variables including, but not limited to, the expected term that stock options will remain outstanding, the expected common stock price volatility over the term of the option, risk-free interest rates and expected dividends.

The fair value of stock options and ESPP awards is recognized over the period during which an optionee is required to provide services in exchange for the stock option award, known as the requisite service period (usually the vesting period) on a straight-line basis. Stock-based compensation expense is recognized based on the fair value determined on the date of grant and is reduced for forfeitures as they occur. For stock options granted to recipients in Belgium, option holders have a period of time (no longer than 30 days) to accept their awards. Accordingly, the grant date is determined based on the date of acceptance, as that is the point when a mutual understanding of the key terms of the awards are established.

The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (i) the expected stock price volatility, (ii) the expected term of the award, (iii) the risk-free rate of interest, and (iv) expected dividends. Due to the lack of company-specific historical implied volatility data, the Company has based its computations of expected volatility on the historical volatility of a representative group of public companies with similar characteristics of the Company, including stage of product development and life science industry focus. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The Company uses 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 and non-employees, whereby, the expected term equals the arithmetic average of the vesting term and the original contractual term of the options due to its lack of sufficient historical data. The risk-free interest rate is based on U.S. Treasury securities with a maturity date commensurate with the expected term of the associated award. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock. The fair value of common stock is determined based on the quoted market price of the common stock.

The fair value of restricted stock units is also recognized over the requisite service period on a straight-line basis. The fair value of restricted stock units is based on the price of the Company's common stock on the grant date.

The Company classifies stock-based compensation expense in its statement of operations and comprehensive income in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Income taxes

The Company provides for income taxes under the asset and liability method. Current income tax expense or benefit represents the amount of income taxes expected to be payable or refundable for the current year. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax bases of assets and liabilities and net operating loss and credit carryforwards, and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all of the tax benefits will not be realized.

The global intangible low-taxed income ("GILTI") provisions require the Company to include in its U.S. income tax return foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets. The Company is electing to account for GILTI tax in the period in which it is incurred.

The Company accounts for uncertain tax positions in accordance with ASC 740-10, *Accounting for Uncertainty in Income Taxes.* The Company assesses all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and the Company will determine whether (i) the factors underlying the sustainability assertion have changed and (ii) the amount of the recognized tax benefit is still appropriate. The recognition and measurement of tax benefits requires significant judgment. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available.

The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes.

Segment information

Operating segments are defined as components of an enterprise for which separate discrete financial information is available for evaluation by the chief operating decision maker (CODM) in deciding how to allocate resources and in assessing operating performance. The Company's CODM is the Chief Executive Officer. The Company views its operations and manages its business in one operating segment, the business of developing cancer immunotherapies.

Net income per share attributable to common stockholders

Basic net income per share and diluted net income per share are computed using the weighted-average number of shares of common stock outstanding for the period. The effect of potentially dilutive shares is computed using the treasury stock method. Except where the result would be antidilutive to net income, diluted net income per share is computed assuming the exercise of common stock options.

Accounting standards not yet effective

In June 2016 the FASB issued ASU No. 2016-13, Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments. This standard requires that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, this standard now requires allowances to be recorded instead of reducing the amortized cost of the investment. The Company adopted this standard as of January 1, 2023. The adoption of this standard did not have a material impact on the Company's consolidated financial position and results of operations.

Note 3. Investment securities and fair value measurements

Certain of the Company's assets and liabilities are recorded at fair value, as described below.

The following tables set forth the Company's financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy:

	December 31, 2022			
(in thousands)	Level 1	Level 2	Level 3	Total
Cash equivalents (money market funds)	$ 92,850	$ —	$ —	$ 92,850
U.S. government agency bonds	-	267,748	-	$ 267,748
U.S. treasury bonds	186,477	-	-	$ 186,477
Corporate debt securities	-	5,349	-	$ 5,349
Totals	$ 279,327	$ 273,097	$ —	$ 552,424

(in thousands)	December 31, 2021 Level 1	Level 2	Level 3	Total
Cash equivalents (money market funds)	$ 797,448	$ —	$ —	$ 797,448
Totals	$ 797,448	$ —	$ —	$ 797,448

Cash equivalents consist of money market funds, which are classified within Level 1 of the fair value hierarchy because they are valued using quoted market prices in an active market. U.S. treasury securities are also classified as Level 1 because they are valued using quoted prices. U.S. government agency and corporate securities are classified within Level 2 of the fair value hierarchy because they are valued using market-based models that consider inputs such as yield, prices of comparable securities, coupon rate, maturity, and credit quality.

During the periods presented, the Company has not changed the manner in which it values assets and liabilities that are measured at fair value. The Company recognizes transfers between levels of the fair value hierarchy as of the end of the reporting period. There were no transfers within the hierarchy during the years ended December 31, 2022 and 2021.

The Company's fixed income securities held as of December 31, 2022 are classified as available-for-sale. The following table presents the amortized cost, fair value, and unrealized losses by major security type, for the fixed income securities held by the Company:

(in thousands)	December 31, 2022 Amortized cost	Gross unrealized gains in AOCI	Gross unrealized losses in AOCI	Fair value
U.S. government agency bonds	$ 254,881	$ 87	$ (211)	$ 254,757
U.S. treasury bonds	186,496	19	(37)	186,478
Corporate debt securities	5,358	-	(9)	5,349
Totals	$ 446,735	$ 106	$ (257)	$ 446,584

The $3 thousand difference between the net unrealized loss reflected in the above table and that per the statement of comprehensive income is due to unrealized losses relating to debt securities which were cash equivalents as of December 31, 2022, and are therefore not included in the table above.

The following table presents the amortized cost and fair value of the Company's fixed income securities by maturity grouping:

(in thousands)	December 31, 2022 Amortized cost	Fair value
Due in one year or less	$ 328,405	$ 328,359
Due after one year through five years	118,330	118,225
Due after five years through ten years	-	—
Due after ten years	-	—
Total	$ 446,735	$ 446,584

There were no securities which were determined to be other-than-temporarily impaired as of the year ended December 31, 2022. There were no sales of securities which resulted in a realized loss during the year ended December 31, 2022. The Company recognized $9.6 million of interest income earned from its available-for-sale debt securities and money market funds. The Company also recognized $1.8 million of accretion on its available-for-sale debt securities, which was recorded to interest income.

Note 4. Consolidated balance sheet components

Property and equipment

Property and equipment, net consisted of the following:

(in thousands)	December 31, 2022	2021
Scientific equipment	$ 3,008	$ 2,970
Furniture & office equipment	1,332	1,002
Leasehold improvements	1,238	1,071
Total	5,578	5,043
Accumulated depreciation and amortization	(3,457)	(2,971)
Property & equipment, net	$ 2,121	$ 2,072

Depreciation and amortization expense was $0.8 million and $0.6 million for the years ended December 31, 2022 and 2021, respectively.

Accrued expenses and other current liabilities

Accrued liabilities consisted of the following:

(in thousands)	December 31, 2022	2021
Accrued clinical trial costs	$ 13,496	$ 12,991
Accrued personnel costs	5,635	3,884
Accrued professional fees	64	25
Accrued other	532	257
Total accrued expenses and other current liabilities	$ 19,727	$ 17,157

Note 5. License and collaboration agreements

Adimab

In January 2017, the Company entered into a collaboration agreement (as amended, the Adimab Agreement) with Adimab, LLC (Adimab). Adimab has developed an antibody discovery and optimization technology platform. This collaboration enables the Company's research and development efforts on discovery and optimization of new antibodies against immuno-oncology targets the Company may identify.

Under the terms of the Adimab Agreement, Adimab has granted the Company a worldwide, non-exclusive research license for a one-year research term period and evaluation period for up to 18 months per research program. The Company is required to use commercially reasonable efforts to perform its research activities under the Adimab Agreement and, if the Company exercises its right to obtain a development and commercialization license, the Company is required to use commercially reasonable efforts to pursue development and commercialization of a product directed to the applicable target. Under the terms of the Adimab Agreement, the Company granted Adimab a worldwide, non-exclusive license under all of its patents and know-how that are reasonably necessary or useful for Adimab to perform its research activities under the Adimab Agreement.

In February 2021, the Company entered into an amendment to the Adimab Agreement (the Amended Adimab Agreement). The Amended Adimab Agreement specifies different milestone payments for new products that are derived from research programs beginning after February 22, 2021 (the New Products). For New Products, on a per target basis, the Company may be required to pay development, regulatory and commercial milestone payments totaling up to an aggregate of $45.8 million for the first three products and additional milestone payments up to $14.5 million for each additional product.

The Company will pay Adimab low to mid single-digit percentage royalties on a country-by-country and product-by-product basis, on worldwide net product sales of licensed products. Royalties are payable on a licensed product-by-licensed product and country-by-country basis until the later of (i) expiration of the last valid claim of a licensed patent right that covers such licensed product in such country, and (ii) ten years following the first commercial sale of such licensed product in such country.

Through December 31, 2022, the Company has paid a total of $5.4 million to Adimab under the Adimab Agreement. In 2022, the Company made a payment of $2.0 million due to reaching an additional milestone (dosing of first patient for Phase 2 clinical trial). As of the date of these consolidated financial statements, the Company has not pursued any additional targets under the Adimab agreement that could potentially result in such milestone payments.

Adimab controls the filing, prosecution, maintenance and enforcement of the intellectual property that it licenses to the Company under the Adimab Agreement. The Company has the right to enforce such licensed intellectual property against infringement if the infringement is competitive with the Company's licensed products and Adimab does not pursue enforcement. The Company controls the filing, prosecution, maintenance and enforcement of the intellectual property the Company licenses to Adimab under the Adimab Agreement and all program antibody patents.

The term of the Adimab Agreement will continue until the last to expire royalty term on a product-by-product and country-by-country basis if the Company exercises its option, or in the event no option is exercised, the conclusion of the last-to-expire evaluation term, unless terminated earlier by either party. Each party has the right to terminate the Adimab Agreement due to the other party's uncured material breach or the Company's abandonment of the product.

GlaxoSmithKline (GSK)

Summary of Agreement

On June 11, 2021, the Company's wholly owned subsidiary, iTeos Belgium S.A., and GSK executed a Collaboration and License Agreement, or the GSK Collaboration Agreement, pursuant to which the Company agreed to grant GSK a license under certain of the Company's intellectual property rights to develop, manufacture, and commercialize products comprised of or containing the Company's antibody product, EOS-448. Under the GSK Collaboration Agreement, GSK agreed to make an upfront nonrefundable payment of $625.0 million to the Company within 10 business days of the date on which the GSK Collaboration Agreement became effective, which occurred on July 26, 2021. Additionally, the Company is eligible to receive up to $1.45 billion in milestone payments, contingent upon the EOS-448 program achieving certain development and commercial milestones. Within the collaboration, GSK and the Company agree to share responsibility and costs for the global development of EOS-448 beyond the Phase 1 study (the "Global Development Plan") and will jointly commercialize and equally split profits in the United States. Outside of the United States, GSK will receive an exclusive license for commercialization, and the Company is eligible to receive tiered double digit royalty payments up to 20% during a customary royalty term.

Collaboration

The Company concluded that the GSK Collaboration Agreement is under the scope of ASC 808 as both parties will actively participate in a joint operating activity and are exposed to significant risks and rewards that depend on the activity's commercial success. ASC 808 provides that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606 when the collaborative arrangement participant is a customer in the context of a unit of account. In those situations, all of the guidance in ASC 606 should be applied, including recognition, measurement, presentation, and disclosure requirements related to such unit of account. The unit-of-account guidance in ASC 808, which aligns with the guidance in ASC 606 (that is, a distinct good or service) is used when an entity is assessing whether the collaborative arrangement or a part of the arrangement is within the scope of ASC 606.

The Company determined that the co-development in Phases 2 and 3 and the co-commercialization efforts of the GSK Collaboration Agreement represent joint operating activities in which both parties are active participants and of which both parties are exposed to significant risks and rewards that are dependent on the success of the activities. Accordingly, the Company is accounting for these activities in accordance with ASC No. 808, *Collaborative Arrangements* (ASC 808). Additionally, the Company has determined that in the context of these activities, GSK does not represent a customer as contemplated by ASC 606-10-15, *Revenue from Contracts with Customers – Scope and Scope Exceptions*. As a result, these activities are accounted for as a component of the related expense in the period incurred in accordance with ASC 730, *Research and Development*. Additionally, reimbursements received from GSK in connection with the joint operating activities are recognized as a reduction to research and development expense.

GSK is responsible for 60% of the costs related to the Global Development Plan. During the year ended December 31, 2022, the Company expensed approximately $30.8 million of costs related to the cost-sharing provisions of the GSK Collaboration Agreement, of which approximately $10.2 million were reimbursable to GSK and recorded to research and development expense during the year ended December 31, 2022. As of December 31, 2022, $4.7 million of the reimbursable expenses have not been paid and are recorded to accrued expenses in the consolidated balance sheet. The Company and GSK have collectively agreed to spend an aggregate of $900.0 million on the Global Development Plan.

Revenue Recognition

The Company also evaluated the elements of the GSK Collaboration Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, GSK, is a customer. The Company's arrangement with GSK contains the following material promises under the contract at inception: (i) transfer of the license under certain of the Company's intellectual property related to EOS-448, (ii) completion of the Phase 1 clinical study related to EOS-448, (iii) transfer of "Know How" under the EOS-448 intellectual property, and (iv) manufacturing until the "Know How" transfer is complete. The Company evaluated the above material promises under ASC 606 and determined that it has one combined performance obligation. These promises are considered to be outputs of the Company's ordinary activities and ongoing major operations. As GSK provided the Company consideration in exchange for these promises, GSK meets the definition of a customer under ASC 606-10-20 in the context of the combined performance obligation. These promises are distinct from the co-development and co-commercialization activities in which the Company and GSK jointly participate. Accordingly, the context in which GSK is a customer is limited to the material promises described above.

The transaction price totaling $625.0 million was comprised of the upfront license payment. As of December 31, 2022, no development or regulatory milestones have been assessed as probable of being reached and thus have been fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to GSK and therefore have also been excluded from the transaction price. The Company is applying the royalty exception for sales-based royalties and will not recognize revenue until the subsequent sale of product occurs.

The transaction price is being recognized as revenue over time as the costs to complete the Phase 1 study, perform interim clinical supply manufacturing, and perform the know-how transfer are incurred. The combined performance obligations are substantially complete as of the year ended December 31, 2022, with an insignificant portion expected to be completed in early 2023. Revenue is recognized using a percent complete method based on costs incurred compared with the total expected costs to be incurred (cost to cost measure of progress). There are no outputs from the performance obligation. As a result, an input method was appropriate. A cost to cost measure of progress provides a faithful depiction of the transfer of services to the customer since the predominant inputs to the performance obligation are labor costs, research and development supplies and manufacturing supplies related to the Phase 1 Study, clinical manufacturing and know-how transfer.

During the year ended December 31, 2022, the Company recognized revenue totaling approximately $267.6 million with respect to the GSK Collaboration Agreement. The revenue is classified as license and collaboration revenue in the accompanying consolidated statements of operations. As of December 31, 2022, there was approximately $12.6 million of deferred revenue related to the GSK Collaboration Agreement of which all was classified as current deferred revenue in the accompanying consolidated balance sheet based on the performance period of the underlying obligations.

Contract Costs

The Company incurred approximately $6.8 million of capitalizable costs to obtain the contact. The Company utilized the practical expedient in ASC 340 and recognized such costs immediately in 2021 as the Company expected to complete its performance obligations under the GSK Collaboration Agreement in less than 12 months.

Contract Assets and Liabilities

The following table presents changes in the Company's GSK contract assets and liabilities during the year ended December 31, 2022:

Year Ended December 31, 2022

(in thousands)	Balance at Beginning of Year	Additions	Deductions	Balance at Year End
Contract liabilities				
Deferred revenue	$ 280,225	$ —	$ (267,630)	$ 12,595

MSD International GmbH

On December 10, 2019, the Company entered into a Clinical Trial Collaboration and Supply Agreement (the MSD Agreement) with MSD International GmbH (MSD), a subsidiary of Merck & Co., Inc. Under the MSD Agreement, the Company will sponsor a clinical trial in which both the Company's compound and MSD's compound will be

dosed in combination. The Company will conduct the research at its own cost and MSD will contribute its compound towards the study at no cost to the Company. The parties will equally own the clinical data and inventions from the study, with the exception of inventions relating solely to each party's compound class. The MSD Agreement will expire upon the delivery of a written report on the results of the study, unless earlier terminated or agreed by the parties.

The Company began receiving compounds from MSD on April 1, 2020 and the Company began the research study in the third quarter of 2020. The terms of the MSD Agreement meet the criteria under ASC 808, as both parties are active participants in the activity and are exposed to the risks and rewards dependent on the commercial success of the activity. ASC 808 does not provide guidance on how to account for the activities under the collaboration, and the Company determined that neither party met the definition of a customer under ASC 606, *Revenue from Contracts with Customers*. Accordingly, the Company considered other guidance to determine the accounting for the respective elements of the arrangement. The Company accounted for the collaboration activities by analogy to ASC Topic 845, *Nonmonetary Transactions*, and recognized nonmonetary income with an offsetting entry to expense for amounts received from MSD within research and development expense in the consolidated statement of operations and comprehensive income.

Note 6. Government grant funding and potential repayment commitments under recoverable cash advance grants (RCAs)

The Company has been awarded grants from a federal region of Belgium (the Walloon Region), and the European Union (collectively, the granting agencies) to fund research and development activities. The grants reimburse a percentage (55-100%) of actual qualifying expenditures. The Company periodically submits proof of qualifying expenditures to the granting agencies for approval and reimbursement. To date, the Company received funding under several grants which included no obligation to repay and two grants that include potential obligations to repay (RCAs).

As the granting agencies do not meet the definition of a customer under Topic 606, qualifying grants receipts are recognized as grant income within other income in the consolidated statements of operations and comprehensive income. Grant income recognized under all of the grants for research and development activities totaled approximately $2.1 million and $10.2 million for the years ended December 31, 2022 and 2021, respectively.

Grants which do not include an obligation to repay

As of December 31, 2022, the total amount that the granting agencies have agreed to fund in the future if the Company incurs qualifying research and development expenses under these grants is $7.4 million.

Grants which include a potential obligation to repay—RCAs

On July 20, 2017, the Company entered into an arrangement whereby the Walloon Region will provide the Company with up to $20.1 million for a research and development program to perform clinical validation of an A_{2A} receptor antagonist drug candidate for immune-oncology (RCA-1). As of December 31, 2022, the Company has received $20.1 million under this grant.

On December 3, 2019, the Company entered into another recoverable cash advance grant with the Walloon Region (RCA-2) for up to $4.6 million to be received to fund a research and development program conducted to develop a TIGIT blocking antibody with anti-tumor properties. As of December 31, 2022, the Company has received $4.6 million under this grant.

Under the terms of both agreements, the Company must decide within 6 months after the end of the research period whether it will further pursue commercial development or out licensing of the drug candidate. The research period for RCA-1 ended in December 2021. The Company decided it would pursue commercialization or out licensing of RCA-1. The Company negotiated an extension on the research period for RCA-2 with the Walloon Region. The original research period for RCA-2 ended February 2021, and was extended to March 2022. The Company must repay 30% of the amount received under the grant by annual installments from 2023 to 2042 (the fixed annual repayments) unless the Company decides not to pursue commercial development or out licensing of the drug candidate, applies for a waiver from the Walloon Region justifying its decision based upon the failure of the program, and returns the intellectual property to the Walloon Region. Because of the requirement to repay 30% of the amounts received under the grant, the Company records the present value of such amounts as grants repayable on the consolidated balance sheets.

In addition, in the event that the Company receives revenue from products or services related to the results of the research, it has to pay to the Walloon Region a 0.33% royalty on revenue resulting from RCA-1 and a 0.15% royalty on revenue resulting from RCA-2 (increased from 0.12% effective December 2021). The maximum amount payable to the Walloon Region under each grant, including the fixed annual repayments, the royalty on revenue, and the interest thereon, is twice the amount of funding received.

The Company assessed whether there is an obligation to make a royalty payment based on the probability of successful completion of the research and development and future sales and commercial success of the drug candidate. For the RCA-1, no grant repayable related to royalties was recorded as of December 30, 2022 or December 31, 2021. For the RCA-2, the Company recorded a royalty accrual of $0.8 million as of December 31, 2022, due to the upfront payment from the GSK Collaboration Agreement. The royalty accrual is included in the accrued expenses and other current liabilities in the consolidated balance sheet. The Company recorded a royalty accrual of $0.9 million as of December 31, 2021.

The Company recorded grant income in the consolidated statement of operations and comprehensive income (for the years ended December 31, 2022 and 2021 for amounts of grants received from the Walloon Region in the period during which the related qualifying expenses were incurred, net of any grants repayable recorded in the consolidated balance sheets.

The Company recorded receivables on the consolidated balance sheets related to amounts the Walloon Region owes the Company based on qualifying expenses incurred by the Company. The Company recorded deferred income in the consolidated balance sheets for amounts received from the Walloon Region in advance of incurring qualifying expenses.

The following table reflects activity for grant programs for the years ended December 31, 2022 and 2021 and end of year balances as of December 31, 2022 and December 31, 2021:

	RCA -1		RCA-2		Other Grants		Total	
(In thousands)	2022	2021	2022	2021	2022	2021	2022	2021
Cash received	$ 2,244	$ 1,990	$ 1,520	585	$ 2,497	$ 592	$ 6,261	$ 3,167
Grant income recognized	364	4,113	478	1,286	1,249	4,782	2,091	$ 10,181
Grants receivable	5	1,832	—	1,097	996	1,093	1,001	$ 4,022
Grants repayable	5,665	5,278	1,312	886	—	—	6,977	$ 6,164

Of the total repayable balance, $0.4 million is the current portion and $6.6 million is the non-current portion. The current portion is recorded to accrued expenses and other liabilities.

Note 7. Stockholders' equity

The Company's restated Certificate of Incorporation authorizes the Company to issue up to 160,000,000 shares, of which (i) 150,000,000 shares are designated as common stock, par value $0.001 per share, and (ii) 10,000,000 shares are designated as undesignated preferred stock, par value $0.001 per share. Each share of common stock entitles the holders to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are not entitled to receive dividends, unless declared by the board of directors.

Note 8. Stock-based compensation

General

The Board of Directors, at its sole discretion, shall determine the exercise price. Stock options expire 7 to 10 years from the date of grant. The stock options generally vest 25% upon the one-year anniversary of the service inception date and then ratably each month over the remaining 36 months. Upon termination of service, any unvested stock options are automatically returned to Company. Vested stock options that are not exercised within the specified period, according to the terms and conditions of the option plan, following the termination as an employee, consultant, or service provider to the Company are surrendered back to the Company. Those stock options are added back to the pool and made available for future grants.

2019 Stock Option and Grant Plan

The Company's 2019 Stock Option and Grant Plan (the 2019 Plan) provided for the Company to grant stock options and other stock-based awards to employees and non-employees to purchase the Company's common

stock. Total authorized options under the 2019 Stock Option and Grant Plan is 3,464,316. Upon the effectiveness of the 2020 Plan (as defined below), no further issuances will be made under the 2019 Plan.

On July 15, 2020, the Company's Board of Directors approved an amendment to stock options outstanding under the 2019 Stock Option and Grant Plan to provide for immediate 100% vesting for all outstanding options under the plan upon the consummation of a Sale Event, as defined by the amendment.

2020 Stock Option and Incentive Plan

The 2020 Stock Option and Incentive Plan (the 2020 Plan) was approved by the Company's board of directors on July 15, 2020, and the Company's stockholders on July 20, 2020 and became effective on July 22, 2020, the date immediately prior to the date on which the registration statement for the Company's IPO became effective. The 2020 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock units, restricted stock awards, unrestricted stock awards, cash-based awards and dividend equivalent rights to the Company's officers, employees, directors and consultants. The number of shares of common stock reserved for issuance as of December 31, 2022 under the 2020 Plan was 7,335,355 and will be increased each January 1 by 5% of the number of shares of the Company's common stock outstanding on the immediately preceding December 31 or such lesser number of shares as determined by the Company's compensation committee of the board of directors. Accordingly, on January 1, 2023, the number of shares of common stock reserved and available for issuance under the 2020 Plan increased by 1,780,560. The 2020 Plan replaced the 2019 Plan, as the Company's board of directors is not expected to make additional awards under the 2019 Plan following the completion of the IPO. However, the 2019 Plan will continue to govern outstanding equity awards granted thereunder.

Employee Stock Purchase Plan

The 2020 Employee Stock Purchase Plan (the 2020 ESPP) was approved by the Company's board of directors on July 15, 2020, and the Company's stockholders on July 20, 2020, and became effective on July 22, 2020, the date immediately prior to the date on which the registration statement for the Company's IPO was declared effective. The number of shares of common stock reserved for issuance as of December 31, 2022 under the 2020 ESPP was 650,191. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1 thereafter by the lesser of 634,969 shares of common stock, 1% of the outstanding number of shares of common stock on the immediately preceding December 31, or such lesser number of shares as determined by the Company's compensation committee. There was no increase to the number of shares of common stock reserved and available for issuance under the 2020 ESPP on January 1, 2023. During the year ended December 31, 2022, 17,740 shares were issued at a price of $14.71 under the 2020 ESPP. The purchase price of the stock is equal to 85% of the lesser of the market value of such shares at either first date of the offering period or the last date of the offering period. The estimated fair value of the issued shares was $6.50 per share. The assumptions utilized to estimate the fair value are include in the assumption table below.

Stock-Based Compensation Expense

The following table summarizes stock option activity for the year ended December 31, 2022:

	Stock Options			
	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (In thousands)
Outstanding as of December 31, 2021	5,207,084	$ 14.35	7.7	
Granted	1,361,467	32.80		
Forfeited	(39,086)	8.00		
Exercised	(127,478)	5.21		
Outstanding as of December 31, 2022	6,401,987	$ 18.50	7.1	$ 40,745
Vested and expected to vest as of December 31, 2022	6,401,987	$ 18.50	7.1	$ 40,745
Exercisable at December 31, 2022	3,278,177	$ 12.79	6.3	$ 29,670

The following table summarizes stock-based compensation expense, and also the allocation within the consolidated statements of operations and comprehensive income:

(in thousands)	Year Ended December 31, 2022	2021
Research and development	$ 4,152	$ 1,906
General and administrative	17,409	11,888
Total stock-based compensation expense	$ 21,561	$ 13,794

The weighted-average grant-date fair value of options awarded during the year ended December 31, 2022 and 2021 was approximately $23.94 per share and $27.46 per share, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2022 and 2021 was $3.2 million and $11.0 million, respectively. The aggregate grant date fair value of stock options vested during the years ended December 31, 2022 and 2021 were $20.4 million and $10.7 million, respectively. As of December 31, 2022, there was a total of $49.2 million of unrecognized employee compensation costs related to non-vested stock option awards expected to be recognized over a weighted average period of 2.5 years.

The Company estimates the fair value of stock-based compensation utilizing the Black-Scholes option pricing model, which is dependent upon several variables, such as expected term, volatility, risk-free interest rate, and expected dividends. Each of these inputs is subjective and generally requires significant judgment to determine.

The following table summarizes the range of key assumptions used to determine the fair value of stock options and ESPP awards granted during:

	Year Ended December 31, 2022	2021
Stock Options:		
Risk-free interest rate	1.37% - 4.23%	0.42% - 1.27%
Expected term (in years)	5.5 - 6	6
Expected volatility	86% - 94%	92% - 100%
Expected dividend yield	0%	0%
Estimated fair value of common stock	$17.50 - $46.56	$20.54 - $46.68
ESPP Awards:		
Risk-free interest rate	1.63%	-
Expected term (in years)	0.5	-
Expected volatility	81%	-
Expected dividend yield	0%	-
Estimated fair value of common stock	$17.30	-

Restricted Stock Units

The Company issued restricted stock units in 2022, which vest over a four-year period. The following table summarizes the Company's restricted stock unit activity:

	Shares	Weighted average grant date fair value
Unvested as of December 31, 2021	—	$ —
Issued	10,000	35.86
Vested	—	—
Cancelled	—	—
Unvested as of December 31, 2022	10,000	$ 35.86

The restricted stock units cliff vest 25% on the anniversary of the grant date. The remainder of the units will vest in quarterly increments over the remaining three years of the vesting period. No restricted stock units had vested as of December 31, 2022. As of December 31, 2022, there was approximately $0.3 million of unrecognized

stock-based compensation expense related to restricted stock units that are expected to vest. These costs are expected to be recognized over a weighted-average period of approximately 3.2 years.

Note 9. Income taxes

For financial reporting purposes, income before income tax expense for the years ended December 31, 2022 and 2021 consisted of the following:

(in thousands)	2022	2021
Domestic	$ (72,940)	$ (47,242)
Foreign	221,676	303,706
Income before income tax expense	$ 148,736	$ 256,464

The Company's worldwide effective tax rate for the years ended December 31, 2022 and 2021 was 35.0% and 16.4%, respectively. The reconciliation of the statutory U.S. federal income tax rate (21%) to the effective income tax rate is as follows:

	2022	2021
U.S. statutory federal income tax rate	21.0%	21.0%
State income taxes	(2.2)	(0.5)
Foreign tax differential	5.2	4.7
Non-deductible/non-taxable permanent differences	0.1	0.1
Innovation income deduction tax exemption	(33.4)	(28.2)
Net GILTI Inclusion Income	18.9	15.2
Unrecognized tax benefits	14.9	6.6
Other	(3.0)	(1.1)
Change in valuation allowance	13.5	(1.4)
Effective income tax rate	35.0%	16.4%

The components of income tax expense for the years ended December 31, 2022 and 2021 consisted of the following:

(in thousands)	2022	2021
Current		
Domestic	$ 50,750	$ 41,535
Foreign	1,334	408
Deferred	—	—
Total income tax expense	$ 52,084	$ 41,943

Deferred income taxes reflected the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes and

operating losses and tax credit carryforwards. The significant components of the Company's deferred tax assets and liabilities are comprised of the following:

	December 31,	
(in thousands)	2022	2021
Deferred tax assets :		
Net operating loss carryforward	$ 13,359	$ 17,097
Foreign research and development expenses	12,355	7,884
Section 174 capitalized research and development expenses	14,856	—
Stock-based compensation	3,860	1,784
Operating lease liabilities	1,201	1,374
Accrued vacation and bonus	552	390
Other	932	17
Total deferred tax assets	47,115	28,546
Valuation allowance	(45,421)	(26,647)
Deferred tax assets, net of valuation allowance	1,694	1,899
Deferred tax liabilities:		
Operating lease right of use assets	(1,196)	(1,371)
Prepaid expenses	(394)	(497)
Depreciation and amortization	(104)	(31)
Total deferred tax liabilities	(1,694)	(1,899)
Deferred tax assets and liabilities, net of valuation allowance	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon its ability to realize its deferred tax assets. Management has considered the Company's history of losses in prior years, the nature of the Company's deferred tax assets, and the timing, likelihood and amount, if any, of future taxable income during the periods in which those temporary differences and carryforwards become deductible and has concluded that it is more likely than not that the company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation will be maintained on the net deferred tax assets until there is sufficient evidence to support the reversal of some portion of these allowances. The valuation allowance increased $18.8 million during the year ended December 31, 2022 primarily due to an increase in cumulative temporary differences related to capitalized research and development under Section 174, stock based compensation and foreign research and development expenses.

The Tax Cuts and Jobs Act, or TCJA, which was enacted in December 2017, will generally allow federal losses generated after 2017 to be carried over indefinitely, but will generally limit the net operating loss ("NOL") deduction to the lesser of the NOL carryover or 80% of a corporation's taxable income (subject to Section 382 of the Internal Revenue Code of 1986, as amended). In addition, there will be no carryback for losses generated after 2017. Losses generated prior to 2018 will generally be deductible to the extent of the lesser of a corporation's NOL carryover or 100% of a corporation's taxable income and be available for twenty years from the period the loss was generated. The Company does not have any NOLs generated prior to 2018. The Coronavirus Aid, Relief and Economic Security ("CARES") Act temporarily allows the Company to carryback NOLs arising in 2018, 2019 and 2020 to the five prior tax years. In addition, NOLs generated in these years could fully offset prior year taxable income without the 80% of the taxable income limitation under the TCJA which was enacted on December 22, 2017.

As of December 31, 2022, the Company has Belgium net operating loss carryforwards for Belgian federal income tax purposes of approximately $44.4 million, that can be carried forward indefinitely.

As of December 31, 2022, the Company has fully utilized its U.S. federal NOL carryforwards and has $38.4 million of state NOL carryforwards, which may be available to offset future state income tax liabilities. They expire at various dates through 2041. As of December 31, 2022, the Company has de minimis U.S. federal and state tax credit carryforwards available to reduce future tax liabilities, which expire at various dates through 2042 and 2037, respectively.

Utilization of net operating loss and research and development credit carryforwards may be subject to limitation under Section 382 and Section 383 of the Internal Revenue Code of 1986, as amended, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the

amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The latest Section 382 study was performed by the Company through January 3, 2022, through which it was noted that a historic ownership change has likely occurred. Nonetheless, the Company has determined that the prospective utilization of all net operating loss and tax credit carryforwards and, therefore, the corresponding federal and state deferred tax assets, should not be restricted by Sections 382 and 383, although ownership changes after January 3, 2022 could impact the Company's ability to utilize these tax attributes in the future. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development credit carryforwards before utilization.

The Company files income tax returns in the U.S., New Hampshire, Massachusetts, Florida and Belgium. The Company is subject to U.S. federal, state and Belgium tax examinations by tax authorities for years 2019 through present. To the extent that the Company has tax attribute carryforwards, the tax years in which the attributes were generated may still be adjusted upon examination by the Internal Revenue Service, state or foreign tax authorities to the extent utilized in a future period.

Unrecognized tax benefits were $39.2 million and $17.0 million as of December 31, 2022 and 2021, respectively. iTeos Belgium is currently under examination by taxing authorities in that country. Their latest assessments of $1.4 million and $0.4 million of additional taxes owed has been included in income tax expense in the 2022 and 2021 statement of operations and other comprehensive income, respectively. During the year ended December 31, 2022, the Company accrued interest relating to uncertain tax positions of $2.2 million. The increase in the unrecognized tax benefits during the year ended December 31, 2022 was caused by the recognition of additional revenue, and the resulting income, during 2022 under the GSK Collaboration Agreement. As the uncertain tax position relates to the Company's allocation of that revenue and resulting income between the U.S. and Belgium under the GSK Collaboration Agreement, the additional recognition of revenue under that agreement increases the liability for the uncertain tax position.

The changes to the unrecognized tax benefits during the year ended December 31, 2022 were as follows:

(in thousands)		
Balance at December 31, 2021	$	17,000
Increase related to current year tax positions		22,200
Balance at December 31, 2022	$	39,200

Note 10. Commitments and contingencies

Purchase commitments

The Company has contractual arrangements with research and development organizations and suppliers; however, these contracts are generally cancelable on 30-60 days' notice and the obligations under these contracts are largely based on services performed. The Company may also enter into contracts in the normal course of business with clinical research organizations for clinical trials, with contract manufacturing organizations for clinical supplies and with other vendors for preclinical studies, supplies and other services and products for operating purposes. These contracts generally provide for termination on notice. As of December 31, 2022 and 2021, there were no amounts accrued related to termination charges.

The Company has entered into a Biologics Master Services Agreement with WuXi Biologics (Hong Kong) Limited (WuXi) herein referred to as the WuXi Agreement. The WuXi Agreement includes the terms and conditions under which WuXi will coordinate the Company's biologics development and manufacturing services. Pursuant to the WuXi Agreement, the Company may be required to pay WuXi a royalty percentage or a one-time milestone payment on global net sales of third-party manufactured products at the Company's election. The royalty or one-time milestone payment is only payable if the Company does not use WuXi as the manufacturer in part, or in totality. As of December 31, 2022 and 2021, there are no minimum commitments under the WuXi Agreement. Additionally, as of December 31, 2022 and 2021, there are no royalties or milestones payable.

Leases

The Company's operating leases are as follows:

- An April 2016 lease for 1,577 square meters of office and laboratory space in Gosselies, Belgium, which commenced in May 2016 and terminated in December 2021. In January 2021, the Company entered into an amendment to extend the lease, effective February 2021 with a termination date of January 2030, and increase the office and laboratory space by 201 square meters. In October 2021, the Company entered into an amendment to increase the office and laboratory space by 453 square meters.
- A November 2021 lease for 9,068 square feet of office space in Watertown, Massachusetts, which commenced in November 2021 and terminates in February 2027. The lease is subject to fixed-rate rent escalations.
- Various car leases that the Company enters into from time to time. The life of each car lease ranges from 48 to 60 months.

The Company identified and assessed the following estimates in recognizing the operating lease right of use assets and corresponding liabilities.

Expected lease term: The expected lease term includes non-cancelable lease periods and, when applicable, periods covered by an option to extend the lease if the Company is reasonably certain to exercise that option, as well as periods covered by an option to terminate the lease if the Company is reasonably certain not to exercise that option.

Incremental borrowing rate: As the discount rates in the Company's lease are not implicit, management estimated the incremental borrowing rate based on the rate of interest the Company would have to pay to borrow a similar amount on a collateralized basis over a similar term.

Lease and non-lease components: The Company is required to pay fees for operating expenses in addition to monthly base rent for certain operating leases (non-lease components). The Company has not elected the practical expedient which allows non-lease components to be combined with lease components for all asset classes. Variable non-lease components are not included within the lease right-of-use asset and lease liability on the consolidated balance sheet, and instead are reflected as expense in the period they are paid.

Rent expense was $0.9 million and $0.7 million for the year ended December 31, 2022 and 2021, respectively.

The following table summarizes lease terms and discount rate:

	December 31, 2022
Weighted-average remaining lease term (years)	5.0
Weighted-average discount rate	4.79%

The following table summarizes the cash flow and other information:

(in thousands)	Year ended December 31, 2022
Operating lease liabilities arising from obtaining right-of-use assets (non-cash)	$ 350
Operating cash flows used in operating leases	$ 860

As of December 31, 2022, the Company had the following future minimum lease payments under non-cancelable operating leases for the future years thereafter (in thousands):

Year ending December 31:		
2023	$	1,059
2024		1,041
2025		1,010
2026		980
2027		489
Thereafter		770
Total Lease Payments		5,349
Less: Interest		(676)
Total Lease Liability	$	4,673
Lease liabilities - current	$	836
Lease liabilities, net of current portion	$	3,837

In November 2021, the Company provided a letter of credit for approximately $142 thousand to secure its obligation under its lease in Watertown, Massachusetts. The Company maintains that amount of cash on hand (restricted) to fund any necessary draws on the letter of credit. In addition, as of December 31, 2022 and 2021, the Company has approximately $92 thousand and $99 thousand on hand serving as a guarantee for its lease obligation in Belgium. These amounts have been classified as restricted cash in the consolidated balance sheets as of December 31, 2022 and 2021.

Note 11. Employee benefit plan

iTeos Belgium sponsors a defined contribution insurance plan (the Plan) for its employees. In the first quarter of each year, iTeos Belgium pays an annual premium to the insurance company which corresponds to 5% of employees' gross salaries. Interest accrues each year into a pool for each employee and when they retire, they collect the total in their accounts. The Company contributed approximately $398 thousand and $254 thousand to the Plan for the years ended December 31, 2022 and 2021, respectively.

iTeos Inc. has a 401(k) defined contribution plan (the 401(k) Plan) for its U.S. employees. The 401(k) plan provides for voluntary tax-deferred salary deductions for all employees of up to 100% of their annual compensation, as limited by an annual maximum amount as determined by the Internal Revenue Service. The Company may match employee contributions in amounts to be determined at the Company's sole discretion. The Company contributed approximately $278 thousand and $82 thousand to the 401(k) Plan for the years ended December 31, 2022 and 2021, respectively.

Note 12. Related party transactions

On June 11, 2018, the Company entered into a Royalty Transfer Agreement with the charitable foundations of two of its investors (MPM Oncology Charitable Foundation, Inc. and UBS Optimus Foundation), which requires it to pay a royalty equal to 1% of its net product sales on any product developed or owned by iTeos Therapeutics, Inc. or iTeos Belgium S.A., each year within 120 days following each year end. Such agreement was entered into as a result of the capital contributions received from the investors. As the Company had no product sales in 2022 and 2021, no royalties were owed to these charitable foundations as of December 31, 2022 and 2021.

Note 13. Net income per share attributable to common stockholders

The Company granted certain stock options under the 2019 Plan, and currently grants certain stock options under the 2020 Plan, which are considered common stock equivalents. For the years ending December 31, 2022 and 2021, the common stock equivalents were included to calculate weighted-average diluted shares outstanding. The Company used the treasury stock method.

The following table summarizes the impact of the treasury stock method:

Net income per shares (in thousands, except per share amounts)	December 31, 2022	December 31, 2021
Numerator		
Net income attributable to common stockholders	$ 96,652	$ 214,521
Denominator		
Weighted-average shares used to compute net income per share, basic	35,552,025	35,181,383
Effect of dilutive securities	2,214,482	2,593,407
Weighted-average shares used to compute net income per share, diluted	37,766,507	37,774,790
Net income per share:		
Basic	$ 2.72	$ 6.10
Diluted	$ 2.56	$ 5.68

Note 14. Subsequent events

The company maintains depository relationships with Silicon Valley Bank (“SVB”). As of March 15, 2023, the amount of the Company’s assets held on deposit with SVB is immaterial with respect to the Company’s total cash, cash equivalents and marketable securities. The Company does not expect that SVB’s liquidity concern will have a significant adverse impact on its operations due to the Company's limited exposure to SVB and the Federal Reserve’s decision to make all of SVB’s depositors whole. The Company will continue to monitor the situation with SVB as it evolves.

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