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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2023

OR

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

For the transition period from _____ to

Commission File Number 001-38915

IDEAYA Biosciences, Inc.
(Exact name of Registrant as specified in its Charter)

Delaware	**47-4268251**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
7000 Shoreline Court, Suite 350 South San Francisco, California	**94080**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (650) 443-6209

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, $0.0001 par value per share	**IDYA**	**Nasdaq Global Select Market**

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

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

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

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

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

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

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

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the shares of common stock on the Nasdaq Global Select Market on June 30, 2023 of $23.50 per share, was $1.3 billion. Shares of common stock held by each executive officer and director and by each other person who may be deemed to be an affiliate of the registrant, have been excluded from this computation. The determination of affiliate status for this purpose is not necessarily a conclusive determination for other purposes.

As of February 16, 2024, the registrant had 74,560,273 shares of common stock, $0.0001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to the 2024 Annual Meeting of Stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K to the extent stated herein. The proxy statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2023.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. All statements other than statements of historical facts contained in this Form 10-K, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations and future results of anticipated products, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this Annual Report on Form 10-K are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of risks, uncertainties and assumptions described under the sections in this Annual Report on Form 10-K entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Annual Report on Form 10-K. These forward-looking statements are subject to numerous risks, including, without limitation, the following:

- the scope, progress, results and costs of developing our product candidates or any other future product candidates, and conducting preclinical studies and clinical trials, including our IDE196 (darovasertib) Phase 1/2 and 2/3 clinical trials, IDE397 Phase 1/2 clinical trials, our IDE161 Phase 1 clinical trial and our GSK101(IDE705) clinical trial;
- our clinical and regulatory development plans;
- the scope, progress, results and costs related to the research and development of our precision medicine target and biomarker discovery platform, including costs related to the development of our proprietary libraries and database of tumor genetic information and specific cancer-target dependency networks;
- our expectations about the impact of macroeconomic developments, such as health epidemics or pandemics, macro-economic uncertainties, social unrest, geopolitical hostilities, natural disasters or other catastrophic events, on our business, and operations, including clinical trials, manufacturing suppliers and collaborators, and on our results of operations and financial condition;
- the availability of companion diagnostics for biomarkers associated with our product candidates and any future product candidates, or the cost of coordinating and/or collaborating with certain diagnostic companies for the manufacture and supply of companion diagnostics;
- the timing of and costs involved in obtaining and maintaining regulatory approval (or certification in certain foreign jurisdictions) for any of current or future product candidates and companion diagnostics, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our expectations regarding the potential market size and size of the potential patient populations for IDE196, IDE397, IDE161, our other product candidates and any future product candidates, if approved for commercial use;
- the timing and amount of any option exercised, milestone, royalty or other payments we may or may not receive pursuant to any current or future collaboration or license agreement, including under the Collaboration, Option and License Agreement with an affiliate of GSK plc, GLAXOSMITHKLINE INTELLECTUAL PROPERTY (NO. 4), Limited (GSK);
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements and the financial terms of any such agreements, including our Collaboration, Option and License Agreement with GSK, our Clinical Trial Collaboration and Supply Agreements with Pfizer Inc., our License Agreement with Novartis, our Option and License Agreement with Cancer Research United Kingdom, or CRUK, and University of Manchester and our Clinical Trial Collaboration and Supply Agreement with Gilead Sciences, Inc.;

- the timing of commencement of future nonclinical studies and clinical trials and research and development programs;
- our ability to acquire, discover, develop and advance product candidates into, and successfully complete, clinical trials;
- our intentions and our ability to establish collaborations and/or partnerships;
- the timing or likelihood of regulatory filings and approvals for our product candidates;
- our commercialization, marketing and manufacturing capabilities and expectations;
- our intentions with respect to the commercialization of our product candidates;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model and strategic plans for our business, product candidates and technology platforms, including additional indications for which we may pursue;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, including the projected terms of patent protection;
- our potential involvement in lawsuits in connection with enforcing our intellectual property rights;
- our potential involvement in third-party interference, opposition, derivation or similar proceedings with respect to our patent rights and other challenges to our patent rights and patent infringement claims;
- estimates of our expenses, future revenue, capital requirements, our needs for additional financing and our ability to obtain additional capital;
- our future financial performance; and
- developments and projections relating to our competitors and our industry, including competing therapies and procedures.

Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not occur or be achieved, and actual results could differ materially from those projected in the forward-looking statements. We qualify all of our forward-looking statements by these cautionary statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

SUMMARY OF PRINCIPAL RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A, “Risk Factors” in this Annual Report on Form 10-K. You should carefully consider these risks and uncertainties when investing in our securities. The principal risks and uncertainties affecting our business include the following:

- We are an early-stage biopharmaceutical company with a limited operating history and no products approved for commercial sale. We have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future, which, together with our limited operating history, makes it difficult to assess our future viability;
- We are very early in our development efforts. Our business is dependent on the successful development of our product candidates, future product candidates, and companion diagnostics for biomarkers associated with our product candidates and future product candidates;

- In connection with the Collaboration, Option and License Agreement with GSK, if GSK terminates any development program under its collaborations with us, whether as a result of our inability to meet milestones or otherwise, any potential revenue from those collaborations will be significantly reduced or eliminated, and our results of operations and financial condition will be materially and adversely affected;
- As an organization, we have never completed a clinical trial, and may be unable to do so for any of our product candidates;
- The successful development of targeted therapeutics, including therapeutics involving direct targeting of an oncogenic pathway and synthetic lethality therapeutics, including our portfolio of synthetic lethality small molecule inhibitors, as well as any related diagnostics, is highly uncertain;
- Preclinical and clinical drug development is a lengthy and expensive process with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates, which could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our business, financial condition, results of operations and prospects. Furthermore, results of earlier studies and trials may not be predictive of future trial results;
- We may find it difficult to enroll patients in our clinical trials given the limited number of patients who have the diseases for which our product candidates are being developed. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected;
- If we are unable to successfully develop molecular diagnostics for biomarkers that enable patient selection and/or that demonstrate drug-target interaction, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates;
- We rely on third parties for the manufacture of our product candidates for preclinical and clinical development and expect to continue to do so for the foreseeable future. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts;
- We face significant competition in an environment of rapid technological and scientific change, and our failure to effectively compete may prevent us from achieving significant market penetration. Most of our competitors have significantly greater resources than we do and we may not be able to successfully compete;
- If we fail to attract and retain senior management and key scientific personnel, our business may be materially and adversely affected;
- Our success depends on our ability to obtain and maintain protection for our intellectual property and our proprietary technologies, to successfully enforce our intellectual property rights and to avoid infringing the rights of others; and
- Our stock price has been and may continue to be volatile and you may not be able to resell shares of our common stock at or above the price you paid.

PART I

Item 1. Business.

Company Overview

We are a precision medicine oncology company committed to the discovery and development of targeted therapeutics for patient populations selected using molecular diagnostics. Our clinical pipeline includes four potential first-in-class clinical-stage product candidates – darovasertib (PKC), IDE397 (MAT2A), IDE161 (PARG) and GSK101 (Pol Theta Helicase). We own or control all commercial rights of the three most-advanced of these product candidates: darovasertib, IDE397, and IDE161. We are also advancing our Werner Helicase program for which we have selected a development candidate in collaboration with GlaxoSmithKline, or GSK and, subject to investigational new drug-, or IND-, enabling studies, are targeting an IND in 2024. We also have multiple earlier-stage preclinical programs. We have established selective, value-accretive collaborations with leading pharmaceutical companies to support our clinical development activities.

Our most advanced clinical program is evaluating darovasertib, or IDE196 which we in-licensed from Novartis, a small molecule protein kinase C, or PKC, inhibitor, in uveal melanoma, or UM. We have initiated a potential registration-enabling Phase 2/3 clinical trial, designated as IDE196-002, to evaluate darovasertib in combination with crizotinib, Pfizer's investigational cMET inhibitor, in patients having metastatic UM, or MUM, with human leukocyte antigen-, or HLA-A*02:01 negative, or HLA-A2(-), serotype, as part of a second Clinical Trial Collaboration and Supply Agreement, or Second Pfizer agreement, with Pfizer. We have achieved double-digit patient enrollment and have opened multiple clinical sites, including international sites, where we are recruiting patients for enrollment in this planned global Phase 2/3 clinical trial. We reported positive interim clinical data in April 2023 from our Phase 2 clinical trial evaluating darovasertib and crizotinib in MUM. We also reported updated darovasertib clinical top line results, circulating tumor DNA, or ctDNA, data and HLA-A2(-)/(+) data subsets from this Phase 2 clinical trial, as well as HLA-A2(-)/(+) prevalence based on our broader clinical experience in MUM, at the European Society for Medical Oncology's Congress in October 2023, or ESMO 2023. We are targeting clinical program update(s) in 2024.

We are also planning to enroll additional HLA-A*02:01 positive, or HLA-A2(+), patients as an independent clinical strategy to address HLA-A2(+) MUM patients, in a clinical study. This strategy reflects observed darovasertib clinical activity irrespective of HLA serotype as reported at ESMO 2023, and demonstrates our commitment to fully address the high unmet medical need in MUM. We are further evaluating darovasertib in combination with crizotinib in a Phase 2 expansion arm of IDE196-001 clinical trial in patients with cutaneous melanoma, alternatively referred to as skin melanoma.

We separately initiated and have achieved double-digit patient enrollment in our Phase 2 clinical trial, designated as IDE196-009, evaluating darovasertib as single-agent neoadjuvant and adjuvant therapy in patients having primary UM, with ongoing enrollment and multiple clinical sites open, and are targeting a clinical efficacy update in mid-year 2024 and regulatory guidance update in 2024. We are also supporting evaluation of darovasertib as single-agent neoadjuvant and adjuvant therapy in primary UM in an ongoing investigator-sponsored clinical trial, or IST, captioned as "Neoadjuvant / Adjuvant trial of Darovasertib in Ocular Melanoma", or NADOM, and led by St. Vincent's Hospital in Sydney with the participation of Alfred Health and the Royal Victorian Eye and Ear Hospital in Melbourne and are targeting a clinical efficacy update in mid-year 2024. We reported proof-of-concept evidence in April 2023, June 2023 and October 2023 for darovasertib as neoadjuvant therapy in primary UM.

IDE397, our small molecule methionine adenosyltransferase 2a, or MAT2A, inhibitor, is being evaluated in a Phase 1/2 clinical trial. We are actively enrolling into the Phase 2 monotherapy expansion cohort in selected priority indications for patients having tumors with methylthioadenosine phosphorylase, or MTAP, gene deletion, including squamous non-small cell lung cancer, or NSCLC, bladder, gastric and esophageal cancers. We observed IDE397 monotherapy responses in multiple priority solid tumor types based on experience across several patients in the early phase of the Phase 2 dose expansion.

In collaboration with Amgen as part of the Amgen Clinical Trial Collaboration and Supply Agreement, or Amgen CTCSA, we initiated patient enrollment in the Amgen-sponsored Phase 1/2 clinical trial evaluating IDE397 in combination with AMG 193, the Amgen investigational MTA-cooperative protein arginine methyltransferase 5, or PRMT5, inhibitor, in patients having tumors with MTAP deletion, or the IDE397/AMG 193 combination study. This potential first-in-class synthetic lethality combination targets mechanistically complementary nodes of the MTAP methylation pathway – MAT2A and PRMT5 – and is supported by data demonstrating preclinical anti-tumor efficacy presented at the 2023 Annual Meeting of the American Association for Cancer Research, or AACR 2023.

We are also planning to evaluate IDE397 in combination with sacituzumab-govitecan-hziy, or Trodelvy, Gilead's Trop-2 directed anti-body conjugate, or ADC, in patients having MTAP deletion bladder cancer, in an IDEAYA-sponsored clinical trial pursuant to a Clinical Study Collaboration and Supply Agreement, or Gilead CSCSA, with Gilead Sciences, Inc., or Gilead.

IDE161, our small molecule poly (ADP-ribose) glycohydrolase, or PARG, inhibitor, is being evaluated in a Phase 1 clinical trial, which is currently in monotherapy expansion, with a strategic focus in estrogen receptor positive, or ER+, human epidermal growth factor receptor 2 negative, or Her2(-),breast cancer with homologous recombination deficiency, or HRD, as well as other solid tumors with HRD, such as endometrial cancer, colorectal cancer and prostate cancer. We are, in parallel, continuing with Phase 1 dose optimization of IDE161 in patients having tumors with HRD. We have observed multiple partial responses, or PRs, by RECIST 1.1. and tumor shrinkage in priority solid tumor types early in the Phase 1 dose escalation and at the expansion dose. We received Fast Track Designation from the U.S. Food and Drug Administration, or FDA, for IDE161 for ovarian cancer and breast cancer indications, specifically for the treatment of (i) adult, pretreated, platinum-resistant advanced or metastatic ovarian cancer patients having tumors with BRCA1/2 mutations and (ii) adult, pretreated, advanced or metastatic hormone receptor positive, or HR+, Her2- and BRCA1/2 mutant breast cancer patients.

GSK101 (IDE705), our Pol Theta Helicase inhibitor, is a potential first-in-class small molecule inhibitor of the helicase domain of Polymerase Theta, or Pol Theta. GSK101 was discovered and evaluated in preclinical studies in collaboration with GSK. GSK is evaluating GSK101 in a GSK-sponsored clinical trial in combination with niraparib, the GSK small molecule inhibitor of poly-(ADP-ribose) polymerase, or PARP, for the treatment of patients having tumors with BRCA or other homologous recombination, or HR, mutations, or HRD. GSK has dosed the first patient in this Phase 1 clinical trial.

GSK is leading clinical development for GSK101 and is responsible for all research and development costs for the Pol Theta program. In August 2023, we earned, and in October 2023 we received, a $7.0 million milestone payment upon acceptance of the IND for GSK101 by the FDA. We are next eligible to receive a potential additional $10.0 million milestone payment upon initiation of Phase 1 clinical dose expansion.

We have selected a Werner Helicase Inhibitor Development Candidate, or DC, in collaboration with GSK. This Werner Helicase Inhibitor DC is targeting the helicase domain of the Werner, or WRN, protein, for patients having tumors with high microsatellite instability, or MSI. In October 2023, we earned a $3.0 million milestone from GSK in connection with IND-enabling studies for the Werner Helicase Inhibitor DC. We are, in collaboration with GSK, targeting an IND submission in 2024 to enable first-in-human clinical evaluation of our Werner Helicase Inhibitor DC in high MSI tumors. We are next eligible to receive a potential additional $7.0 million milestone payment upon IND clearance for the Werner Helicase Inhibitor DC.

We have multiple wholly owned preclinical-stage programs on undisclosed targets to enable the next wave of precision medicine therapeutics in our pipeline. These preclinical programs are focused on opportunities that we believe have the potential to be first-in-class and/or best-in-class. We are targeting multiple DC nominations for these programs in 2024.

We have established a robust precision medicine research platform with capabilities for identification and validation of new targets and biomarkers, drug discovery and translational biology. Our approach integrates small molecule drug discovery with extensive capabilities in identifying and validating translational biomarkers to develop targeted therapies for select patient populations that are most likely to benefit from these targeted therapies. Our small molecule drug discovery expertise includes discovery and development of small molecule therapeutics. The drug discovery platform includes our proprietary chemical library, INQUIRE™, structure-based drug design enabled by extensive structural biology and crystallography capabilities, and our proprietary content-based machine-learning engine, HARMONY™, providing effective and efficient molecular design and structure-activity-relationship, or SAR, cycles. We have deep research and development expertise in synthetic lethality—which represents an emerging class of precision medicine targets. We are applying these capabilities to develop a robust pipeline in precision medicine oncology.

We have assembled a team of cancer biologists, drug discovery chemists, translational biologists and drug development professionals with broad experience at leading oncology organizations. Our team is led by our Chief Executive Officer, Yujiro S Hata. We are also guided by a renowned scientific advisory board made up of key scientific and clinical thought leaders.

Strategy

Our objective is to develop and commercialize innovative precision medicine drugs that indirectly or directly target the genetic drivers of cancer in order to provide therapies for defined patient populations. The principal components of our strategy are to:

Continue to efficiently develop our clinical-stage product candidates, darovasertib, IDE397, IDE161, and GSK101. We are evaluating darovasertib in combination with crizotinib in a potential registrational clinical trial in patients having MUM. We are also evaluating darovasertib as monotherapy in a Phase 2 clinical trial in primary UM. We are further evaluating darovasertib in combination with crizotinib in a Phase 2 clinical trial in patients with cutaneous melanoma. We are currently evaluating IDE397 in a Phase 2 monotherapy expansion cohort in selected priority indications for patients having tumors with MTAP gene deletion, including NSCLC, bladder, gastric and esophageal cancers. We are currently evaluating IDE161 in a Phase 1 expansion trial in homologous recombination deficiency, or HRD, solid tumor types, including ER+ HER- breast, colorectal, endometrial, and prostate cancers. We received Fast Track Designation from the FDA for IDE161 for ovarian cancer and breast cancer indications, specifically for the treatment of (i) adult, pretreated, platinum-resistant advanced or metastatic ovarian cancer patients having tumors with BRCA1/2 mutations and (ii) adult, pretreated, advanced or metastatic hormone receptor positive, or HR+, Her2- and BRCA1/2 mutant breast cancer patients.

Advance our preclinical pipeline of small molecule product candidates in synthetic lethality into clinical development. Our synthetic lethality pipeline includes multiple preclinical research programs, including our Werner Helicase program. We have selected a development candidate in collaboration with GSK and, subject to IND-enabling studies, are targeting an IND submission in 2024. We are also continuing to invest in our earlier-stage pre-clinical programs and have established selective, value-accretive collaborations with leading pharmaceutical companies to support our clinical development activities.

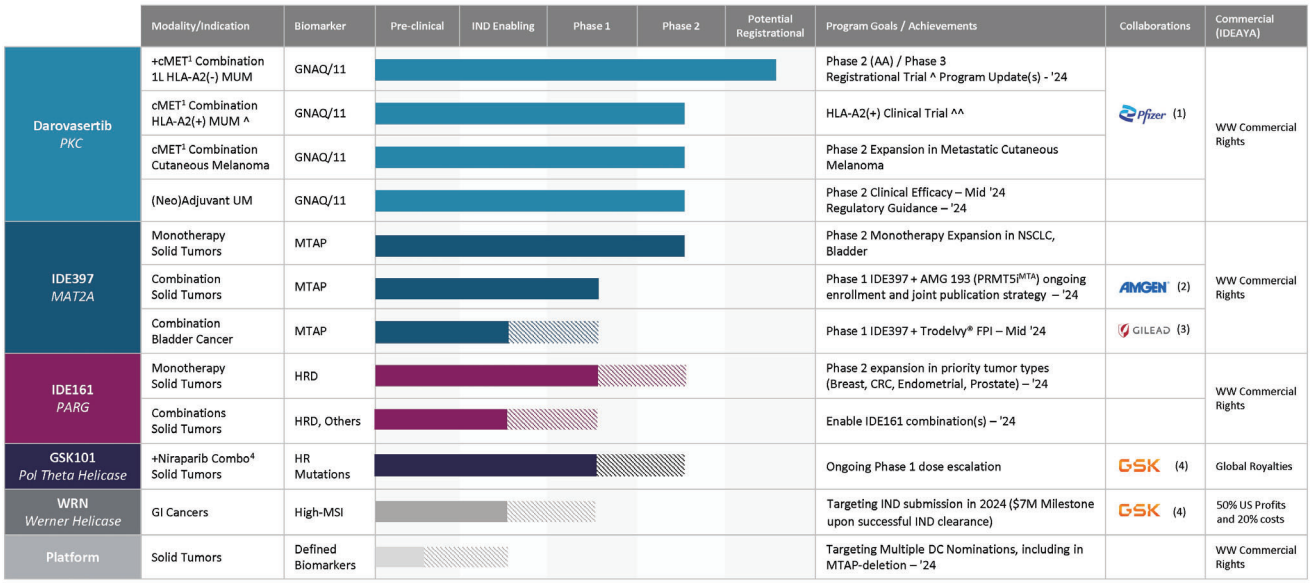
Broaden our pipeline of targeted therapies and apply our core capabilities to establish a leading franchise in the field of synthetic lethality. We are continuing our target identification and validation activities for advancing new synthetic lethality targets and associated biomarkers, with active programs for several next-generation synthetic lethality targets. We continue to invest in core functional capabilities, including in drug discovery, bioinformatics and translational biology.

Collaborate with leaders in the field of diagnostics to enable the identification of defined patient populations for our product candidates. Our precision medicine approach leverages the availability or development of companion diagnostics to identify patients for which our product candidates will be most effective.

Collaborate under our existing strategic partnerships and identify additional strategic collaborations to accelerate development timelines and maximize the commercial potential of our targeted product candidates. We have entered into the Pfizer Agreements for evaluation of the darovasertib in combination with crizotinib in MUM and cutaneous melanoma. We entered into the Amgen CTCSA to clinically evaluate IDE397 in combination with AMG 193, the Amgen investigational MTA-cooperative PRMT5 inhibitor, in patients having MTAP-deletion solid tumors. We have entered into the Gilead CSCSA to clinically evaluate IDE397 in combination with sacituzumab-govitecan-hziy (Trodelvy), Gilead's Trop-2 directed ADC, in patients having MTAP-deletion bladder cancer. We have entered into a strategic partnership and collaboration with GSK for our synthetic lethality programs targeting Pol Theta and Werner Helicase pursuant to the Collaboration, Option and License Agreement with GSK, or GSK Collaboration Agreement. We will selectively evaluate strategic collaborations for our targeted product candidates with biopharmaceutical partners whose research, development, commercial, marketing, and geographic capabilities complement our own.

Pipeline – Overview and Program Goals

We are applying our capabilities and approach to develop a portfolio of targeted therapeutics for patient populations, selected using molecular diagnostics.



(1) Pursuant to Pfizer Agreements
(2) Pursuant to Amgen CTCSA
(3) Pursuant to Gilead CSCSA
(4) Pursuant to GSK Collaboration, Option and License Agreement

Our clinical pipeline currently includes four potential first-in-class clinical-stage product candidates: darovasertib (PKC), IDE397 (MAT2A), IDE161(PARG) and GSK101 (Pol Theta Helicase). We own or control all commercial rights of the three most-advanced of these product candidates: darovasertib, IDE397, and IDE161.

Our pipeline also includes preclinical research programs directed to targeted therapeutic targets, including our Werner Helicase program for which we have selected a development candidate in collaboration with GSK and, subject to IND-enabling studies, we are targeting an IND submission in 2024. We also have earlier-stage preclinical programs, the profiles of which are summarized below.

All data and the status of each program are as of February 1, 2024, unless otherwise noted.

Darovasertib - (GNAQ or GNA11 Mutations)

- We are evaluating darovasertib in combination with crizotinib, an investigational cMET inhibitor in a potential registrational clinical trial in patients having MUM. We have initiated a potential registration-enabling Phase 2/3 clinical trial to evaluate the darovasertib and crizotinib combination in MUM patients with human leukocyte antigen-, or HLA-A*02:01 negative, or HLA-A2(-), serotype. We have achieved double-digit patient enrollment and have opened multiple clinical sites, including international sites, where we are recruiting patients for enrollment in this planned global Phase 2/3 clinical trial. We are targeting clinical program update(s) in 2024.
- We are planning to enroll additional HLA-A*02:01 positive, or HLA-A2(+), patients as an independent clinical strategy to address HLA-A2(+) MUM patients, in a clinical study.
- We have initiated a Phase 2 expansion arm in our IDE196-001 clinical trial evaluating the darovasertib and crizotinib combination in GNAQ/11 metastatic cutaneous melanoma, based on the observed preliminary clinical efficacy.

- We separately initiated and have achieved double-digit patient enrollment in our Phase 2 clinical trial evaluating darovasertib as single-agent neoadjuvant and adjuvant therapy in patients having primary UM, with ongoing enrollment and multiple clinical sites open, and are targeting a clinical efficacy update in mid-year 2024 and regulatory guidance update in 2024. We are also supporting evaluation of darovasertib as single-agent neoadjuvant and adjuvant therapy in primary UM in an ongoing investigator-sponsored clinical trial, or IST, captioned as "Neoadjuvant / Adjuvant trial of Darovasertib in Ocular Melanoma", or NADOM, and led by St. Vincent's Hospital in Sydney with the participation of Alfred Health and the Royal Victorian Eye and Ear Hospital in Melbourne and are targeting a clinical efficacy update in mid-year 2024.
- We own or control all commercial rights in our darovasertib program in uveal melanoma, including in MUM and in primary UM, subject to certain economic obligations pursuant to our exclusive, worldwide license to darovasertib with Novartis.

IDE397 (MTAP Gene Deletion)

- We are enrolling patients into a Phase 2 clinical trial designated as IDE397-001 to evaluate IDE397 for patients having certain tumors with MTAP gene deletion.
- We are proceeding with enrollment of MTAP-deletion patients into a monotherapy Phase 2 expansion cohort with an initial focus on high priority solid tumor types, including squamous NSCLC, bladder, esophageal and gastric cancers.
- In June 2023, we announced selection of a Phase 2 monotherapy expansion dose for IDE397 and in connection therewith, reported preliminary evidence of clinical activity as monotherapy.
- We are collaborating with Amgen to clinically evaluate IDE397 in combination with AMG 193, the Amgen investigational MTA-cooperative PRMT5 inhibitor, in patients having tumors with MTAP deletion, in an Amgen-sponsored clinical trial pursuant to the Amgen CTCSA.
- In April 2023, we co-presented preclinical efficacy data with Amgen at the 2023 Annual Meeting of the American Association for Cancer Research, or AACR 2023, for the IDE397 and AMG 193 combination in a NSCLC MTAP-null cell-derived xenograft, or CDX, model. The data collectively demonstrates that combined pharmacological inhibition of MAT2A and PRMT5 deepens the biological response through maximal pathway suppression.
- In August 2023, Amgen initiated and dosed a first patient in the IDE397 /AMG 193 combination study, following clearance of the Amgen-sponsored IND and FDA authorization to proceed with the clinical trial. This Phase 1/2 clinical trial will evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of IDE397 in combination with AMG 193, with an initial focus for expansion in NSCLC patients and an estimated enrollment of approximately 180 patients. We are targeting the development of a joint publication strategy in 2024.
- We are collaborating with Gilead to clinically evaluate IDE397 in combination with Trodelvy, the Gilead Trop-2 directed ADC, in patients having MTAP deletion bladder cancer, in an IDEAYA-sponsored clinical trial pursuant to the Gilead CSCSA. We anticipate enrolling the first patient in this clinical trial in mid-year 2024.
- We own all right, title and interest in and to IDE397 and the MAT2A program, including all worldwide commercial rights thereto.

PARG Program (HRD, including BRCA)

- We are progressing with enrollment of patients having tumors with HRD into the Phase 1 expansion portion of the Phase 1/2 clinical trial in selected priority tumors. In parallel, we are also continuing with Phase 1 dose optimization to confirm a move-forward expansion dose for the planned Phase 2 portion of the clinical trial. We are targeting clinical program update(s) in 2024. We are also validating IDE161 combination opportunities preclinically and targeting identification of potential combination(s) in 2024.
- In connection with the Phase 1 expansion announced in September 2023, we disclosed preliminary clinical proof-of-concept for IDE161 in HRD solid tumors based on early clinical data from the dose escalation cohorts. These clinical data showed dose-dependent pharmacodynamic modulation of poly-ADP ribose (PAR) proteins in peripheral blood, demonstrating IDE161 target engagement. In addition, we announced a greater than 50% PSA reduction in a prostate cancer patient in January 2023.

- In September 2023, we received Fast Track Designation from the FDA for IDE161 for ovarian cancer and breast cancer indications, specifically for the treatment of (i) adult, pretreated, platinum-resistant advanced or metastatic ovarian cancer patients having tumors with BRCA1/2 mutations and (ii) adult, pretreated, advanced or metastatic hormone receptor positive, or HR+, Her2- and BRCA1/2 mutant breast cancer patients.
- The expansion portion of the Phase 1 trial will include HRD solid tumor types, including endometrial, colorectal, prostate, and ER+ HER2- breast cancers.
- We are targeting IDE161 clinical program update(s) and enabling clinical combination(s) in 2024.

Pol Theta Program (HR mutations, including BRCA, or HRD)

- In November 2023, GSK initiated and dosed a first patient in the Phase 1 clinical trial for GSK101, following submission of the GSK-sponsored IND and FDA allowance to proceed with the clinical trial. GSK intends to clinically evaluate GSK101 in combination with niraparib, the GSK small molecule inhibitor of PARP for the treatment of patients having tumors with BRCA or other HRD.
- GSK is leading clinical development of GSK101 pursuant to the GSK Collaboration Agreement.
- In August 2023, we earned and in October 2023 we received a $7.0 million payment for a milestone based on acceptance of the IND by the FDA.
- We have the potential to receive an additional $10.0 million milestone payment upon initiation of Phase 1 clinical dose expansion.

WRN Program (High MSI)

- We selected a Werner Helicase Inhibitor DC in collaboration with GSK. Subject to successful completion of ongoing IND-enabling studies, we are targeting an IND submission in 2024 to enable first-in-human clinical evaluation of Werner Helicase Inhibitor DC for patients having tumors with high MSI.
- We are collaborating with GSK on the ongoing IND-enabling studies and, subject to IND submission and FDA allowance to proceed with clinical development, GSK will lead clinical development for the Werner Helicase program.
- In October 2023, we earned a $3 million milestone in connection with IND-enabling studies. We have the potential to earn up to an additional $17 million aggregate milestone payments through early Phase 1 clinical studies, including $7.0 million upon IND clearance.

Other Pipeline Programs (Defined Biomarkers)

- We have initiated early preclinical research programs focused on pharmacological inhibition of several new targets, or NTs, for patients with solid tumors characterized by defined biomarkers based on genetic mutations and/or molecular signatures. We believe these research programs have the potential for discovery and development of first-in-class or unique-in-class or best-in-class therapeutics.
- We are targeting development candidate nominations in 2024 for multiple NTs, including a development candidate to treat MTAP-deletion solid tumors.
- We own or control all commercial rights in our next-generation programs.

New Target and Biomarker Discovery Platform

- We have invested significantly and continue to invest in capabilities for identification and validation of new precision medicine targets and biomarkers for patient selection. For targets of interest, we advance our research to discover therapeutic drugs and to further qualify relevant biomarkers.
- We own or control all commercial rights in programs directed to targets identified in on our new target and biomarker discovery platform.

Scientific Rationale – Synthetic Lethality

Synthetic lethality is emerging as an important therapeutic paradigm in the treatment of cancer. It was first defined by Calvin Bridges in 1922 based on the observation that certain combinations of gene mutations resulted in lethality despite the fact the single mutations in either gene were viable.

Cancer cells often contain genetic changes that lead to alterations in pathways such as DNA repair and metabolism. These changes endow the cancer cells with certain properties such as the ability to replicate by bypassing normal control mechanisms. However, removing these important regulators of cell function may also make these cancer cells more dependent on backup pathways that can then be targeted to achieve a therapeutic effect. We are using small molecule inhibitors against targets in DNA damage repair, or DDR, pathways or in tumor metabolism pathways, that have potentially less effects on the viability of normal cells, but are designed to result in lethality in cancer cells having specific underlying genetic alterations. Cancer targets based on synthetic lethality are ideal for precision medicine approaches because each product candidate inherently has a tumor-associated genetic biomarker to facilitate patient selection.

Darovasertib – PKC Inhibitor Clinical Candidate in Uveal Melanoma

Darovasertib (IDE196) is our most advanced clinical-stage product candidate. Darovasertib is a potent, selective small molecule inhibitor of PKC, which we are developing for genetically-defined cancers having GNAQ or GNA11 gene mutations. PKC is a protein kinase that functions downstream of the GTPases GNAQ and GNA11.

We are pursuing a clinical strategy for darovasertib to broadly address uveal melanoma, alternatively referred to as ocular melanoma, as both primary and metastatic disease. Greater than 90% of uveal melanoma patients have tumors harboring GNAQ or GNA11 mutations. There are no FDA approved systemic therapies for primary UM, as either neoadjuvant or adjuvant therapies. There are likewise no FDA approved therapies for patients having MUM with HLA-A*02:01 negative, or HLA-A2(-), serotype. These primary UM patients and HLA-A2(-) MUM patients collectively represent approximately 85% of all ocular melanoma patients. We have a separate, independent clinical strategy to address HLA-A*02:01 positive, or HLA-A2(+), MUM patients.

The potentially addressable patient population for MUM is estimated to include an annual incidence of approximately 4,500 patients across the United States, or U.S., and Europe, with an estimated total prevalence of approximately 14,000 patients in the U.S. and Europe. (Neo)Adjuvant UM represents a significant expansion opportunity for darovasertib – with a potential annual incidence of approximately 8,700 patients aggregate in U.S. and Europe and with an estimated total prevalence of approximately 100,000 patients in the U.S. and Europe.

We own or control all commercial rights in our darovasertib program in uveal melanoma, including in MUM and in primary UM, subject to certain economic obligations pursuant to our exclusive, worldwide license to darovasertib with Novartis.

Darovasertib – Potential Registration-Enabling Clinical Trial in First-Line HLA-A2(-) Metastatic Uveal Melanoma

We have achieved double-digit patient enrollment and have opened multiple clinical sites, including international sites, where we are recruiting patients for enrollment in our potentially registration-enabling Phase 2/3 clinical trial, designated as IDE196-002, to evaluate darovasertib and crizotinib as a combination therapy in HLA-A2(-) MUM. We are the sponsor of this registrational Phase 2/3 clinical trial and are also collaborating with Pfizer for supply of crizotinib on this Phase 2/3 registrational trial, pursuant to the Second Pfizer Agreement. We are targeting clinical program update(s) in 2024.

The protocol of the Phase 2/3 clinical trial design incorporates guidance and feedback following our Type C meeting with the FDA in March 2023. This protocol includes an integrated Phase 2/3 open-label study-in-study design in first-line MUM patients with an HLA-A2(-) serotype. The clinical trial design employs a Phase 2 portion with median progression free survival, or PFS, as a primary endpoint for potential accelerated approval. Patients enrolled in Phase 2 will continue on treatment within the same study and will be considered, together with additional enrolled patients, to evaluate overall survival, or OS, as the primary endpoint of the Phase 3 portion of the clinical trial to support a potential confirmational approval.

In the Phase 2 portion of the clinical trial, approximately 230 patients will be randomized on a 2:1 basis for treatment with the darovasertib and crizotinib combination in the treatment arm or investigators choice in the control arm, selected from (a) a combination of ipilimumab (ipi) and nivolumab (nivo), (b) PD1-targeted monotherapy or (c) dacarbazine. The treatment arm of the Phase 2 portion of the clinical trial includes a nested study to confirm the move forward combination dose for the integrated Phase 2/3 clinical trial – including cohorts at the Phase 2 expansion doses of (i) darovasertib 300 mg BID + crizotinib 200 mg BID and (ii) darovasertib 200 mg BID + crizotinib 200 mg BID. Under the nested study design, patients enrolled in the cohort at the move forward dose will be included within the Phase 2/3 registrational clinical trial. The Phase 2 portion of the clinical trial contemplates an efficacy and safety data set of approximately 200 patients randomized 2:1 with the treatment arm at the move forward dose to support a potential accelerated approval based on median PFS by blinded independent central review, or BICR, as a primary endpoint. Accelerated approval is intended to allow for earlier approval of drugs that treat serious conditions and fill an unmet medical need based on a demonstration of effectiveness on a surrogate endpoint.

Patients enrolled in Phase 2 at the selected dose would continue on treatment and be included in the Phase 3 study analysis, supplemented by enrollment of approximately 120 additional patients into the Phase 3 portion of the clinical trial, with 2:1 randomization on the same basis as the Phase 2 portion. Efficacy data from the Phase 3 could support potential approval using median OS as a primary endpoint.

On May 12, 2023, we expanded our relationship with Pfizer to support the Phase 2/3 registrational trial to evaluate darovasertib and crizotinib as a combination therapy in MUM by entering into Amendment No. 1 to the Second Pfizer Agreement. Under the as-amended Second Pfizer Agreement, Pfizer will provide us with a first defined quantity of crizotinib at no cost, as well as an additional second defined quantity of crizotinib at a lump-sum cost. We anticipate that the supply of crizotinib under the Second Pfizer Agreement, as amended, will be sufficient to support the planned Phase 2 and Phase 3 portions of the Phase 2/3 potentially registrational clinical trial.

In parallel, we are continuing to evaluate darovasertib in our ongoing Phase 2 clinical trial, designated as IDE196-001, as a combination therapy with crizotinib in MUM patients. We are the sponsor of this Phase 2 clinical trial, and are collaborating with Pfizer on this Phase 2 clinical trial pursuant to the Pfizer Agreement.

In April 2023, we reported clinical data, including a safety and clinical efficacy interim results, from the Phase 2 expansion cohort evaluating darovasertib and crizotinib combination in MUM. In October 2023, we updated this clinical data and also reported darovasertib clinical ctDNA data and HLA-A2(-)/(+) data subsets from this Phase 2 clinical trial, as well as HLA-A2(-)/(+) prevalence based on our broader clinical experience in MUM, at ESMO 2023.

The Phase 2 clinical data, as reported in October 2023, were based on twenty (20) evaluable first-line and sixty-three (63) evaluable any-line patients enrolled as of September 22, 2022 in the darovasertib and crizotinib combination study at the expansion dose of 300 mg twice-a-day darovasertib and 200 mg twice-a-day crizotinib. Reported data were preliminary and based on investigator review from an unlocked database as of the data analyses cutoff date of August 22, 2023.

The evaluable patients generally had a significant disease burden and the evaluable any-line patients were heavily pre-treated. Key parameters for characterizing disease burden include baseline lactate dehydrogenase, or LDH, size of the largest metastatic lesion and degree of multi-site metastases. These evaluable patients had baseline LDH which was greater than the upper limit of normal in 60% of any-line and 50% of first-line patients. The largest metastatic lesion was greater than 3.0 cm in 65% of any-line and 60% of first-line patients, and greater than 8.0 cm in 10% of any-line and 15% of first-line patients. The patient metastases included both hepatic and extrahepatic loci in 64% of any-line and 50% of first-line patients. Among any-line patients, 68% had received one or more prior lines of therapy and 43% had received two or more prior lines of therapy.

In the twenty (20) evaluable first-line MUM patients in the expansion cohort, the investigator-reviewed data by RECIST 1.1 included: (i) 45% Overall Response Rate, or ORR, in First-Line MUM: 9 of 20 evaluable patients had a confirmed PR; (ii) 90% Disease Control Rate, or DCR, in First-Line MUM: 18 of 20 evaluable patients showed disease control, including 9 confirmed PRs and 9 stable disease; and (iii) ~7 months median PFS in First-Line MUM.

In the sixty-three (63) evaluable any-line MUM patients at the expansion dose, the investigator-reviewed data by RECIST 1.1 included: (i) 30% ORR in Any-Line MUM: 19 of 63 evaluable patients had a confirmed PR; (ii) 89% DCR in Any-Line MUM: 56 of 63 evaluable patients showed disease control, including 19 confirmed PRs and 37 stable disease; and (iii) ~7 months median PFS in Any-Line MUM. Notably, the observed median PFS was enhanced from the median PFS of ~5 months as previously reported in September 2022 based on thirty-five (35) evaluable Any-Line MUM patients.

There was a subset of nineteen (19) evaluable hepatic-only MUM patients – including first-line and pre-treated patients with only hepatic metastases, for whom the investigator-reviewed data by RECIST 1.1 included: (i) 37% ORR in Hepatic-Only MUM: 7 of 19 evaluable patients had a confirmed partial response (PR); (ii) 100% DCR in Hepatic-Only MUM: 19 of 19 evaluable patients showed disease control, including 7 confirmed PRs and 12 stable disease; and (iii) ~11 months median PFS in Hepatic-Only MUM.

Treatment durations as of the August 22, 2023 data analyses cutoff date were observed for the Any-Line (n=63) patients: approximately 50% of patients were treated for greater than six months, and approximately 30% of patients were treated for greater than one year. Multiple patients with confirmed PRs by RECIST 1.1 have been on treatment greater than 24 months, with the potential for further enhancement on the duration of treatment analysis as approximately 20% (13 out of 63 evaluable patients) of any-line MUM patients are continuing on treatment.

Based on the two-year PFS Kaplan-Meier curve of the darovasertib and crizotinib combination in any-line MUM, the combination provides a promising PFS trend compared to other therapies, including tebentafusp. The observed tail of the PFS curve implies durable benefit in a significant proportion of patients who remain progression free as far out as two years.

Circulating tumor DNA (ctDNA) molecular responses reported at ESMO 2023 were determined based on measured changes in mean allele frequency (MAF) on-treatment as compared to MAF levels at baseline for a subset of any-line MUM patients (n=32). Patients whose ctDNA showed a reduction of greater than 50% MAF following treatment were characterized as having a ctDNA molecular response, or MR.

A reduction in MAF was observed in all but one patient. Significantly, ctDNA MRs were observed in 30 of 32 evaluable patients, reflecting a molecular response rate of 94%. The determined ctDNA molecular responses were deep and sustained, with approximately 80% of measured patients having >80% reduction in MAF. The ctDNA molecular responses correlated with observed efficacy, including confirmed PRs as determined by RECIST 1.1.

Clinical efficacy was observed in both HLA-A2(-) and HLA-A2(+) patients. There were 50 all-line MUM patients with known HLA-A2 status among the 63 patients evaluable for efficacy, with 31 of these being HLA-A2(-) and 19 being HLA-A2(+). The reported efficacy data by HLA-A2 serotype was based on a preliminary analysis of an unlocked database as of August 22, 2023 by investigator review and RECIST 1.1. For HLA-A2(-) MUM patients, confirmed partial responses (PRs) were observed in 9 of 31 (29% ORR) any-line and in 5 of 12 (42% ORR) first-line patients. For HLA-A2(+) MUM patents, confirmed PRs were also observed in 6 of 19 (32% ORR) any-line and in 3 of 5 (60% ORR) first-line patients.

As reported in April 2023, the darovasertib and crizotinib combination therapy continued to observe a manageable safety profile in MUM patients (n=68) at the combination expansion doses, with a low rate (10%) of drug-related serious adverse events, or SAEs. Patients reported predominantly Grade 1 or 2 drug-related adverse events, or AE's: 31% of patients reported at least one drug-related Grade 3 AE; no patients observed a drug-related Grade 4 AE; and one patient observed a Grade 5 AE. The reported Grade 5 SAE was, we believe, not likely related to study therapies and most likely due to disease progression. Drug-related adverse events observed in the darovasertib and crizotinib combination in MUM patients as related to darovasertib as of August 22, 2023 primarily include: SAEs of diarrhea, vomiting, sepsis, respiratory failure, syncope, hypotension and toxic epidermal necrolysis; and AEs, that occurred in greater than 20% of patients, of diarrhea, nausea, edema peripheral, vomiting, dermatitis acneiform, fatigue, hypotension, hypoalbuminaemia, dizziness and decreased appetite. The treating investigator assessed the Grade 5 SAE as being of unknown cause, most likely related to disease progression, and possibly related to the study therapies. Principal investigators on the study reviewed the Grade 5 SAE and concluded that the event was most likely due to disease progression. As the sponsor of the clinical trial, we likewise concluded the Grade 5 SAE was most likely due to disease progression and not likely related to study therapies. Five (7%) of patients permanently discontinued treatment with darovasertib and crizotinib due to a drug-related adverse event.

We consider that these data demonstrate robust clinical efficacy of the darovasertib and crizotinib combination in first-line and any-line MUM patients, with a manageable safety profile, and that collectively, these data support the potential registration-enabling Phase 2/3 clinical trial to evaluate darovasertib and crizotinib as a combination therapy in MUM.

We are continuing to evaluate patients in our Phase 2 clinical trial for darovasertib in combination with crizotinib in MUM. In May 2023, we continued our relationship with Pfizer by entering into Amendment No. 4 to the Pfizer Agreement relating to the supply of crizotinib in support of this Phase 2 clinical trial, pursuant to which Pfizer will continue to provide IDEAYA with an additional defined quantity of crizotinib at no cost.

We also expanded our relationship with Pfizer in May 2023 under an Amendment No. 1 to the Second Pfizer Agreement to support the Phase 2/3 registrational trial to evaluate darovasertib and crizotinib as a combination therapy in MUM. Under the as-amended Second Pfizer Agreement, Pfizer will provide us with a first defined quantity of crizotinib at no cost, as well as an additional second defined quantity of crizotinib at a lump-sum cost.

*Prevalence of HLA-A2*02:01 Negative Serotype in MUM*

Data from darovasertib clinical trials in MUM demonstrate that approximately 70% of MUM patients with known HLA-A*02:01, or HLA-A2 status were HLA-A2(-). As reported at ESMO 2023, the HLA-A2 status was known in subsets of patients enrolled in clinical trials evaluating darovasertib. Prevalence of HLA-A2(+) and HLA-A2(-) in MUM patients was determined from a first data set of n=149 MUM patients treated with darovasertib as monotherapy or in a combination arm of a clinical trial, and separately in a second data set of n=118 MUM patients treated with the darovasertib and crizotinib combination. These data include 102 of 149 (68%) of patients in the all-treatment subset and 81 of 118 (69%) patients in the darovasertib and crizotinib combination treatment subset.

*Darovasertib – Strategy for HLA-A*02:01 Positive MUM*

Based on clinical data from the Phase 2 clinical trial evaluating darovasertib and crizotinib in MUM as reported at ESMO 2023, and based on the darovasertib mechanism of action, we anticipate darovasertib may have clinical activity independent of HLA-A2 status in GNAQ/11-mutation cancers.

We are planning to enroll additional HLA-A*02:01 positive, or HLA-A2(+), patients as an independent clinical strategy to address HLA-A2(+) MUM patients, in a clinical study. This strategy reflects observed darovasertib clinical activity irrespective of HLA serotype as reported at ESMO 2023, and demonstrates our commitment to fully address the high unmet medical need in MUM. Such clinical trial data from darovasertib and crizotinib combination treatment in HLA-A2(+) MUM could support publication and potential inclusion in NCCN Clinical Practice Guidelines in Oncology.

Darovasertib – Orphan Drug Designation in UM and Fast Track Designation in MUM

In April 2022, the FDA designated darovasertib as an Orphan Drug in UM, including primary and metastatic disease under 21 C.F.R Part 316. Under an Orphan Drug designation, darovasertib may be entitled to certain tax credits for qualifying clinical trial expenses, exemption from certain user fees and, subject to FDA approval of a New Drug Application, or NDA, for darovasertib in UM, eligibility for seven years of statutory marketing exclusivity. As an FDA-designated Orphan Drug, darovasertib may also be excluded from certain mandatory price negotiation provisions of the 2022 Inflation Reduction Act, if approved.

In November 2022, the FDA granted Fast Track designation to IDEAYA's development program investigating darovasertib in combination with crizotinib in adult patients being treated for MUM. The Fast Track designation makes our darovasertib and crizotinib development program eligible for various expedited regulatory review processes, including generally more frequent FDA interactions, such as meetings and written communications, potential eligibility for rolling review of a future NDA and potential accelerated approval and priority review of an NDA.

Darovasertib - Neoadjuvant and Adjuvant Therapy in Uveal Melanoma (UM)

We are clinically evaluating the potential for darovasertib as neoadjuvant or adjuvant therapy, or both, also referred to as (neo)adjuvant therapy, in primary, non-metastatic UM patients. In April 2023, June 2023 and October 2023, we reported preliminary clinical data in the neoadjuvant setting showing evidence of anti-tumor activity that we believe supports further clinical evaluation of darovasertib to determine its potential as a neoadjuvant therapy to either save the eye by avoiding enucleation, or to reduce the tumor thickness in the eye, enabling treatment with less radiation to preserve vision, and as an adjuvant therapy, to potentially extend relapse free survival.

We have initiated and dosed our first patient in a company-sponsored Phase 2 clinical trial designated as IDE196-009, with ongoing enrollment and multiple clinical sites open. The purpose of the clinical trial is to evaluate single-agent darovasertib as neoadjuvant treatment of primary UM prior to primary interventional treatment of enucleation or radiation therapy and also as adjuvant therapy following the primary treatment. As of October 23, 2023, six patients have enrolled in the trial, including four enucleation patients and two plaque-therapy patients.

The IDE196-009 clinical protocol includes neoadjuvant treatment with darovasertib to maximum benefit up to 6 months, primary treatment, then up to 6 months of follow-up adjuvant therapy.

In the neoadjuvant setting, one cohort of UM patients with large tumors will be treated with darovasertib until maximum benefit or six months, at which time they will undergo a primary interventional treatment. The neoadjuvant endpoint for this large-sized tumor cohort is eye preservation. For example, a patient who would otherwise have undergone enucleation would instead be eligible for radiation treatment. Another neoadjuvant cohort of UM patients with small or medium tumors will be treated with darovasertib until maximum benefit or six months, at which time they will undergo radiation therapy. Neoadjuvant endpoints for this small- or medium-sized tumor cohort include (i) reducing the radiation dose that the patient receives, relative to the radiation dose they would have otherwise received without the neoadjuvant treatment, and (ii) functional vision preservation.

In the adjuvant setting, each of the two neoadjuvant cohorts will be treated with darovasertib for up to six months as follow-up adjuvant therapy after the primary interventional treatment. The adjuvant endpoints for this portion of the clinical trial include relapse free survival and useful vision.

We are additionally supporting evaluation of darovasertib as (neo)adjuvant therapy in primary UM in the ongoing NADOM IST. Pursuant to an as-amended protocol for the NADOM study, uveal melanoma patients who would otherwise undergo enucleation are instead treated with single agent darovasertib as neoadjuvant treatment for up to six months or maximum benefit. This reflects an increase in potential treatment duration versus the initial approach of one month neoadjuvant therapy, following which these patients will undergo a primary interventional treatment. Patients will subsequently be treated with darovasertib for up to six months as follow-up adjuvant therapy after the primary interventional treatment.

In October 2023, we reported clinical data demonstrating clinical activity for darovasertib as neoadjuvant therapy in primary UM, including tumor shrinkage in ocular tumor lesions. The preliminary interim update was based on investigator review with an enrollment and data cut-off as of July 17, 2023, in the enucleation cohort of the NADOM IST. In total, 11 patients eligible to receive six months of neoadjuvant therapy have been enrolled as of October 23, 2023 in the neoadjuvant UM enucleation cohort of the NADOM IST.

The company reported that seven patients were treated to maximal response or have ongoing treatment with darovasertib in the neo-adjuvant setting as of the data cut-off date of July 17, 2023. Six of these seven patients were considered evaluable based on evaluation with at least one ultrasound scan. Two evaluable patients had a confirmed eye preservation and avoided enucleation, based on conversion of their primary treatment from the planned enucleation to plaque brachytherapy. A third evaluable patient was confirmed as plaque-eligible and treatment of this patient is ongoing with darovasertib neo-adjuvant treatment until maximal benefit. These data reflect eye preservation in three of six evaluable patients – a 50% eye preservation rate. Of the evaluable six patients, approximately 83% of patients had tumor shrinkage.

Two patients enrolled into the IST did not complete their treatment to maximal response. One of these patients had sub-retinal blood present at baseline and with lack of shrinkage and visual deterioration and the patient discontinued treatment after 6 weeks. A second of these patients had a Grade 3 drug-related AE of dermatitis and discontinued treatment before a first scan.

Enrollment into the IST is ongoing. As of October 23, 2023, two out of four additional patients enrolled after the data cutoff date of July 17, 2023, are likely plaque eligible – based on an observed 22% ocular tumor shrinkage at 1-month and 20% ocular tumor shrinkage at 2-months, and are continuing darovasertib neoadjuvant therapy until maximal benefit. One patient is being enucleated. The status of the fourth patient was not reported.

In April 2023, we reported on a compassionate use case for a primary UM patient who was already blind in one eye from vascular disease and developed a large uveal melanoma lesion in his other eye which also had an associated cataract. The patient sought neoadjuvant treatment with the darovasertib and crizotinib combination under a compassionate use protocol with a goal to avoid enucleation and potentially preserve vision in the affected eye. The preliminary clinical data showed prompt responsiveness to treatment, including observed progressive tumor shrinkage over each prior month of treatment. Namely, the patient experienced ~30% tumor shrinkage after one month that continued up to ~80% after 4 months of treatment, in each case as determined by investigator measurement of apical height. After 1 month the ocular lesion size was sufficiently reduced to approach the threshold for radiation therapy (e.g., plaque brachytherapy). The patient thus avoided enucleation of the eye having the uveal melanoma, which reflects an initial reported case of systemic neoadjuvant therapy resulting in eye preservation by avoiding enucleation. Additionally, the patient has restored normal vision of the eye following the course of neoadjuvant treatment and treatment of the associated cataract, with a reported post-treatment vision score of 6/5 (measurement in meters: 6/6 m = 20/20 ft), reflecting a greater than 20 fold improvement in vision.

In June 2023, we reported a second case of a primary UM patient who was spared enucleation, which was also the first reported case of a primary UM patient who was treated with darovasertib as monotherapy neoadjuvant therapy and was spared enucleation in the Phase 1 (neo)adjuvant IST. In this reported case, the UM patient observed a 24% reduction in tumor size following four months of neoadjuvant treatment with darovasertib as monotherapy. The reduction in tumor size enabled plaque brachytherapy as a primary interventional treatment rather than an originally planned enucleation.

We believe that these clinical observations provide a basis for further clinical investigation to evaluate whether darovasertib can improve current primary treatment paradigms, which typically include radiotherapies or enucleation of the eye as primary interventional treatments. Our regulatory strategy includes evaluation of potential clinical endpoints such as vision and organ preservation which would be temporally proximal to the primary interventional treatments, potentially enabling a discussion with regulatory authorities on an accelerated approval pathway.

Darovasertib – Expansion Opportunity in Skin Melanoma

We have initiated a Phase 2 expansion arm in our IDE196-001 clinical trial evaluating the darovasertib and crizotinib combination in GNAQ/11 metastatic cutaneous melanoma, also referred to as skin melanoma, based on the observed preliminary clinical efficacy. In the darovasertib monotherapy cutaneous melanoma cohort (n=8), five of seven evaluable patients had tumor shrinkage (approximately 71%) with one patient having a PR and remaining on treatment over 10 months after previously receiving multiple lines of immunotherapy. In the darovasertib plus binimetinib cutaneous melanoma cohort (n=2), one of two cutaneous melanoma patients with a PR demonstrated 50% tumor shrinkage and remained on treatment approximately 600 days after previously receiving multiple lines of immunotherapy. In the darovasertib plus crizotinib cutaneous melanoma cohort (n=2), one of two cutaneous melanoma patients had tumor shrinkage of 60% with one patient having a PR and remaining on treatment approximately 600 days after previously receiving multiple lines of immunotherapy.

Darovasertib, as monotherapy or in combination with either binimetinib or crizotinib, has indicated a manageable safety profile in cutaneous melanoma patients with certain drug-related AEs being reported in all cohorts. These preliminary clinical data support initiation of a Phase 2 expansion of the darovasertib and crizotinib combination in GNAQ/11 metastatic cutaneous melanoma to advance the darovasertib and crizotinib combination. There are currently no FDA approved therapies in this indication in this genetically-defined patient population.

The GNAQ/11 prevalence in cutaneous melanoma has been reported at approximately 5% in The Cancer Genome Atlas. The GNAQ/11 cutaneous melanoma estimated annual incidence is approximately 5,000 patients in the United States and 8,000 patients in the EU28, and the estimated total prevalence of GNAQ/11 cutaneous melanoma is approximately 70,000 patients in the United States and 110,000 patients in the EU28. It has been reported that approximately 12.5% to 15% of cutaneous melanoma patients have been reported to develop metastatic disease.

IDE397 – MAT2A Inhibitor in Tumors with MTAP Deletion

IDE397 is a clinical-stage, potent, selective small molecule inhibitor of MAT2A, which we are developing for patients having solid tumors with MTAP deletion. The prevalence of MTAP deletion is estimated to be approximately 15% of human solid tumors. MTAP deletion in patient tumors is identified by commercial or institutional next generation sequencing, or NGS, panels or by MTAP immunohistochemistry, or IHC, assay with confirmation by NGS.

MTAP-null cells lack the ability to metabolize 5-methylthioadenosine, or MTA, which is an essential step in a biochemical pathway involved in salvaging the metabolite S-adenosyl methionine, or SAM. Increased levels of MTA partially inhibit the methyltransferase PRMT5 for which SAM is the methyl-donor substrate for methylation of various proteins. This partial inhibition of PRMT5 by increased levels of MTA renders MTAP-null cells more dependent on the activity of MAT2A, an enzyme that is responsible for the synthesis of SAM. Because of this enhanced dependence, loss of MTAP results in synthetic lethality when MAT2A is pharmacologically inhibited.

We are enrolling patients into a Phase 2 clinical trial designated as IDE397-001 to evaluate IDE397 for patients having certain tumors with MTAP gene deletion. We are proceeding with enrollment of MTAP-deletion patients into a monotherapy Phase 2 expansion cohort with an initial focus on high priority solid tumor types, including squamous NSCLC, bladder, esophageal and gastric cancers. In June 2023, we announced selection of a Phase 2 monotherapy expansion dose for IDE397 and in connection therewith, reported preliminary evidence of clinical activity as monotherapy. We observed tumor shrinkage in multiple patients treated with IDE397 monotherapy in our high-priority MTAP-deletion solid tumor types based on experience across several patients in the early phase of the monotherapy dose expansion. Specifically, there have been eight patients dosed in the Phase 2 expansion in the high priority solid tumor types of squamous NSCLC and bladder

cancer, of which two patients have not yet had a first tumor scan assessment. The PRs include an earlier reported 33% tumor shrinkage by CT-PET (without contrast) for a squamous NSCLC patient, and a confirmed PR (47% tumor shrinkage) by RECIST 1.1 with IDE397 in a previously undisclosed tumor type (bladder cancer). This bladder cancer patient has converted to a complete response by RECIST 1.1 at the week 18 CT-scan. In addition, of patients evaluable for ctDNA pre and post treatment, a ctDNA molecular response rate of 83% was observed in these MTAP-deletion priority tumor types. As of the October 13, 2023 cut-off date, we have observed low rates of drug-related discontinuations and SAEs in the dose escalation and expansion phases. Patients reported predominantly Grade 1 or 2 drug-related AEs: nine patients reported at least one Grade 3 drug-related AE; no patients observed a Grade 4 drug-related AE or Grade 5 drug-related AE.

We are collaborating with Amgen to clinically evaluate IDE397 in combination with AMG 193, the Amgen investigational MTA-cooperative PRMT5 inhibitor, in patients having tumors with MTAP deletion, in an Amgen-sponsored clinical trial pursuant to the Amgen CTCSA.

The combination of IDE397 with AMG 193 is a novel and potential first-in-class synthetic lethality combination which targets two distinct and mechanistically complementary nodes of the MTAP methylation pathway – MAT2A and PRMT5, providing a complementary approach for targeting MTAP-null tumors.

In August 2023, Amgen initiated and has dosed a first patient in the IDE397 /AMG 193 combination study, following FDA authorization to proceed with the clinical trial. This Phase 1/2 clinical trial (NCT: 05975073) will evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of IDE397 in combination with AMG 193, with an initial focus for expansion in NSCLC patients and an estimated enrollment of approximately 180 patients.

In April 2023, we co-presented preclinical efficacy data with Amgen at the 2023 Annual Meeting of the American Association for Cancer Research, or AACR 2023, for the IDE397 and AMG 193 combination in a NSCLC MTAP-null cell-derived xenograft, or CDX, model. As reflected in these published xenograft data, we observed complete responses following approximately 30 days of combination treatment, starting at study-day 7 through study-day 39, at doses below the maximally efficacious preclinical dose for each of IDE397, such as 1/10th of maximally efficacious dose, and AMG 193. The complete responses were durable from approximately study-day 40 to study-day 100. The IDE397 and AMG 193 combination was well tolerated, with no observed body weight loss through the approximate 30 days of combination treatment.

We also presented preclinical efficacy data showing deep and durable anti-tumor efficacy and pharmacodynamic, or PD, responses for IDE397 in combination with representative MTA-cooperative PRMT5 inhibitors in NSCLC MTAP-null cell-derived xenograft, or CDX, models, and for one representative compound, also in a pancreatic MTAP-null CDX model.

In addition, we presented further supporting preclinical data at AACR 2023, including the results of gene expression analysis of hallmark pathways, alternative splicing analysis and retained intron analysis. These data collectively demonstrate that combined pharmacological inhibition of MAT2A and PRMT5 deepens the biological response through maximal pathway suppression. The enhanced combination effect was observed selectively in MTAP-null relative to MTAP wild-type models.

We believe that the preclinical efficacy data, considered together with the biological mechanistic response data, as presented at AACR 2023 supports our plans to clinically evaluate IDE397 in combination with AMG 193. We own all right, title and interest in and to IDE397 and the MAT2A program, including all worldwide commercial rights thereto.

We are collaborating with Gilead to clinically evaluate IDE397 in combination with Trodelvy, the Gilead Trop-2 directed ADC, in patients having tumors with MTAP deletion, in patients having MTAP deletion bladder cancer, in an IDEAYA-sponsored clinical trial pursuant to the Gilead CSCSA.

IDE161 – PARG Inhibitor in Tumors with Homologous Recombination Deficiency

We are evaluating IDE161, a small molecule inhibitor of PARG being evaluated in a Phase 1/2 clinical trial designated as IDE161-001 for patients having tumors with HRD and potentially other genetic and/or molecular signatures. PARG is a novel target in a clinically validated biological pathway. PARG functions as a regulator of DNA repair in the same biochemical pathway as PARP. PARG hydrolyzes poly (ADP-ribose), or PAR, chains that are polymerized by PARP enzymes, completing the PAR cycle. Small molecule inhibitors of PARG result in a dose dependent increase in cellular PAR after DNA damage. PARG is a mechanistically distinct target relative to PARP.

We are progressing with enrollment of patients having tumors with HRD into the Phase 1 expansion portion of the Phase 1/2 clinical trial in selected priority tumors. In parallel, we are also continuing with Phase 1 dose optimization to confirm a move-forward expansion dose for the planned Phase 2 portion of the clinical trial. We are targeting clinical program update(s) in 2024. We are also validating IDE161 combination opportunities preclinically and targeting identification of potential combination(s) in 2024.

The expansion portion of the Phase 1 trial will include patients having HRD-associated breast cancer and ovarian cancer, as well as a basket of other selected solid tumors. The breast cancer focus is on ER+, Her2-, HRD+ tumors, which represent approximately 10% to 14% of breast cancer patients. The ovarian cancer focus represents approximately 50% of ovarian cancer where HRD is observed. Selected other solid tumors with HRD, such as HRD+ endometrial cancer, will also be evaluated in the Phase 1 expansion portion of the clinical trial.

In connection with the Phase 1 expansion announced in September 2023, we disclosed preliminary clinical proof-of-concept for IDE161 in HRD solid tumors based on early clinical data from the dose escalation cohorts. These clinical data showed dose-dependent pharmacodynamic modulation of PAR proteins in peripheral blood, demonstrating IDE161 target engagement. These clinical data also demonstrated IDE161 exposure levels in humans which correlate to preclinical exposures that were efficacious in achieving tumor regressions in xenograft models. We observed preliminary tumor shrinkage observed in multiple HRD solid tumor patients, including an BRCA1/2 endometrial cancer subject with a first imaging assessment of a partial response in the target lesion, a complete response in the non-target lesion and an 87% reduction in the CA-125 tumor marker (2,638 units/ml at baseline to 360 units/ml at 6-weeks).

We have observed multiple PRs by RECIST 1.1 and tumor shrinkage in priority solid tumor types early in the Phase 1 dose escalation and at the expansion dose. As of October 13, 2023, there have been a total of seven patients treated at the expansion dose, of which two patients have not yet had a first scan tumor assessment. We observed preliminary tumor shrinkage in multiple HRD solid tumor patients, including an BRCA1/2 endometrial cancer subject with a confirmed PR in the target lesion as of the second imaging assessment, a complete response in the non-target lesion and an 87% reduction in the CA-125 tumor marker (2,722 units/ml at baseline to 360 units/ml at six-weeks). At the IDE161 expansion dose, we have observed no drug-related discontinuations or SAEs as of the October 13, 2023 cut-off date.

In September 2023, we received Fast Track Designation from the FDA for IDE161 for ovarian cancer and breast cancer indications. Fast Track is a FDA process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. Specifically, for IDE161, Fast Track Designation was received for the treatment of adult patients having advanced or metastatic ovarian cancer with germline or somatic BRCA 1/2 mutations who are platinum resistant and have received prior antiangiogenic and PARP inhibitor therapies. The Fast Track Designation was also received for IDE161 for the treatment of adult patients having advanced or metastatic HR+, Her2- breast cancer with germline or somatic BRCA 1/2 mutations who have progressed following treatment with at least one line of a hormonal therapy, a CDK4/6 inhibitor therapy and a PARP inhibitor therapy.

Under the Fast Track designation, the IDE161 development program in BRCA1/2 mutant (m) breast and ovarian cancers, as specified in the respective Fast Track designation, is eligible for various expedited regulatory review processes, including generally more frequent FDA interactions (e.g., meetings, written communications), potential eligibility for rolling review of an and potential accelerated approval and priority review of a future NDA.

We entered into an exclusive license under the Evaluation, Option and License Agreement, by and among the Company, Cancer Research Technologies Ltd., also known as Cancer Research United Kingdom, or CRT, and the University of Manchester, pursuant to which we hold exclusive worldwide license rights covering a broad class of PARG inhibitors.

In April 2023, we incurred an obligation to pay milestone payments in an aggregate amount of £750,000 to CRT based upon the achievement of certain milestones relating to first and second tumor histologies in connection with the Phase 1 portion of the IDE161-001 Phase 1/2 clinical trial in oncologic diseases. The Company will be obligated to make additional payments to CRT aggregating up to £18.75 million upon the achievement of specific development and regulatory approval events for development of a PARG inhibitor in oncologic diseases, including an aggregate of up to £1.5 million and up to £2.25 for the achievement of certain Phase 2 and Phase 3 development milestones, respectively, in each case as relating to first and second tumor histologies.

We own or control all commercial rights in our PARG program, subject to certain economic obligations pursuant to our exclusive, worldwide license to certain PARG inhibitors, including IDE161, with CRT and University of Manchester.

GSK101 (IDE705) - Pol Theta Helicase Inhibitor in tumors with Homologous Recombination Deficiency

We discovered GSK101 (IDE705), our Pol Theta Helicase inhibitor clinical development candidate, and evaluated GSK101 in preclinical studies in collaboration with GSK. GSK101 targets the helicase domain of the Pol Theta protein for patients having solid tumors with BRCA or other mutations associated with HRD.

Pol Theta is involved in a DNA repair process called microhomology mediated end joining, or MMEJ, that is utilized when homologous recombination mediated repair is compromised, as happens in the case of certain BRCA1 or BRCA2 mutations. The expression of Pol Theta is largely absent in normal cells, but tumor cells harboring double strand break repair defects, such as BRCA1 or BRCA2 mutations, show higher Pol Theta expression and synthetic lethality when Pol Theta is inhibited. Pol Theta is a large protein with two functional domains: a DNA polymerase domain and an ATP-dependent DNA helicase domain, sometimes referred to as an ATPase domain, linked by a RAD51 central region.

GSK is evaluating GSK101 in combination with niraparib, the GSK small molecule inhibitor of PARP for the treatment of patients having tumors with BRCA or other HR mutations, or HRD, in a GSK-sponsored Phase 1 clinical trial. GSK has dosed the first patient in this trial.

GSK is leading clinical development of GSK101 pursuant to the GSK Collaboration Agreement. GSK is responsible for all research and development costs for the Pol Theta program.

We have the potential to receive an additional $10.0 million milestone payment upon initiation of Phase 1 clinical dose expansion. In August 2023, we achieved and earned a $7.0 million milestone based on acceptance of the IND by the FDA, for which payment was received in October 2023. An earlier preclinical development $3.0 million milestone payment from GSK was achieved in August 2022 in connection with ongoing IND-enabling studies to support evaluation of GSK101.

We have the potential to earn further aggregate late-stage development and regulatory milestones of up to $465 million. Upon commercialization, we will be eligible to receive up to $475 million of commercial milestones, and tiered royalties on global net sales of GSK101 – ranging from high single-digit to sub-teen double-digit percentages, subject to certain customary reductions.

WRN Inhibitors in Tumors with High Microsatellite Instability

We are advancing our preclinical IND-enabling studies and other preclinical research in collaboration with GSK for an inhibitor targeting Werner Helicase for patients having tumors with high MSI.

WRN protein is a RecQ enzyme involved in the maintenance of genome integrity. Germline loss of function mutations in WRN lead to premature aging and pre-disposition to cancer. MSI is a change in the DNA content of a tumor cell in which the number of repeats of microsatellites, short repeated sequences of DNA, differ as cells divide. High MSI is present in about 15% of gastrointestinal tumor cancers, including in approximately 22% of stomach adenocarcinoma and 16% of colorectal cancer. Tumors with high MSI are routinely assessed in multiple diagnostic profiling tests.

WRN is a protein having several functional domains, and we have shown that the helicase functional domain of WRN is responsible for this synthetic lethal interaction, as reflected in our publication in Cell Press - iScience, Werner Syndrome Helicase is Required for the Survival of Cancer Cells with Microsatellite Instability (March 2019).

We have demonstrated *in vivo* efficacy with tumor regression and PD response in a relevant high MSI model. We have observed selectivity of our Werner Helicase inhibitor and validation of the synthetic lethal relationship to tumors with high MSI over tumors with microsatellite stable, or MSS, based on a lack of *in vivo* pharmacological response in relevant MSS xenograft models.

We selected a Werner Helicase Inhibitor DC in collaboration with GSK. Subject to successful completion of ongoing IND-enabling studies, we are targeting an IND submission in 2024 to enable first-in-human clinical evaluation of Werner Helicase Inhibitor DC for patients having tumors with high MSI.

We are collaborating with GSK on the ongoing IND-enabling studies and, subject to IND submission and clearance, GSK will lead clinical development for the Werner Helicase program. GSK is responsible for 80% of global research and development costs and IDEAYA is responsible for 20% of such costs. GSK holds a global, exclusive license to develop and commercialize the Werner Helicase Inhibitor DC.

In October 2023, we achieved and earned a $3 million milestone in connection with IND-enabling studies. We have the potential to earn up to an additional $17 million aggregate milestone payments through early Phase 1 clinical studies, including $7.0 million upon IND clearance. We are also eligible to receive additional future aggregate total development milestones of up to $465 million. Upon commercialization, we will be eligible to receive up to $475 million of commercial milestones, 50% of U.S. net profits and tiered royalties on global non-U.S. net sales of the Werner Helicase Inhibitor DC – ranging from high single-digit to sub-teen double-digit percentages, subject to certain customary reductions.

Next-Generation Precision Medicine Pipeline Programs

We have initiated early preclinical research programs focused on pharmacological inhibition of several new targets, or NTs, for patients with solid tumors characterized by defined biomarkers based on genetic mutations and/or molecular signatures. We believe these research programs have the potential for discovery and development of first-in-class or unique-in-class or best-in-class therapeutics. We are targeting development candidate nominations in 2024 for multiple NTs. Collectively, we believe these efforts will further advance our multi-pronged clinical and business strategy. We own or control all commercial rights in our next-generation NT programs.

New Target and Biomarker Discovery Platform

Since inception of the company, our core research has and continues to be focused on precision medicine oncology, with synthetic lethality as a central tenet. We have invested significantly and continue to invest in capabilities for identification and validation of new precision medicine targets and biomarkers for patient selection. For targets of interest, we advance our research to discover therapeutic drugs and to further qualify relevant biomarkers.

DECIPHER™ Dual CRISPER Synthetic Lethality Library – UCSD

We have constructed our DECIPHER Dual CRISPR library for synthetic lethality target and biomarker discovery in collaboration with the University of California, San Diego, and bioinformatics analysis and validation are ongoing. The DECIPHER 1.0 library is focused on DNA Damage Repair targets across various
tumor suppressor genes and oncogenes of interest that were selected based on their known prevalence and role in solid tumors, enabling evaluation of approximately 50,000 independent gene knockout combinations of DDR pathway related drug targets across known tumor suppressor genes.

PAGEO™ Paralogous Gene Evaluation in Ovarian Cancer and Dep Map Consortium – Broad Institute

We have an ongoing strategic collaboration with the Broad Institute focused on synthetic lethality target and biomarker discovery. This collaboration will use the large-scale CRISPR paralog screening platform developed at the laboratory of William R. Sellers, M.D., Core Institute Member, Broad Institute, to evaluate functionally redundant paralogous genes across ovarian cancer subtypes and to generate novel target and biomarker hypotheses. Dr. Sellers, who also serves on our Scientific Advisory Board, is the principal investigator for the strategic collaboration. We have also become a member of the Broad DepMap (Cancer Dependency Map) consortium led by the Broad Institute to further enhance our efforts in bioinformatics and cell-based screening for synthetic lethality target and biomarker discovery and validation.

Drug Discovery and Program Biomarker Discovery Platform

We are also continuing to invest in our capabilities to advance our research on newly identified synthetic lethality targets of interest, including to enable discovery of therapeutic drugs and program relevant biomarkers. These investments include both additional research personnel and capital investments, which will enhance our capabilities broadly, including in target validation, biological assay development, protein synthesis, structural biology, computational chemistry, and analytical chemistry, among other core functional areas.

As examples of aspects of our drug discovery platform, we use our INQUIRE™ Chemical Library to enhance our synthetic lethality drug discovery platform. INQUIRE is a proprietary, expert-curated small-molecule library of over 200,000 chemical compounds, which we believe will enhance our hit discovery capabilities across a broad range of novel synthetic lethality targets and historically difficult-to-drug target classes, such as helicases and endonucleases.

We use our HARMONY ™ machine-learning engine to empower evaluation and decisions related to structure-activity-relationships analyses, empowering our drug-discovery platform.

Competition

Our industry is very competitive and subject to change based on ongoing advances in technology. Although we believe that our approach, strategy, scientific capabilities, knowledge and experience provide us with competitive advantages, we expect to have substantial competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. 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 product candidates in our pipeline, and will face competition with respect to future product candidates, from segments of the pharmaceutical, biotechnology and other related markets that pursue targeted approaches to addressing activating genetic and other molecular alterations in cancer.

For darovasertib, we are not aware of other companies actively developing clinical-stage therapeutics directed to PKC as a target for solid tumors. MingSight is developing a PKC beta inhibitor in chronic lymphocytic leukemia, or CLL, and diabetic macular edema, both in Phase 1 studies. Varian Biopharmaceuticals is advancing a preclinical-stage atypical PCK iota inhibitor, including as a dermatologic gel formulation for potential topical treatment of Basal Cell Carcinoma, or BCC. Exscientia is developing a PKC theta inhibitor in inflammatory diseases in Phase 1 studies. Varsity Pharma is developing a PKC inhibitor in CLL. We are aware of other companies that are conducting research and development of potential therapies for primary UM or for MUM based on other targets and approaches. For example, Aura Biosciences is developing AU-011 a virus-like drug conjugate (VDC) as local treatment for early-stage choroidal melanoma. Immunocore is developing and commercializing Tebentafusp, also known under its branded name as Kimmtrak for the treatment of adult patients with HLA-A*02:01-positive unresectable or metastatic uveal melanoma. Novartis is developing DYP688, an antibody-drug-conjugate, or ADC, with a GNAQ-11 inhibitor payload in a Phase 1/2 clinical trial in MUM.

For IDE397, Servier Pharmaceuticals, LLC, or Servier, is evaluating a small molecule MAT2A inhibitor designated as S95035 in a Phase 1 trial and Insilico Medicine has a small molecule MAT2A inhibitor in IND-enabling studies.

For IDE161, we are not aware of any other clinical-stage therapies targeting PARG. Several companies are conducting preclinical research to develop PARG inhibitors, including Nodus Oncology, SynRx, 858 Therapeutics and Satya Pharma Innovations.

For GSK101 (IDE705), Artios Pharma is developing two clinical-stage therapies targeting Pol Theta, both in Phase 1/2 studies. Additionally, Repare Therapeutics and Breakpoint Therapeutics have Pol Theta inhibitors in IND-enabling studies.

For our preclinical pipeline of synthetic lethality therapeutics, potential competition includes established companies as well as earlier-stage emerging biotechnology companies. Multiple established companies have been involved with research and development in synthetic lethality, such as AstraZeneca (Lynparza), Pfizer (Talzenna), GSK (Zejula) and Roche. Additionally, several other early-stage companies, including 858 Therapeutics, Anticancer Bioscience, Artios, Breakpoint Therapeutics, FoRx Therapeutics, Repare Therapeutics, Ryvu Therapeutics, Tango, Vividion, Xpose, and Eikon Therapeutics.

Intellectual Property

Intellectual property, including patents, trade secrets, trademarks and copyrights, is important to our business. We endeavor to establish, maintain and enforce intellectual property rights that protect our business interests.

Our patent portfolio, including patents owned by or exclusively licensed to us, is built on a program-by-program basis with a goal of establishing broad protection that generally includes, for each product candidate compound and for selected alternative back-up compounds, claims directed to composition of matter, pharmaceutical compositions, and methods of treatment using such pharmaceutical compositions. For some programs, our portfolio may also include claims directed to methods of treatment involving biomarker-enabled patient identification or selection, methods of treatment involving particular dosing approaches, polymorphs, formulations and/or methods of synthesis. We are seeking and maintaining patent protection in the United States and key foreign jurisdictions.

As of February 3, 2024, we own or exclusively in-license patents and patent applications, comprising approximately 71 distinct patent families, protecting our technology across our pipeline. Excluding applications that we are not currently prosecuting, our portfolio consists of 16 issued U.S. patents, approximately 48 pending U.S. applications, 21 pending applications under the Patent Cooperation Treaty, or PCT, 44 issued foreign patents and approximately 160 pending foreign applications in approximately 44 foreign jurisdictions, including without limitation countries included in major markets in North America, Europe, and Asia, each having expiration dates ranging from 2035 to 2044. The nominal expiration of our patents and patent applications does not account for any applicable patent term adjustments or extensions.

As of February 3, 2024, as relating to our PKC program, including darovasertib, we own or have exclusively in-licensed from Novartis patents and patent applications comprising approximately six issued U.S. patents, approximately 31 issued foreign patents, approximately eight pending U.S. applications, three pending PCT application, and approximately 33 pending applications in approximately 20 foreign jurisdictions which we are currently prosecuting, including without limitation countries included in major markets in North America, Europe, and Asia. These in-licensed patents and applications are directed to composition of matter, pharmaceutical compositions and methods of treatment, including treatment of uveal melanoma. These solely owned or in-licensed patent applications, if granted, would expire between 2035 and 2043, without taking into account any applicable patent term adjustments or extensions. In addition, the PKC program portfolio includes two U.S. patent application and two PCT applications which are jointly owned with Pfizer directed to methods of treatment for certain combination treatments.

As of February 3, 2024, as relating to our MAT2A program, including IDE397, we own patents and patent applications comprising approximately three issued U.S. patents, approximately two issued foreign patent, 10 pending U.S. applications, approximately eight pending PCT applications and approximately 52 pending foreign applications in approximately 28 foreign jurisdictions which we are currently prosecuting, including without limitation countries included in major markets in North America, Europe, and Asia. These solely owned or in-licensed patent applications, if granted, would expire between 2039 and 2043, without taking into account any applicable patent term adjustments or extensions. In addition, the MAT2A program portfolio also includes one pending U.S. application and one pending foreign application directed to methods of treatment of cancer which is jointly owned with GSK pursuant to the GSK Collaboration Agreement, as well as one pending PCT application and two foreign applications directed to methods of treatment of cancer which is jointly owned with Amgen pursuant to the Amgen CTCSA.

As of February 3, 2024, as relating to our PARG program, including IDE161, we own or have exclusively in-licensed from Cancer Research UK and University of Manchester, patents and patent applications comprising approximately two issued U.S. patents, 10 issued foreign patents, 13 pending U.S. application, and approximately 26 pending foreign applications in approximately 18 foreign jurisdictions which we are currently prosecuting, including without limitation countries included in major markets in North America, Europe, and Asia. These solely owned or in-licensed patent applications, if granted, would expire between 2035 and 2044, without taking into account any applicable patent term adjustments or extensions.

As of February 3, 2024, as relating to our Pol Theta program, GSK holds a global, exclusive license to develop and commercialize Pol Theta products arising out of the Pol theta program.

Our patent portfolio also supports programs in our synthetic lethality preclinical pipeline, including U.S. patent applications directed to composition of matter, pharmaceutical compositions and/or methods of treatment of cancer for each of our Pol Theta (HR), WRN (high MSI), and certain next-generation SLT programs.

Strategic Relationships

We own or control all commercial rights in our three most advanced programs, each of which are clinical-stage programs – darovasertib, IDE397 and IDE161. We have entered into strategic relationships for these programs – for example, to in-license certain intellectual property rights or to enable evaluation of combination therapies, such as through combination drug supply or clinical trial collaborations to evaluate combinations. For darovasertib, we have an exclusive license agreement with Novartis and separately, we have established clinical trial collaboration and supply agreements with Pfizer in support of our clinical evaluation of darovasertib in combination with crizotinib in MUM and cutaneous melanoma. For IDE397, we entered into the Amgen CTCSA to clinically evaluate IDE397 in combination with AMG 193, the Amgen investigational MTA-cooperative PRMT5 inhibitor, in patients having MTAP-null solid tumors, and we entered into the Gilead GSCSA to clinically evaluate IDE397 in combination with Trodelvy, the Gilead Trop-2 directed ADC, in patients having MTAP deletion bladder cancer. For PARG, we have an exclusive in-license agreement with Cancer Research UK and University of Manchester.

We have entered into a strategic partnership and collaboration with GSK for our preclinical synthetic lethality programs targeting Pol Theta and Werner Helicase, pursuant to the GSK Collaboration Agreement. We own all commercial rights in our earlier next-generation synthetic lethality programs, for which our small molecule compounds are being discovered and/or developed internally with our own resources, as supplemented by certain service providers such as CROs.

We have established collaborative relationships with other companies for access to their proprietary database of patient samples, and/or for their genetic screening services on their proprietary platform. We have established certain development manufacturing and service relationships with CMOs for darovasertib, IDE397, and IDE161 We have an agreement with STA Pharmaceutical Hong Kong Limited, or STA Pharmaceutical, for the synthesis of the API for darovasertib, and agreements with STA Pharmaceutical and Patheon Inc. for formulation and manufacturing of darovasertib drug product. We have an agreement with STA Pharmaceutical for the synthesis of the API, formulation and manufacturing of IDE197 drug product. We have an agreement with Pharmaron for the synthesis of the API and formulation for IDE161, and with STA Pharmaceutical for the manufacturing of IDE161 drug product. We have established arrangements with CMOs as well for packaging, labeling and distribution of darovasertib, IDE397, and IDE161. We also have established clinical services relationship with CROs to support our conduct of clinical trials for our darovasertib, IDE397, and IDE161programs.

In addition to these existing strategic license relationships, existing and planned development manufacturing and service arrangements, and existing and planned clinical services arrangements, we have various existing agreements and relationships with service providers, such as CROs, which are enabling execution of various research and development activities for each of our pipeline programs. In particular, such agreements are directed to chemistry and compound synthesis, compound analysis and characterization, structural biology, computational biology, biological assay and model development, *in vitro* screening, *in vivo* screening, translational biomarker diagnostic development, bioinformatics, toxicology and formulation, among other activities.

We may also evaluate future strategic opportunities to accelerate development timelines and maximize the commercial potential of our product candidates. We plan to selectively evaluate strategic collaborations with biopharmaceutical partners whose research, development, commercial, marketing, and geographic capabilities complement our own.

Agreements

Clinical Trial Collaboration and Supply Agreements with Pfizer for Darovasertib

In March 2020, we entered into the Pfizer Agreement. Pursuant to the Pfizer Agreement, as amended in September 2020, April 2021, August 2021 and May 2023, Pfizer supplies us with their MEK inhibitor, binimetinib, and their cMET inhibitor, crizotinib, to evaluate combinations of darovasertib independently with each of the Pfizer compounds, in patients with tumors harboring activating GNAQ or GNA11 mutations. Under the Pfizer Agreement, we are the sponsor of the combination studies and will provide darovasertib and pay for the costs of the combination studies. Pfizer will provide binimetinib and crizotinib for use in the clinical trial at no cost to us. The Pfizer Agreement provides that we and Pfizer will jointly own clinical data generated from the clinical trial and will also jointly own inventions, if any, relating to the combined use of darovasertib and binimetinib, or independently, to the combined use of darovasertib and crizotinib. We and Pfizer have formed a joint development committee responsible for coordinating all regulatory and other activities under the agreement.

Pfizer may terminate the agreement if Pfizer believes binimetinib or crizotinib is being used in an unsafe manner. Either party may terminate the agreement for patient safety reasons, if any regulatory action prevents the supply of its drug or if a party ceases development of its drug. Either party may terminate the agreement for the other party's material breach that remains uncured for thirty days. If the agreement is terminated, we must return any unused binimetinib or unused crizotinib, as applicable, to Pfizer. If Pfizer terminates the agreement because of our material breach, we will be required to reimburse Pfizer certain manufacturing costs for the binimetinib or crizotinib supplied under the agreement.

We have further expanded the scope of our relationship with Pfizer, entering into additional agreements to facilitate evaluation of darovasertib in combination with crizotinib in a potential registrational clinical trial in MUM and separately, in combination with crizotinib in other cMET-driven tumor indications.

In March 2022, we and Pfizer entered into the Second Pfizer Agreement pursuant to which we may, subject to FDA feedback and guidance, evaluate darovasertib and crizotinib as a combination therapy in MUM in a planned Phase 2/3 potential registration-enabling clinical trial. Pursuant to the Second Pfizer Agreement, we are the sponsor of the planned combination trial and we will provide darovasertib and pay for the costs of the combination trial; Pfizer will provide crizotinib for the planned combination trial at no cost to us for up to an agreed-upon number of MUM patients. We and Pfizer will jointly own clinical data from the planned combination trial and all inventions relating to the combined use of darovasertib and crizotinib. We and Pfizer have formed a joint development committee responsible for coordinating all regulatory and other activities under the Second Pfizer Agreement.

Separately, in March 2022, we and Pfizer also entered into the Third Pfizer Agreement pursuant to which we may, subject to preclinical validation and FDA feedback and guidance, evaluate darovasertib and crizotinib, as a combination therapy in cMET-driven tumors such as NSCLC and/or HCC in a Phase 1 clinical trial. Pursuant to the Third Pfizer Agreement, we are the sponsor of the planned combination trial, and we will provide darovasertib and pay for the costs of the combination trial; Pfizer will provide crizotinib for the planned combination trial at no cost to us. We and Pfizer will jointly own clinical data from the planned combination trial and all inventions relating to the combined use of darovasertib and crizotinib. We and Pfizer had formed a joint development committee responsible for coordinating all regulatory and other activities under the Third Pfizer Agreement.

In May 2023, we continued our relationship with Pfizer by entering into Amendment No. 4 to the Pfizer Agreement relating to the supply of crizotinib in support of this Phase 2 clinical trial, pursuant to which Pfizer will continue to provide us with an additional defined quantity of crizotinib at no cost.

We also expanded our relationship with Pfizer in May 2023 under an Amendment No. 1 to the Second Pfizer Agreement to support the Phase 2/3 registrational trial to evaluate darovasertib and crizotinib as a combination therapy in MUM. Under the as-amended Second Pfizer Agreement, Pfizer will provide us with a first defined quantity of crizotinib at no cost, as well as an additional second defined quantity of crizotinib at a lump-sum cost. Under Amendment No. 1 to the Second Pfizer Agreement, we also terminated the Third Pfizer Agreement.

Exclusive License Agreement with Novartis for Darovasertib

In September 2018, we entered into a license agreement with Novartis International Pharmaceuticals Ltd. (Novartis) to develop and commercialize Novartis' LXS196 (also known as IDE196), a Phase 1 protein kinase C (PKC) inhibitor, for the treatment of cancers having GNAQ and GNA11 mutations. We have renamed Novartis' LXS196 oncology as IDE196, and which has a non-proprietary name of darovasertib.

Under the license agreement, Novartis granted to us a worldwide, exclusive, sublicensable license to research, develop, manufacture, and commercialize certain defined compounds and products, including IDE196 and certain other PKC inhibitors as well as companion diagnostic products, collectively referred to as the licensed products, for any purpose. The license grant is subject to Novartis' retained rights to complete its ongoing Phase 1 clinical trial of darovasertib, designated in their clinical trial as LXS196. Novartis also agreed to transfer to us certain materials and know-how relating to the licensed products or arising from the ongoing Phase 1 clinical trial of darovasertib.

We are solely responsible for the manufacturing and commercialization of the licensed products, subject to Novartis' rights under the ongoing clinical trial of darovasertib. We have certain obligations to supply darovasertib and licensed products for compassionate use, named patient and similar programs in connection with the ongoing clinical trial. We are obligated to use commercially reasonable efforts to develop one licensed product and to commercialize and obtain regulatory approval for at least one licensed product in the United States and in specified European countries.

All inventions, know-how, data and results resulting from our activities under the license agreement, including activities relating to our own clinical trials, will be exclusively owned by us. All inventions, know-how, data and results resulting from Novartis' activities connected with Novartis' ongoing Phase 1 clinical trial for IDE196 will be exclusively owned by Novartis, and subject to the license to us. Ownership of all other inventions and know-how will be determined according to U.S. patent law, with Novartis' interest subject to the license to us.

We control the prosecution and maintenance of the patents exclusively licensed to us, with Novartis retaining step-in rights if we do not continue such prosecution and maintenance. If we fail to maintain or prosecute any exclusively licensed patent and Novartis exercises this step-in right, our license to the relevant patents will terminate in the relevant country. We have the first right to enforce any exclusively licensed patents, while Novartis retains the right to representation. If we do not bring an action to enforce any exclusively licensed patent, Novartis has the right to bring such action, and we will have the right to representation.

We paid Novartis an upfront payment of $2.5 million and issued 263,615 shares of our Series B redeemable convertible preferred stock concurrently with the execution of the license agreement. Subject to completion of certain clinical and regulatory development milestones, we agreed to make milestone payments in the aggregate of up to $9.0 million, and subject to achievement of certain commercial sales milestones, we agreed to make milestone payments in the aggregate of up to $20.0 million. We also agreed to pay mid to high single-digit tiered royalty payments based on annual worldwide net sales of licensed products, payable on a licensed product-by-licensed product and country by country basis until the latest of the expiration of the last to expire exclusively licensed patent, the expiration of regulatory exclusivity, and the ten year anniversary of the first commercial sale of such product in such country. The royalty payments are subject to reductions for lack of patent coverage, loss of market exclusivity, and payment obligations for third-party licenses.

The license agreement continues in force on a licensed product-by-licensed product and country by country basis until the latest of the expiration of the last to expire exclusively licensed patent, the expiration of regulatory exclusivity, and the ten year anniversary of the first commercial sale of such product in such country.

We may terminate the license agreement in its entirety or on a licensed product-by-licensed product basis without cause on 60 days' prior written notice. Either party may terminate the license agreement for the other party's material breach that remains uncured for 90 days. In addition, Novartis has the right to terminate the license agreement immediately upon our insolvency.

Upon termination by Novartis for material breach or for our insolvency, or upon termination by us without cause, at Novartis' written request and in return for consideration that will be negotiated at such time, we will grant to Novartis a perpetual, irrevocable, worldwide, sublicensable, nonexclusive or exclusive license, under all patent rights and know-how controlled by us that are related to and actually used as of the date of termination in the development, manufacture, and commercialization of licensed products, for Novartis to develop, manufacture, and commercialize the licensed products.

Clinical Trial Collaboration and Supply Agreement with Amgen for IDE397

In July 2022, we entered into the Amgen CTCSA to clinically evaluate IDE397 in combination with AMG 193 in patients having MTAP-null solid tumors, in a Phase 1/2 clinical trial. Under the mutually non-exclusive Amgen CTCSA, we will provide IDE397 drug supply to Amgen, who will be the sponsor of the Phase 1 clinical combination trial evaluating IDE397 and AMG 193. Each party will pay for fifty percent (50%) of the external third-party costs of the combination study. Each party will be responsible for its own internal costs and expenses in support of the combination study. We and Amgen will jointly oversee clinical development of the combination therapy through a Joint Oversight Committee responsible for coordinating all regulatory and other activities under the Amgen CTCSA. The parties will jointly own collaboration data and combination-related intellectual property, if any, arising from the combination clinical trial. We and Amgen each retain commercial rights to our respective compounds, including with respect to use as a monotherapy agent or combination agent.

Clinical Trial Collaboration and Supply Agreement with Gilead for IDE397

In November 2023, we entered into the Gilead CSCSA with Gilead to clinically evaluate IDE397 in combination with Trodelvy (sacituzumab-govitecan-hziy), a Trop-2 directed ADC, in patients having MTAP-deletion bladder cancer, in a Phase 1 clinical trial. Under the mutually non-exclusive Gilead CSCSA, we will receive Trodelvy drug supply from Gilead and will sponsor the Phase 1 clinical combination trial evaluating ID397 and Trodelvy. Gilead will bear internal or external costs incurred in connection with its supply of Trodelvy. We will bear all internal and external costs and expenses associated with the conduct of the combination study. We and Gilead will jointly oversee clinical development of the combination therapy through a Joint Steering Committee responsible for coordinating all regulatory and other activities under the Gilead CSCSA. We and Gilead each retain commercial rights to our respective compounds, including with respect to use as a monotherapy agent or combination agent.

Exclusive Option and License Agreement with Cancer Research UK for IDE161

In April 2017, we entered into the CRUK/Manchester Agreement with Cancer Research UK and University of Manchester, which was amended on April 24, 2019 and on March 3, 2020, for the development and commercialization of licensed products comprising pharmaceutical preparations of PARG inhibitors for all therapeutic uses.

Under this agreement, Cancer Research UK and University of Manchester have granted to us, and we have in turn granted to Cancer Research UK and University of Manchester, non-exclusive, sublicensable, royalty-free licenses to carry out non-clinical research during the research term, which ended with our exercise of our option described below. The non-clinical research was governed by a joint research committee comprised of representatives from each party. During the research term, no party was to undertake a drug discovery program in PARG inhibitors other than under this agreement.

Cancer Research UK also granted us the exclusive option to obtain an exclusive, sublicensable, worldwide, royalty-bearing license, under certain Cancer Research UK background intellectual property and Cancer Research UK's interest in any intellectual property jointly developed under the agreement, to research, develop, manufacture, and commercialize licensed products, as well as a non-exclusive, sublicensable, royalty-free, freedom-to-operate license under related intellectual property. Cancer Research UK and University of Manchester retain certain rights under the licensed intellectual property for academic, non-commercial research and teaching.

In the March 2020 second amendment to the CRUK/Manchester Agreement, the parties reduced the license fee due at exercise of our option, extended the research period to March 2021, and also extended the option period, during which we have rights to exercise an option to certain license rights. The expanded collaborative research included evaluation of an IDEAYA proprietary small molecule PARG inhibitor in multiple *in vitro* and *in vivo* ovarian cancer xenograft models. This research was also evaluating replication stress signature as a potential patient selection biomarker. The extended option period was for up to four additional years from March 2020, including an initial one year period to March 2021 and an additional eighteen month extension to September 2022, which has now been elected pursuant to our certification of ongoing program research activities.

In January 2022, we exercised our option for an exclusive worldwide license rights covering a broad class of PARG inhibitors from Cancer Research Technology Ltd. (CRT) and the University of Manchester, and in connection therewith, paid a one-time option exercise fee of £250,000.

Following our option exercise, we gained sole control and responsibility for the research, development, manufacture, and commercialization of the licensed PARG inhibitors. Cancer Research UK also transferred its know how relating to the research, development or manufacturing of the licensed PARG inhibitors to us.

We were obligated to use reasonable efforts to research a PARG inhibitor during the research term, and we are obligated to develop a PARG inhibitor for the treatment of a cancer indication now that we exercised the option.

Each party is the sole owner of any intellectual property it develops solely under the agreement, and the parties will be joint owners of any jointly developed intellectual property. Each party grants the other a non-exclusive, fully-paid, royalty free, irrevocable, sublicensable, perpetual license to its rights in such jointly created intellectual property to make, use and sell inventions claimed in the joint patents, except for those joint patents exclusively licensed to us under the agreement following our exercise of the option.

Before our exercise of the option, Cancer Research UK was responsible for the prosecution and maintenance of Cancer Research UK background patents specifically relating to PARG, while we were responsible for the prosecution and maintenance of patents covering inventions developed under the agreement as project intellectual property. Cancer Research UK and University of Manchester had the first right to enforce the patents covering inventions developed under the agreement as project intellectual property and we had the right to participate in such actions.

Following our exercise of the option, we have assumed Cancer Research UK's prosecution and maintenance responsibilities for the Cancer Research UK background patents specifically relating to PARG and we obtained the first right to enforce such patents as well as the patents covering inventions developed under the agreement as project intellectual property, and Cancer Research UK will have the right to participate.

We pay all expenses associated with prosecution and maintenance and each party bears its own costs for enforcement. If we abandon the patents covering inventions developed under the agreement as project intellectual property, Cancer Research UK will thereafter be responsible for prosecuting and maintaining such patents. If we abandon such patents, Cancer Research UK and University of Manchester will be responsible for paying the expenses associated with the prosecution and maintenance of such patents.

In addition to an upfront fee of £100,000 and a one-time option exercise fee of £250,000, each of which have been paid, we have certain potential milestone-dependent financial obligations, including: (a) subject to completion of specific development and regulatory approval events for development of a PARG inhibitor in oncologic diseases, payments of up to £19.5 million per broad disease classification block – for example, in oncologic diseases, up to £13.0 million aggregate for a first achievement of such clinical and regulatory milestones and up to £6.5 million aggregate for a second achievement of such clinical and regulatory milestones; (b) subject to certain sales-based milestones based on net sales of licensed products. payments of up to £9 million per broad disease classification block – for example, in oncologic diseases, up to £6.0 million aggregate for a first achievement of such sales milestones and up to £3.0 million aggregate for a second achievement of such sales milestones; and (c) low single-digit tiered royalty payments based on aggregate worldwide net sales of all products, payable on a product-by-product and country-by-country basis until the later of the last-to-expire patent covering such product in such country and the ten year anniversary of the first commercial sale of such licensed product in such country.

The royalty payments are subject to reductions for payment obligations in the event third-party licenses are required to develop or commercialize the product or if the product is not covered by certain patents.

In April 2023, we incurred an obligation to pay milestone payments in an aggregate amount of £750,000 to CRT based upon the achievement of certain milestones relating to first and second tumor histologies in connection with the Phase 1 portion of the Phase 1/2 clinical trial in oncologic diseases.

Certain of the clinical and regulatory milestones are related to and may be due and payable by us if certain milestones are achieved in connection with the IDE161-001 Phase 1/2 clinical trial. We will be obligated to make future milestone payments to CRT aggregating up to £18.75 million upon the achievement of specific development and regulatory approval events for development of a PARG inhibitor in oncologic diseases, including an aggregate of up to £1.5 million and up to £2.25 for the achievement of certain Phase 2 and Phase 3 development milestones, respectively, in each case as relating to first (e.g., a breast cancer) and second (e.g., ovarian cancer) tumor histologies.

Following our exercise of the option, if we sublicense certain intellectual property developed under the agreement or Cancer Research UK background patents specifically relating to PARG, we will also have an obligation to pay to Cancer Research UK low double digit percentage of sublicense revenue we receive, if any. If the agreement is terminated due to our material breach, then we are eligible to receive a percentage of sublicensing revenue that Cancer Research UK receives for licensing intellectual property.

If the agreement is terminated by Cancer Research UK and University of Manchester pursuant to any of their termination rights, then Cancer Research UK and University of Manchester will have exclusive, worldwide rights to project intellectual property. If we terminate the agreement for material breach, then the licenses we receive upon exercise of the option survive, and our payment obligations will be reduced. Following our exercise of the option, the licenses we receive upon exercise of the option survive expiration of the agreement.

Collaboration, Option and License Agreement with GSK for Pol Theta and Werner Helicase

In June 2020, we entered into the GSK Collaboration Agreement, with GSK, pursuant to which we and GSK have entered into a collaboration for its synthetic lethality programs targeting MAT2A, Pol Theta and Werner Helicase. On July 27, 2020, we and GSK received Hart-Scott-Rodino Antitrust Improvements Act clearance, or HSR Clearance, and the GSK Collaboration Agreement became effective. Pursuant to the GSK Collaboration Agreement, GSK paid the Company $100.0 million on July 31, 2020. As of December 31, 2023 GSK has made aggregate payments to us in the amount of $13.0 million for the achievement of certain development and regulatory milestones with respect to Pol Theta and WRN products.

GSK Collaboration – MAT2A Program

Under the MAT2A program, we led research and development through early clinical development stage, and GSK had an exclusive option to obtain an exclusive license to continue development of and commercialize MAT2A products arising out of the MAT2A program, or the Option. We delivered an Option data package resulting from our conduct of a dose escalation portion of a MAT2A Phase 1 monotherapy clinical trial pursuant to the GSK Collaboration Agreement, following which the Option was exercisable within a specified time period.

In January 2022, GSK waived its rights under the GSK Collaboration Agreement to initiate, or request that we initiate, prior to GSK's exercise of the Option, a Phase 1 combination clinical trial for a MAT2A product and GSK's Type I PRMT inhibitor (GSK3368715) product, or the MAT2A Combination Trial. Accordingly, we have no further obligation under the GSK Collaboration Agreement to supply MAT2A product for the MAT2A Combination Trial at its own cost. Our obligation to supply the MAT2A compound for the MAT2A Combination Study was deemed a material right under the GSK Collaboration Agreement.

In August 2022, we received notice from GSK waiving its rights to exercise its Option, or the MAT2A Option Waiver, pursuant to the GSK Collaboration Agreement. As such, we retain and fully own all right, title and interest in and to IDE397 and the MAT2A program, including all worldwide commercial rights thereto. We will be responsible for the costs of further research and clinical development activities that we conduct for the MAT2A program following the MAT2A Option Waiver.

GSK Collaboration - Pol Theta Program

Pursuant to the GSK Collaboration Agreement, GSK holds a global, exclusive license to develop and commercialize Pol Theta products arising out of the Pol Theta program. We and GSK collaborated on preclinical research for the Pol Theta program, and GSK is leading clinical development for the Pol Theta program. GSK is responsible for all research and development costs for the Pol Theta program.

We will be eligible to receive total development and regulatory milestones of up to $485.0 million, with respect to each Pol Theta product, including as applicable, for multiple Pol Theta products that target certain alternative protein domains or are based on alternative modalities. Additionally, we will be eligible to receive up to $475 million of commercial milestones with respect to the Pol Theta product. We are also entitled to receive tiered royalties on global net sales of Pol Theta products by GSK, its affiliates and their sublicensees ranging from high single digit to sub-teen double digit percentages, subject to certain customary reductions.

In June 2022, we announced the nomination of a Pol Theta Helicase Inhibitor DC and in August 2022, announced the achievement of an initial preclinical development milestone in connection with ongoing IND-enabling studies to support evaluation of Pol Theta Helicase Inhibitor DC, triggering a $3.0 million milestone payment, which we received in October 2022.

An IND was submitted and was cleared by the FDA in August 2023 to enable clinical evaluation in combination with niraparib, triggering a $7.0 million milestone payment.

We have the potential to achieve an additional $10.0 million development milestone upon initiation of Phase 1 clinical dose expansion, as well as potential further aggregate late-stage development and regulatory milestones of up to $465 million. Upon commercialization, we will be eligible to receive up to $475.0 million of commercial milestones, and tiered royalties on global net sales of GSK101 – ranging from high single-digit to sub-teen double-digit percentages, subject to certain customary reductions.

GSK Collaboration - Werner Helicase Program

Pursuant to the GSK Collaboration Agreement, GSK holds a global, exclusive license to develop and commercialize WRN products arising out of the WRN program. We and GSK are collaborating on ongoing preclinical research for the WRN program, and GSK will lead clinical development for the WRN program, with IDEAYA responsible for 20% and GSK responsible for 80% of such global research and development costs. The cost-sharing percentages will be adjusted based on the actual ratio of U.S. to global profits for WRN products, as measured three and six years after global commercial launch thereof.

We will be eligible to receive total development milestones of up to $485.0 million, with respect to each WRN product, including as applicable, for multiple WRN products that are based on alternative modalities. Additionally, we will be eligible to receive up to $475 million of commercial milestones with respect to the WRN product. We will be entitled to receive 50% of U.S. net profits and tiered royalties on global non-U.S. net sales of WRN products by GSK, its affiliates and their sublicensees ranging from high single digit to sub-teen double digit percentages, subject to certain customary reductions. We will have a right to opt-out of the 50% U.S. net profit share and corresponding research and development cost share for the WRN program, and would be eligible to receive tiered royalties on U.S. net sales of WRN products by GSK, its affiliates and their sublicensees at the same royalty rates as for global non-U.S. net sales thereafter, with economic adjustments based on the stage of the WRN program at the time of opt-out.

In October 2023, we announced the nomination of a Werner Helicase Inhibitor DC and the achievement of an initial preclinical development milestone in connection with ongoing IND-enabling studies to support evaluation of Werner Helicase Inhibitor DC, triggering a $3.0 million milestone payment.

We have the potential to achieve an additional $17.0 million development milestones through early Phase 1 clinical studies, including $7.0 million upon IND clearance, as well as potential further aggregate late-stage development and regulatory milestones of up to $465 million. Upon commercialization, we will be eligible to receive up to $475.0 million of commercial milestones, 50% of U.S. net profits and tiered royalties on global non-U.S. net sales of the Werner Helicase Inhibitor DC – ranging from high single-digit to sub-teen double-digit percentages, subject to certain customary reductions.

GSK Collaboration - General

Under the terms of the GSK Collaboration Agreement, subject to certain exceptions, we and GSK will not, directly or through third parties, develop or commercialize other products whose primary and intended mechanism of action is the modulation of WRN or Pol Theta for an agreed upon period of time. We and GSK have formed a joint steering committee, joint development committees, and joint commercialization committees responsible for coordinating all activities under the GSK Collaboration Agreement. Ownership of intellectual property developed under the GSK Collaboration Agreement is allocated between or shared by the parties depending on development and subject matter.

GSK's royalty obligations continue with respect to each country and each product until the later of (i) the date on which such product is no longer covered by certain intellectual property rights in such country and (ii) the 10th anniversary of the first commercial sale of such product in such country.

Each party has the right to sublicense its rights under the GSK Collaboration Agreement subject to certain conditions.

The GSK Collaboration Agreement will continue in effect on a product-by-product and country-by-country basis until the expiration of the obligation to make payments under the GSK Collaboration Agreement with respect to such product in each country, unless earlier terminated by either party pursuant to its terms. Either party may terminate the GSK Collaboration Agreement for the other party's insolvency or certain uncured breaches. We may terminate the GSK Collaboration Agreement if GSK or any of its sublicensees or affiliates challenge certain patents of ours. GSK may terminate the GSK Collaboration Agreement in its entirety or on a target-by-target basis upon 90-day notice to us.

Sales and Marketing

We intend to become a fully-integrated biopharmaceutical company. This will enable us to realize our goal of delivering transformative drugs to patients. We currently hold worldwide commercialization rights to each of our product candidates, and intend to retain significant rights in key markets. In light of our stage of development, we have not yet established sales and marketing capabilities. We are planning for potential commercial operations, including for sales and marketing capabilities, subject to further process of our potentially registrational Phase 2/3 clinical trial for darovasertib.

We plan to build our own sales force to commercialize approved products, if any, in the United States and potentially in Europe and other selected foreign countries, and we expect to initiate commercial readiness activities in anticipation of receiving marketing approvals. We believe a moderately sized specialty sales force would enable us to reach oncologists who specialize in treating the patient populations for our product candidates. We may enter into distribution and other marketing arrangements with third parties for any of our product candidates that obtain marketing approval.

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.

Manufacturing

We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and our biomarker diagnostics for preclinical and clinical testing, as well as for future commercial manufacture of any drugs and diagnostics that we may commercialize. We do not own or operate, and currently have no plans to establish, any manufacturing facilities.

In general, we plan to establish agreements with contract manufacturing organizations, or CMOs, for synthesis of the active pharmaceutical ingredient, or API, manufacturing of drug product comprising such API, as well as packaging, labeling and distribution.

We have also established supply arrangements with one or more CMOs for each of our development programs in support of our current clinical development needs.

Our lead product candidates darovasertib, IDE397, IDE161 and Pol Theta are each small molecules that can be manufactured in reliable and reproducible synthetic processes from readily available starting materials. We believe the synthetic chemistry is amenable to scale-up using standard manufacturing equipment and processes. We expect that the compounds being discovered and developed for our other pipeline programs, including WRN, and other future programs, will also be small molecule product candidates that can be produced at contract manufacturing facilities.

In many cases, we anticipate that the biomarker diagnostic may be commercially available on an existing third-party diagnostic panel or assay. In cases where such biomarker diagnostic is not already commercially available, we generally

expect to establish agreements with strategic partners for clinical supply of companion diagnostics for biomarkers associated with the targeted therapeutics we are developing.

Government Regulation

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

U.S. Drug Development Process

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

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

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

Once a pharmaceutical product candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. A clinical hold also may be imposed by the FDA at any time during a clinical trial due to safety concerns or non-compliance with specific FDA requirements, and the clinical trial may not continue until the FDA notifies the sponsor that the hold has been lifted.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. They must be conducted under protocols detailing the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND. An IRB at each institution participating in the clinical trial must review

and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the clinical trial and the consent form that must be provided to each clinical trial subject or his or her legal representative, monitor the clinical trial until completed and otherwise comply with IRB regulations.

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

- *Phase 1:* The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients. Sponsors sometimes designate their Phase 1 clinical trials as Phase 1a or Phase 1b. Phase 1b clinical trials are typically aimed at confirming dosing, pharmacokinetics and safety in a larger number of patients. Some Phase 1b studies evaluate biomarkers or surrogate markers that may be associated with efficacy in patients with specific types of diseases.
- *Phase 2:* This phase involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and appropriate dosage.
- *Phase 3:* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population, generally at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product labeling.

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

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

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

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

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

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose specified clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, clinical trial sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these clinical trials can be delayed until the new product or new indication being studied has been approved.

U.S. Review and Approval Process

The results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Under the Prescription Drug User Fee Act, or PDUFA, the FDA has agreed to certain performance goals in the review of NDAs through a two-tiered classification system, standard review and priority review. According to the current PDUFA performance goals for new molecular entity NDAs, the FDA endeavors to review and act on applications within ten months of the 60-day filing date under standard review, and within six months of the 60-day filing date under priority review.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. Before approving an NDA, the FDA will 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, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

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

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase 4 testing, which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized. The FDA may also place other conditions on approval including the requirement for a risk evaluation and mitigation strategy, or REMS, to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Marketing approval may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

Pediatric Use

Even when not pursuing a pediatric indication, under the Pediatric Research Equity Act, or PREA, an NDA or supplement thereto must contain data that is adequate to assess the safety and effectiveness of the drug product 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. In addition, any sponsor planning to submit an NDA or supplement subject to PREA must submit an initial pediatric study plan, or iPSP, to the IND early in development. The iPSP must contain an outline of the proposed pediatric trials the sponsor plans to conduct, including trial objectives and design, any deferral or waiver requests, and other information required by regulation. The FDA must then review the information submitted, consult with the sponsor, and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time. 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.

Separately, the FDA may issue a Written Request for pediatric studies relating to a drug product if it has determined that information related to the use of the drug in the pediatric population may produce health benefits. If the sponsor conducts the studies pursuant to the Written Request and submits the study reports within the specified timeline, the drug may be entitled to pediatric exclusivity. Pediatric exclusivity is a type of non-patent marketing exclusivity which, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing exclusivity. Sponsors may submit a proposal asking the FDA to issue a Written Request for this purpose.

U.S. Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States or, if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the drug product available in the United States for the disease or condition will be recovered from sales of the product in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its designated orphan use are disclosed publicly by the FDA. Orphan drug designation conveys certain financial incentives, including opportunities for grant funding, tax credits for certain clinical trial costs and certain user-fee waivers. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other application to market the same drug for the same indication for seven years, except in limited circumstances, such as a subsequent product demonstration of clinical superiority to the product with orphan drug exclusivity. Competitors may receive approval of different drugs for the indication for which the orphan product has exclusivity or obtain approval for the same drug but for a different indication from that for which the orphan product has exclusivity. Our product candidates could also be blocked from approval if a competitor obtains approval of the same drug for the same rare disease or condition before we do.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may also 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 April 2022, the FDA designated darovasertib as an orphan drug for the treatment of UM, including MUM, and we may seek orphan drug designation for additional product candidates in the future. Orphan drug designation does not guarantee that any product candidate will be approved for the designated rare disease or condition, if at all.

U.S. Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates intended to treat serious or life-threatening diseases or conditions.

New drug products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a fast track product has opportunities for frequent interactions with the review team during product development and, once an NDA is submitted, the product may be eligible for priority review. A fast track product may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A product intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product, including involvement of senior managers.

After an NDA is submitted for a product, including a product with a fast track designation and/or breakthrough therapy designation, the NDA may be eligible for priority review. A product is eligible for priority review if it has the potential to provide a significant improvement in the treatment or prevention of a serious disease or condition compared to marketed products. If the drug contains a new molecular entity, priority review designation means the FDA's goal is to take an action on the marketing application within six months of the 60-day filing date, compared with ten months under standard review.

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will require the sponsor to perform one or more adequate and well-controlled post-marketing confirmatory trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. The FDA may withdraw approval of a drug or indication approved under the accelerated approval pathway if a trial required to verify the predicted clinical benefit fails to verify such benefit or if the applicant fails to conduct any required post-approval trial with due diligence. Recently, the Food and Drug Omnibus Reform Act, or FDORA, enacted as part of the year-end omnibus spending bill in December 2022, included several reforms intended to expand the FDA's ability to regulate products receiving accelerated approval, including by increasing the FDA's oversight over the conduct of confirmatory trials; however, the ultimate impact of these reforms remains unclear.

Even if a product qualifies for one or more of these expedited development and review programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. In November 2022, the FDA granted fast track designation to darovasertib in combination with crizotinib for treatment of adult patients with MUM. We also expect to pursue breakthrough therapy designation and accelerated approval for darovasertib and may explore some of these opportunities for our other product candidates as appropriate. We received Fast Track Designation from the U.S. Food and Drug Administration, or FDA for IDE161 for ovarian cancer and breast cancer indications.

U.S. Post-approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP regulations and other laws and regulations. In addition, the FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

Any drug products manufactured or distributed by us or our partners pursuant to FDA approvals will be subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market and imposes requirements and restrictions on drug manufacturers, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds on post-approval clinical trials, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties.

U.S. Marketing Exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application, or ANDA, or an NDA submitted under Section 505(b)(2) of the FDCA, or 505(b)(2) NDA, submitted by another company for another drug that contains the same active moiety. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for a change to a previously approved drug, such as a new indication or condition of use, submitted in an NDA, or supplement to an existing NDA, if one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use.

Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Other types of non-patent exclusivity include seven-year orphan drug exclusivity and six-month pediatric exclusivity (each discussed above).

FDA Regulation of Companion Diagnostics

We are collaborating or expect to collaborate with strategic partners or CROs to manufacture and supply *in vitro* diagnostics to identify patients with biomarkers associated with the targeted therapeutics we are developing. These diagnostics, often referred to as 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.

Under the FDCA, medical devices are classified into one of three classes – Class I, Class II or Class III – depending on the degree of risk associated with each medical device and the extent of control needed to provide reasonable assurances with respect to safety and effectiveness. Class I devices are those for which safety and effectiveness can be reasonably assured by adherence to a set of regulations, referred to as General Controls, which require compliance with the applicable portions of the FDA's Quality System Regulation, or QSR, facility registration and product listing, reporting of adverse events and

malfunctions, and appropriate, truthful and non-misleading labeling and promotional materials. Class II devices are those that are subject to the General Controls, as well as Special Controls, which can include performance standards, guidelines and postmarket surveillance. Most Class II devices are subject to premarket review and clearance by the FDA. Premarket review and clearance by the FDA is accomplished through the 510(k) premarket notification process. Under the 510(k) process, the manufacturer must submit to the FDA a premarket notification, demonstrating that the device is "substantially equivalent" to a predicate device. To be "substantially equivalent," the proposed device must have the same intended use as the predicate device, and either have the same technological characteristics as the predicate device or have different technological characteristics and not raise different questions of safety or effectiveness than the predicate device. Class III devices include devices deemed by the FDA to pose the greatest risk such as life-supporting or life-sustaining devices, or implantable devices, in addition to new devices deemed not substantially equivalent following the 510(k) process. The safety and effectiveness of Class III devices cannot be reasonably assured solely by the General Controls and Special Controls. Therefore, these devices are generally subject to the premarket approval, or PMA, application process, which is generally more costly and time-consuming than the 510(k) process.

Alternatively, a device might be the subject of a *de novo* classification request, which seeks marketing authorization and reclassification as a lower-risk Class I or Class II device for a new device that otherwise would automatically be regulated as a Class III device requiring a PMA approval. Specifically, medical device types that the FDA has not previously classified as Class I, II or III are automatically classified into Class III regardless of the level of risk they pose. The Food and Drug Administration Modernization Act of 1997 established a new route to market for low to moderate risk medical devices that are automatically placed into Class III due to the absence of a predicate device, called the "Request for Evaluation of Automatic Class III Designation," or the *de novo* classification procedure. This procedure allows a manufacturer whose novel device is automatically classified into Class III to request down-classification of its medical device into Class I or Class II on the basis that the device presents low or moderate risk, rather than requiring the submission and approval of a PMA application.

If the use of a companion diagnostic is essential to the safe and effective use of a drug or biologic product, then the FDA generally will require approval or clearance of the diagnostic contemporaneously with the approval of the therapeutic product. In July 2014, the FDA issued a final guidance document addressing the development and approval process for *in vitro* companion diagnostic devices. According to the guidance, for novel product candidates such as ours, a companion diagnostic device and its corresponding drug or biologic candidate should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product labeling. The guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a drug generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a drug are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE. In July 2016, the FDA issued a draft guidance document intended to further assist sponsors of therapeutic products and sponsors of *in vitro* companion diagnostic devices on issues related to co-development of these products. In December 2018, the FDA issued another draft guidance document to facilitate class labeling on *in vitro* companion diagnostic devices for oncology therapeutic products, under which a companion diagnostic's labeling may identify a specific group or class of therapeutic products, rather than specific products, where scientifically appropriate.

The FDA generally requires companion diagnostics intended to select the patients who will respond to cancer treatment to obtain approval of a PMA for that diagnostic contemporaneously with approval of the therapeutic, though 510(k) clearance or grant of a *de novo* classification request are also possible. The review of these *in vitro* companion diagnostics in conjunction with the review of a cancer therapeutic involves coordination of review by the FDA's Center for Biologics Evaluation and Research or Center for Drug Evaluation and Research and by the FDA's Center for Devices and Radiological Health. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results when the same sample is tested multiple times by multiple users at multiple laboratories. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution.

If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the clinical trials are conducted and then the data submitted in an amendment to the PMA. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing. PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trials or other data that may be expensive and time-consuming to generate and that can substantially delay approval.

If a companion diagnostic is the subject of a *de novo* classification request in lieu of a PMA, the FDA is required to classify the device within 120 days following receipt of the *de novo* submission. If the manufacturer seeks reclassification into Class II, the manufacturer must include a draft proposal for special controls that are necessary to provide a reasonable assurance of the safety and effectiveness of the medical device. The FDA may reject the reclassification petition if it identifies a legally marketed predicate device that would be appropriate for a 510(k) or determines that the device is not low to moderate risk or that general controls would be inadequate to control the risks and special controls cannot be developed. If the *de novo* request is granted, the new device may be legally marketed (in compliance with applicable regulatory controls), a new classification regulation for the device type will be established, and the device may serve as a predicate device for 510(k) submissions for future devices of the same type.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

Regulation Outside the United States

To the extent that any of our product candidates, once approved, are sold in a foreign country, we would be subject to numerous and varying foreign laws and regulations regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products, and may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals. The foreign regulatory approval process includes all of the risks associated with FDA approval set forth above, as well as additional country-specific regulation.

Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. The approval process varies from country to country, can involve additional testing beyond that required by FDA, and may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing, promotion, and reimbursement vary greatly from country to country.

Non-clinical Studies and Clinical Trials

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

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products, e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies,

both *in vitro* and *in vivo*, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use, or ICH, guidelines on Good Clinical Practices, or GCP, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the EU Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the EU Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice, or GMP. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

In order to market our future products in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization, or MA. To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MA application, or MAA. There are two types of MAs:

- "Centralized MAs" are 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 European Medicines Agency, or EMA, and are valid throughout the entire territory of the EU. The centralized procedure is mandatory for certain types of medicinal products, such as (i) medicinal products derived from biotechnological processes, (ii) designated orphan medicinal products, (iii) advanced therapy medicinal products, or ATMPs (such as gene therapy, somatic cell therapy and tissue engineered products) and (iv) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as AIDS/HIV, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases and other immune dysfunctions. The centralized procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU; and
- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and 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 EU member states, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a

national MA in any member state at the time of application, it can be approved simultaneously in various member state through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops.

In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIority MEdicines, or PRIME, scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. In March 2016, the EMA launched an initiative, the PRIME scheme, a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Moreover, in the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can become a "standard" MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed. Furthermore, MA may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the EU 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. MAs have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance.

Data and Marketing Exclusivity

In the EU, new products authorized for marketing, or reference products, generally receive eight years of data exclusivity and an additional two years of market exclusivity upon MA. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical or biological entity, and products may not qualify for data exclusivity.

Pediatric Development

In the EEA, MAAs for new medicinal products have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO. 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 when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all EU member states and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted.

Orphan Medicinal Products

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product can be designated as an orphan if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects not more than five in ten thousand persons in the EU when the application is made, or (b) the product, without the benefits derived from the orphan status, would not generate sufficient return to justify the necessary investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized for marketing in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

In the EU, an application for designation as an orphan product can be made any time prior to the filing of a MAA. An EU orphan designation entitles a party to incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized procedure. Upon grant of a MA, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved indication. During this market exclusivity period, competent authorities cannot accept another MAA, or grant a MA, or accept an application to extend a MA for a similar medicinal product for the same indication. The period of market exclusivity is extended by two years for orphan medicines that have also complied with an agreed PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The orphan exclusivity period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example because the product is sufficiently profitable not to justify market exclusivity, or where the prevalence of the condition has increased above the threshold. Additionally, MA may be granted to a similar product for the same indication at any time if (i) the applicant consents to a second orphan medicinal product application, (ii) the applicant cannot supply sufficient quantities of the product, or (iii) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Regulation of Companion Diagnostics

In the EU, *in vitro* diagnostic medical devices, or IVD MDs, were regulated by the EU Directive on *in vitro* diagnostic medical devices (Directive No. 98/79/EC, as amended), or IVDD, which regulated the placing on the market, the CE marking, the essential requirements, the conformity assessment procedures, the registration obligations for manufacturers and devices as well as the vigilance procedure. IVD MDs had to comply with the requirements provided for in the IVDD, and with further requirements implemented at national level (as the case may be).

The regulation of companion diagnostics is subject to further requirements since Regulation (EU) No 2017/746, or IVDR, became applicable on May 26, 2022 but there is a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the Regulation. The IVDR introduced a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue an EU certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a MAA for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent authorities or the EMA.

The aforementioned EU rules are generally applicable in the EEA.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations as we begin to directly commercialize our products. In March 2010, the Patient Protection and Affordable Care Act, or ACA, was signed into law which substantially changed the way healthcare is financed by both governmental and private insurers in the United States and significantly affected the pharmaceutical industry. The ACA contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and fraud and abuse changes. Additionally, the ACA increases the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; requires collection of rebates for drugs paid by Medicaid managed care organizations; requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 70 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected, expands of eligibility criteria for Medicaid programs, creates a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research and establishes a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the U.S. Supreme Court's decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers, which will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. In addition, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drug products. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023), and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the drug price negotiation program is currently subject to legal challenges. For that and other reasons, it is currently unclear how the IRA will be effectuated. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare product candidates and services, which could result in reduced demand for our product candidates once approved or additional pricing pressures.

In the EU, similar developments may affect our ability to profitably commercialize our products, if approved. On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

Other Healthcare Laws

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, and transparency laws and regulations with respect to drug pricing and payments and other transfers of value to physicians and other healthcare providers, as well as similar foreign laws in the jurisdictions outside the United States. If their operations are found to be in violation of any of such laws or any other governmental regulations that apply, they may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment.

Data Privacy and Security Laws

Pharmaceutical companies may be subject to numerous federal, state, and foreign laws, regulations and standards which govern the collection, use, disclosure and protection of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Coverage and Reimbursement

Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. These third-party payors are increasingly reducing reimbursements for medical products, drugs and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

In addition, in many countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. In the EU, governments influence the price of products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. The downward pressure on healthcare costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low-priced markets exert a commercial pressure on pricing within a country.

We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability. Furthermore, there can be no assurance that our products will be considered medically reasonable and necessary for a specific indication, that our products will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payors' reimbursement policies will not adversely affect our ability to sell our products profitably.

Human Capital

At IDEAYA, we view our employees as among our most valuable assets. Our ability to hire and retain highly skilled professionals remains an important element to our success in discovering and developing targeted therapeutics. Our employees are at the heart of our values of passionate commitment, fearless innovation, courageous integrity, respectful teamwork, objective decision-making and empowered accountability. We offer our employees a challenging work environment, ongoing skills development, attractive career advancement, and a culture that rewards entrepreneurial initiative and exceptional execution.

In 2020, we established an internal human resources departments part of our commitment to our human resources programs and our employee work experience. We believe our employees and our company benefit from and excel in a diverse, inclusive and safe work environment. Our employees come from numerous countries and bring diversity to our workplace across many critical categories. We believe the variety of experiences, backgrounds and perspectives of our employees bring to their work every day makes IDEAYA stronger and more successful. As of December 31, 2023, females make up 46% of our workforce, 13% of our executive team, and 37.5% of our board of directors.

As of December 31, 2023, we had a total of 124 employees. Of these employees, 98 were primarily engaged in research and development activities and 26 were primarily engaged in general and administrative activities. Of our total employees, 98 hold biology, chemistry or other relevant scientific degrees, including 55 Ph.D.'s. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Corporate Information

We were founded in June 2015 as a Delaware corporation. Our principal executive offices are located at 7000 Shoreline Court, Suite 350, South San Francisco, California 94080, and our telephone number is (650) 443-6209. Our website address is www.ideayabio.com.

We file electronically with the Securities and Exchange Commission (SEC) our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended. Our SEC filings are available to the public on the SEC's website at www.sec.gov. At our corporate website, www.ideayabio.com, we make available free of charge a variety of information for investors, including copies of these reports, and any amendments to these reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The information on, or that can be accessed through, our website is not part of this report and is not incorporated by reference herein. We have included our website address as an inactive textual reference only. We also use our website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD.

We use IDEAYA Biosciences, Inc.®, the IDEAYA logo, and other marks as trademarks in the United States and other countries. This Annual Report on Form 10-K contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report on Form 10-K, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by any other entity.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10-K, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations, growth prospects and stock price. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Many of the following risks and uncertainties are, and will be, exacerbated by the COVID-19 pandemic, the ongoing Ukraine-Russia conflict, the Israel Hamas conflict, or banking sector volatility and any worsening of the global business and economic environment as a result. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

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

We are an early-stage biopharmaceutical company with a limited operating history and no products approved for commercial sale. We have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future, which, together with our limited operating history, makes it difficult to assess our future viability.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are an early-stage biopharmaceutical company, and we have only a limited operating history upon which you can evaluate our business and prospects. We currently have no products approved for commercial sale, have not generated any revenue from sales of products and have incurred losses in each year since our inception in June 2015. In addition, we have limited experience as a company and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. Four of our product candidates, IDE397, darovasertib (IDE196), IDE161 and GSK101 (being developed by GSK under the Collaboration, Option and License Agreement with GSK), are currently in ongoing clinical trials.

We have had significant operating losses since our inception. Our net losses for the twelve months ended December 31, 2023 and 2022 were $113.0 million and $58.7 million, respectively. As of December 31, 2023, we had an accumulated deficit of $348.4 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Three of our product candidates are in early phase clinical trials being conducted by us. We have multiple other product candidates in preclinical development, as well as early-stage research programs. Our product candidates will require substantial additional development time and resources before we will be able to apply for or receive regulatory approvals and, if approved, begin generating revenue from product sales. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. We also do not yet have a sales organization or commercial infrastructure and, accordingly, we will incur significant expenses to develop a sales organization or commercial infrastructure in advance of regulatory approval and generating any commercial product sales. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we continue to develop IDE397, darovasertib, IDE161, our other product candidates and any future product candidates, conduct clinical trials and pursue research and development activities. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital.

Our operating results may fluctuate significantly, which will make our future results difficult to predict and could cause our results to fall below expectations.

Our quarterly and annual operating results may fluctuate significantly, which will make it difficult for us to predict our future results. These fluctuations may occur due to a variety of factors, many of which are outside of our control and may be difficult to predict, including:

- the timing and cost of, and level of investment in, research, development and commercialization activities, which may change from time to time;
- the timing and status of enrollment for our clinical trials;
- the timing of regulatory approvals, if any, in the United States and internationally;
- the cost of manufacturing, as well as building out our supply chain, which may vary depending on the quantity of productions, and the terms of any agreements we enter into with third-party suppliers;

- timing and amount of any option exercise, milestone, royalty or other payments we may or may not receive pursuant to any current or future collaboration or license agreement, including under the Collaboration, Option and License Agreement with GSK;
- timing and amount of any milestone, royalty or other payments due under any current or future collaboration or license agreement, including the License Agreement with Novartis or the Option and License Agreement with CRT and University of Manchester;
- coverage and reimbursement policies with respect to any future approved products, and potential future drugs that compete with our products;
- expenditures that we may incur to acquire, develop or commercialize additional products and technologies;
- the level of demand for any future approved products, which may vary significantly over time;
- future accounting pronouncements or changes in our accounting policies; and
- the timing and success or failure of preclinical studies and clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or collaboration partners.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

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

Since our inception, we have invested a significant portion of our efforts and financial resources in research and development activities for our precision medicine target and biomarker discovery platform and our initial preclinical and clinical product candidates. Preclinical studies and clinical trials and additional research and development activities will require substantial funds to complete. As of December 31, 2023, we had cash, cash equivalents and marketable securities of $632.6 million.

We believe that we will continue to expend substantial resources for the foreseeable future in connection with the research and development of our precision medicine target and biomarker discovery platform, clinical and preclinical product candidates, and any other future product candidates we may choose to pursue, as well as other corporate uses. Specifically, in the near term, we expect to incur substantial expenses as we advance our synthetic lethality product candidates through preclinical studies, advance darovasertib, IDE397 and IDE161 through clinical development, seek regulatory approval, prepare for and, if approved, proceed to commercialization, and continue our research and development efforts. These expenses will include our cost sharing obligations with GSK for research and development for our WRN program and our cost sharing obligations with Amgen for the Phase 1/2 clinical trial to evaluate IDE397 in combination with AMG 193. These expenditures will include costs associated with conducting preclinical studies and clinical trials, obtaining regulatory approvals, and manufacturing and supply, as well as marketing and selling any products approved for sale. In addition, other unanticipated costs may arise. Because the outcome of any preclinical study or clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully develop and commercialize our product candidates or any future product candidates.

We believe that our existing cash, cash equivalents and marketable securities will allow us to fund our planned operations for at least 12 months from the date of the issuance of the financial statements included in this Form 10-K. However, our operating plans and other demands on our capital resources may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Such financing may result in dilution to stockholders, imposition of burdensome debt covenants and repayment obligations, or other restrictions that may adversely affect our business. If we raise additional funds through licensing or collaboration

arrangements with third parties, we may have to relinquish valuable rights to our product candidates, or grant licenses on terms that are not favorable to us. Attempting to secure additional financing may also divert our management from our day-to-day activities, which may adversely affect our ability to develop our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all.

Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of developing our product candidates or any other future product candidates, and conducting preclinical studies and clinical trials, including our ongoing clinical trials for IDE397, darovasertib and IDE161;
- the scope, progress, results and costs related to the research and development of our precision medicine target and biomarker discovery platform, including costs related to the development of our proprietary libraries and database of tumor genetic information and specific cancer-target dependency networks;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates or any future product candidates, or any applicable diagnostics;
- the number and characteristics of any additional product candidates we develop or acquire;
- the cost of coordinating and/or collaborating with certain diagnostic companies for manufacturing and supply of companion diagnostics for biomarkers associated with our product candidates and any future product candidates;
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements and the financial terms of any such agreements, including the Collaboration, Option and License Agreement with GSK, the License Agreement with Novartis and the Option and License Agreement with Cancer Research Technology Ltd., or CRT, and University of Manchester;
- the timing and amount of any option exercise, milestone, royalty or other payments we may or may not receive pursuant to any current or future collaboration or license agreement, including under the Collaboration, Option and License Agreement with GSK;
- the timing and amount of any milestone, royalty or other payments we are required to make pursuant to any current or future collaboration or license agreement, including under the License Agreement with Novartis or the Option and License Agreement with CRT and University of Manchester;
- potential delays in our ongoing clinical programs as a result of any public health outbreaks, epidemics or pandemics (such as the COVID-19 pandemic);
- the cost of manufacturing our product candidates and any future products we successfully commercialize;
- the cost of commercialization activities, including the cost of building a sales force in anticipation of product commercialization and distribution costs;
- any product liability or other lawsuits related to our product candidates or future approved products;
- the expenses needed to attract, hire and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property portfolio; and
- the timing, receipt and amount of sales of any future approved products, if any.

Our ability to raise additional funds will depend on financial, economic and other factors, including the ongoing effects of the COVID-19 pandemic, the Ukraine-Russia conflict, the Israel-Hamas conflict, and closure of or liquidity issues at financial institutions (including, for example, Silicon Valley Bank), many of which are beyond our control. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. Furthermore, we maintain the majority of our cash and cash equivalents in accounts with major U.S. and multi-national financial institutions, and our deposits at certain of these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. If adequate funds are not available to us on a timely basis, we may be required to:

- delay, limit, reduce or terminate preclinical studies, clinical trials or other research and development activities or eliminate one or more of our development programs altogether; or
- delay, limit, reduce or terminate our efforts to establish manufacturing and sales and marketing capabilities or other activities that may be necessary to commercialize darovasertib, if approved, IDE397, if approved, IDE161, if approved, or any other future approved products, or reduce our flexibility in developing or maintaining our sales and marketing strategy.

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

To date, we have primarily financed our operations through the sale of equity securities and payments received under our collaboration agreements. We will be required to seek additional funding in the future and currently intend to do so through collaborations, public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources. If we raise additional funds by issuing equity securities, our stockholders may suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, is likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights or jointly own some aspects of our technologies or product candidates that we would otherwise pursue on our own.

Risks Related to Our Business

We are early in our development efforts. Our business is dependent on the successful development of our product candidates, future product candidates, and companion diagnostics for biomarkers associated with our product candidates and future product candidates.

Our current product candidates are in early stages of development and we are further developing our precision medicine target and biomarker discovery platform. We have no products approved for sale and our three most advanced product candidates, IDE397, darovasertib and IDE161, are in the early stages of clinical development and will require additional clinical development, regulatory review and approval in each jurisdiction in which we intend to market them, access to sufficient commercial manufacturing capacity, and significant sales and marketing efforts before we can generate any revenue from product sales. Our other product candidates have not been tested in clinical trials. The success of our business, including our ability to finance our company and generate revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of our product candidates, which may never occur. In the future, we may also become dependent on other product candidates that we may develop or acquire; however, given our early stage of development, it may be many years, if at all, before we have demonstrated the safety and efficacy of a product candidate sufficient to support approval for commercialization.

We have not previously submitted a new drug application, or NDA, to the FDA or similar approval filings to a comparable foreign regulatory authority, for any product candidate. An NDA or other relevant regulatory filing must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe and effective for each desired indication. The NDA or other relevant regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the product. We cannot be certain that our current or future product candidates will be successful in clinical trials or receive regulatory approval. Further, even if they are successful in clinical trials, our product candidates or any future product candidates may not receive regulatory approval. If we do not receive regulatory approvals for current or future product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approval to market a product candidate, our revenue will depend, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights, as well as the availability of competitive products, whether there is sufficient third-party reimbursement and adoption by physicians.

We plan to seek regulatory approval to commercialize our product candidates both in the United States and in select foreign countries. While the scope of regulatory approval generally is similar in other countries, in order to obtain separate regulatory approval in other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy. Other countries also have their own regulations governing, among other things, clinical trials and commercial sales, as well as pricing and distribution of drugs, and we may be required to expend significant resources to obtain regulatory approval and to comply with ongoing regulations in these jurisdictions.

The clinical and commercial success of our current and any future product candidates will depend on a number of factors, including the following:

- our ability to raise any additional required capital on acceptable terms, or at all;
- our ability to develop and successfully utilize our precision medicine target and biomarker discovery platform;
- timely and successful completion of our preclinical studies and clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- acceptance of INDs by the FDA, or similar regulatory filing by a comparable foreign regulatory authority for the conduct of clinical trials of our product candidates and our proposed design of future clinical trials;
- whether we are required by the FDA or a comparable foreign regulatory agency to conduct additional clinical trials or other studies beyond those planned to support approval of our product candidates;
- our ability to timely execute our ongoing clinical trials and enroll a sufficient number of patients on a timely basis to evaluate our product candidates in clinical development;
- acceptance of our proposed indications and primary endpoint assessments of our product candidates by the FDA and comparable foreign regulatory authorities;
- the availability or successful development of companion diagnostics for biomarkers associated with our product candidates or any other future product candidates;
- our ability to make arrangements with third-party manufacturers for, or establish, commercial manufacturing capabilities, and to consistently manufacture our product candidates on a timely basis;
- our ability, and the ability of any third parties with whom we contract, to remain in good standing with regulatory agencies and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices, or cGMPs, or similar foreign requirements;
- our ability to demonstrate to the satisfaction of the FDA and comparable foreign regulatory authorities the safety, efficacy and acceptable risk-benefit profile of our product candidates;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates, either as monotherapy or in combination with other drugs, or future approved products, if any;
- the timely receipt of necessary marketing approvals from the FDA and comparable foreign regulatory authorities;
- achieving and maintaining, and, where applicable, ensuring that our third-party contractors achieve and maintain, compliance with our contractual obligations and with all regulatory requirements applicable to our current product candidates or any future product candidates or approved products, if any;
- the willingness of physicians, operators of hospitals and clinics and patients to use or adopt any approved products, as well as the willingness of physicians and other health-care providers to incorporate molecular diagnostics or genetic sequencing into their clinical practice;
- our ability to successfully develop a commercial strategy and thereafter commercialize any approved products in the United States and internationally, whether alone or in collaboration with others;
- the availability and level of coverage and adequate reimbursement from managed care plans, private insurers, government payors, such as Medicare and Medicaid, and other third-party payors for any of our product candidates that may be approved;
- the convenience of our treatment or dosing regimen;
- our ability to compete with other approved therapies, if any;
- acceptance by physicians, payors and patients of the benefits, safety and efficacy of our product candidates or any future product candidates, if approved, including relative to alternative and competing treatments;
- patient demand for any approved products;

- our ability to establish and enforce intellectual property rights in and to our product candidates; and
- our ability to avoid third-party patent interference, opposition, derivation, intellectual property challenges, intellectual property infringement claims or similar proceedings with respect to our intellectual property rights.

These factors, many of which are beyond our control, could cause us to experience significant delays or an inability to obtain regulatory approvals or commercialize our current or future product candidates. Even if regulatory approvals are obtained, we may never be able to successfully commercialize any products. Accordingly, we cannot provide assurances that we will be able to generate sufficient revenue through the sale of products to continue our business or achieve profitability.

In connection with the Collaboration, Option and License Agreement with GSK, if GSK terminates any development program under its collaborations with us, whether as a result of our inability to meet milestones or otherwise, any potential revenue from those collaborations will be significantly reduced or non-existent, and our results of operations and financial condition will be materially and adversely affected.

We have invested a significant portion of our time and financial resources in the development of multiple product candidates that are included in our strategic partnership and collaboration with GSK, under the Collaboration, Option and License Agreement entered into on June 15, 2020, or the GSK Collaboration Agreement. The programs currently included in the GSK Collaboration Agreement are the Pol Theta and Werner Helicase (WRN) programs.

Under the GSK Collaboration Agreement, we will be eligible to receive from GSK future development and regulatory milestones of up to $475 million for the Pol Theta and $482.0 million for the WRN product, and commercial milestones of up to $475 million, with respect to the Pol Theta and WRN product. Additionally, we are entitled to receive 50% of U.S. net profits and tiered royalties on global non-U.S. net sales of WRN products by GSK, its affiliates and their sublicensees ranging from high single digit to sub-teen double digit percentages, subject to certain customary reductions. We are entitled to receive tiered royalties on global net sales of Pol Theta products by GSK, its affiliates and their sublicensees ranging from high single digit to sub-teen double digit percentages, subject to certain customary reductions. We have a right to opt-out of the 50% U.S. net profit share and corresponding development cost share for the WRN program, and would be eligible to receive tiered royalties on U.S. net sales of WRN products by GSK, its affiliates and their sublicensees at the same royalty rates as for global non-U.S. net sales thereafter, with potential positive economic adjustments based on the stage of the WRN program, as applicable, at the time of opt-out. There is no guarantee that we will be able to successfully continue to advance the Pol Theta and WRN programs and receive regulatory filing milestone payments related to any Pol Theta or WRN product. GSK may terminate the entire GSK Collaboration Agreement or any collaboration program on a target-by-target basis for any or no reason upon written notice to us after expiration of a defined notice period. The GSK Collaboration Agreement or any program under the GSK Collaboration Agreement may also be terminated by either party for the other party's insolvency or certain uncured breaches. We may terminate the GSK Collaboration Agreement if GSK or any of its sublicensees or affiliates challenge certain of our patents. Depending on the timing of any such termination we may not be entitled to receive the option exercise fees, or potential milestone payments, as these payments terminate with termination of the GSK Collaboration Agreement.

If GSK terminates its rights and obligations with respect to a program or the entire GSK Collaboration Agreement, then depending on the timing of such event:

- the development of our product candidates subject to the GSK Collaboration Agreement may be terminated or significantly delayed;
- our cash expenditures could increase significantly if it is necessary for us to hire additional employees and allocate scarce resources to the development and commercialization of product candidates that were previously funded by GSK;
- we would bear all of the risks and costs related to the further development and commercialization of product candidates that were previously the subject of the GSK Collaboration Agreement, including the reimbursement of third parties; and
- in order to fund further development and commercialization, we may need to seek out and establish alternative collaboration arrangements with third-party collaboration partners; this may not be possible, or we may not be able to do so on terms which are acceptable to us, in which case it may be necessary for us to limit the size or scope of one or more of our programs or increase our expenditures and seek additional funding by other means.

Any of these events would have a material adverse effect on our results of operations and financial condition.

As an organization, we have never completed a clinical trial, and may be unable to do so for any of our product candidates.

We will need to successfully initiate and complete our own Phase 1 clinical trials and later-stage and pivotal clinical trials in order to obtain FDA or a comparable foreign regulatory body's approval to market our product candidates. Carrying out clinical trials and the submission of regulatory filings is a complicated process. As an organization, we have not yet completed any clinical trials for any of our product candidates. We have limited experience in preparing, submitting and prosecuting regulatory filings, and have not previously submitted any NDA or other comparable foreign regulatory submission for any product candidate. In addition, we have had limited interactions with the FDA and cannot be certain how many additional clinical trials of darovasertib, IDE397 or IDE161 or how many clinical trials of any of our other product candidates will be required or whether the FDA will agree with the design or implementation of our clinical trials. We are required to comply with certain regulatory requirements, and the FDA may identify specific clinical or other development-related requirements that we must satisfy, as a condition to initiating or continuing our clinical trials; if we fail to meet such a requirement, the FDA may issue a clinical hold or designate other conditions on our clinical trials. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to regulatory submission of a marketing application for, and approval of, darovasertib, IDE397, IDE161, or any of our other 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 darovasertib, IDE397, IDE161, or any other product candidate.

The successful development of targeted therapeutics, including therapeutics involving direct targeting of an oncogenic pathway and synthetic lethality therapeutics, including our portfolio of synthetic lethality small molecule inhibitors, as well as any related diagnostics, is highly uncertain.

Successful development of targeted therapeutics, including therapeutics involving direct targeting oncogenic pathways and synthetic lethality therapeutics, such as our portfolio of synthetic lethality small molecule inhibitors, as well as any related diagnostics, is highly uncertain and is dependent on numerous factors, many of which are beyond our control. Our precision medicine target and biomarker discovery platform is based on new technologies and methods relating to drug target and biomarker identification, screening and validation, including Dual CRISPR genetic screening and bioinformatics and we have not, to date, sought regulatory approval for any therapeutics developed through our precision medicine target and biomarker discovery platform. As such, it is difficult to accurately predict the developmental challenges we or our collaboration partners may incur for our current and future product candidates as we proceed through product discovery, identification, preclinical studies and clinical trials.

Our precision medicine target and biomarker discovery platform is novel and may not be effective at identifying targets and/or biomarkers for product candidates. We therefore cannot provide any assurance that we will be able to successfully identify additional product candidates or biomarkers, advance any of these additional product candidates or diagnostics for their associated biomarkers through the development process.

Additionally, particular patient genetic alterations, such as mutations, deletions or fusions may not be functionally active genetic drivers of the disease. Further, whether a genetic alteration is functionally active may be difficult to ascertain from preclinical cancer models, may be tissue-type dependent and may vary from patient to patient within a specific indication. If that was the case, we would need to functionally validate such genetic alterations, for example, using *in vitro* and *in vivo* models, potentially across more than one tumor-tissue type and across multiple cell lines. If some of the genetic alterations are not functionally validated, this would reduce the size of our addressable patient population. Even if genetic alterations are preclinically validated, the relevance of these alterations may not translate into a human clinical setting, which could adversely impact our clinical trial results and our commercial opportunities.

Targeted therapeutics that appear promising in the early phases of development may fail to reach the market for several reasons, including:

- research or preclinical studies may show our targeted small molecule inhibitors or antagonists to be less effective than desired or to have harmful or problematic side effects or toxicities;
- failure to accurately identify, validate or develop clinically relevant biomarkers for our targeted therapeutic product candidates;

- clinical trial results may show our targeted therapeutic small molecule inhibitors to be less effective than expected based on preclinical studies (e.g., a clinical trial could fail to meet its primary endpoint(s)) or to have unacceptable side effects or toxicities;
- failure to receive the necessary regulatory approvals or a delay in receiving such approvals. Among other things, such delays may be caused by slow enrollment in clinical trials, patients dropping out of trials, length of time to achieve trial endpoints, additional time requirements for data analysis, IND preparation, discussions with the FDA or similar foreign regulatory authorities, an FDA or similar foreign regulatory authority request for additional preclinical or clinical data, or unexpected safety or manufacturing issues;
- manufacturing costs, formulation issues, pricing or reimbursement issues, or other factors that may make our targeted therapeutic small molecule inhibitors uneconomical; and
- proprietary rights of others and their competing products and technologies that may prevent our targeted therapeutic small molecule inhibitors, or the diagnostics for biomarkers associated with such small molecule inhibitors, from being commercialized.

As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our precision medicine target and biomarker discovery platform will result in the identification, development, and regulatory approval of any products. The length of time necessary to complete clinical trials and to submit an application for marketing approval for a decision by a regulatory authority may be difficult to predict for targeted therapeutic small molecule inhibitors, in large part because of the limited regulatory history associated with them. The clinical trial requirements of the FDA and other comparable foreign regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. Except for certain PARP inhibitors, no products based on synthetic lethality have been approved to date by regulators. As a result, the regulatory approval process for product candidates such as ours is uncertain and may be more expensive and take longer than the approval process for product candidates based on other, better known or more extensively studied technologies. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or other comparable regions of the world or how long it will take to commercialize our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market would adversely affect our business, financial condition, results of operations and prospects.

Even if we are successful in obtaining regulatory approval, commercial success of any approved products will also depend in large part on the availability of insurance coverage and adequate reimbursement from third-party payors, including government payors, such as the Medicare and Medicaid programs, and managed care organizations, which may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. Third-party payors could require us to conduct additional studies, including post-marketing studies related to the cost-effectiveness of a product, to qualify for reimbursement, which could be costly and divert our resources. If government and other healthcare payors were not to provide adequate insurance coverage and reimbursement levels for one any of our products once approved, market acceptance and commercial success would be limited.

In addition, if any of our products is approved for marketing, we will be subject to significant regulatory obligations regarding the submission of safety and other post-marketing information and reports and registration, and will need to continue to comply (or ensure that our third-party providers comply) with cGMPs, or similar applicable foreign requirements and GCPs for any clinical trials that we conduct post-approval. In addition, there is always the risk that we or a regulatory authority might identify previously unknown problems with a product post-approval, such as adverse events, or AEs, of unanticipated severity or frequency. Compliance with these requirements is costly and any failure to comply or other post-approval issues with our product candidates could have a material adverse effect on our business, financial condition, results of operations and prospects.

Preclinical and clinical drug development is a lengthy and expensive process with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates, which could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our business, financial condition, results of operations and prospects. Furthermore, results of earlier studies and trials may not be predictive of future trial results.

Before we can initiate clinical trials for our product candidates, we must submit the results of preclinical studies to the FDA or a comparable foreign regulatory authority along with other information, including information about product candidate chemistry, manufacturing and controls, diagnostics for biomarkers for our product candidates and our proposed clinical trial protocol, as part of an IND application or similar regulatory filing.

Before obtaining marketing approval from regulatory authorities for the sale of any products, we, or our collaboration partners must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are expensive and can take many years to complete, and their outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. In addition, we may rely in part on preclinical, clinical and quality data generated by contract research organizations, or CROs, and other third parties for regulatory submissions for our product candidates. While we have or will have agreements governing these third parties' services, we have limited influence over their actual performance. Further, pursuant to our license agreement with Novartis, we have a right of reference to certain data from Novartis' Phase 1 clinical trial data for our regulatory filings for darovasertib.

If these third parties, including Novartis, fail to make data available to us, or, if applicable, make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may be significantly delayed and we may need to conduct additional studies or trials or collect additional data independently. In either case, our development costs would increase.

Our clinical trial collaboration and supply agreements with Pfizer, Amgen and Gilead for the supply of crizotinib, AMG 193 and Trodelvy, respectively, support our plans to evaluate the safety and efficacy of darovasertib in combination with crizotinib, IDE397 in combination with AMG 193, and IDE397 in combination with Trodelvy. If any of these strategic collaborators delay or fail to supply their compound in support of these combination trials, fail to sponsor or appropriately conduct the combination trial (in the case of Amgen), or we fail to reach an agreement with any of these strategic collaborators for the continued supply of their compound beyond the terms of the current supply agreements, the development programs as pertaining to these combinations may be significantly delayed, and our development costs may increase. In each case, this may require us to establish additional supply agreements and rely upon third parties for supply of such combination agents, or if such combination agents are commercially available, in the absence of a supply agreement, we may incur the cost of purchasing such combination agents and may be at risk of having insufficient supply. We may initiate clinical trials in which our product candidates, including darovasertib, IDE397 or IDE161, are combined with one or more other pharmaceutical agents that have not yet been approved by the FDA or comparable foreign regulatory authorities; in such situations, we may be relying on third parties for obtaining appropriate regulatory approvals and we may have no or limited influence over whether or not such regulatory approvals are achieved for such combination agents.

We and our strategic collaborators also may experience numerous unforeseen events during, or as a result of, any preclinical studies or clinical trials that could delay or prevent us or our strategic collaborators from successfully developing our product candidates, including:

- we may be unable to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- the FDA or a comparable foreign regulatory authority disagreeing as to the design or implementation of our clinical trials;
- delays in obtaining regulatory authorization to commence a clinical trial;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining IRB or ethics committee approval or positive opinion at each clinical trial site;
- recruiting an adequate number of suitable patients to participate in a clinical trial, particularly if any public health outbreak, epidemic or pandemic leads to clinical site closures;
- having patients complete a clinical trial or return for post-treatment follow-up;

- clinical sites deviating from clinical trial protocol or dropping out of a clinical trial;
- addressing subject safety concerns that arise during the course of a clinical trial;
- adding a sufficient number of clinical trial sites;
- obtaining sufficient quantities of product candidate for use in preclinical studies or clinical trials from third-party suppliers; or
- accessing third-party products or product candidates for use in combination with our product candidates in preclinical studies or clinical trials, including third-party product candidates that have not yet been approved by the FDA or comparable foreign regulatory authorities.

We and our strategic collaborators may experience numerous adverse or unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon our development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- we or our third-party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls, or be unable to produce sufficient product supply to conduct and complete preclinical studies or clinical trials of our product candidates in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the quality of our product candidates or other materials necessary to conduct preclinical studies or clinical trials of our product candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- collaborators may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

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

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements, which could be expensive and time-consuming; or
- have the treatment removed from the market after obtaining marketing approval.

We and our strategic collaborators could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or another comparable foreign regulatory authority. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs or other foreign regulatory authorities or ethics committees for reexamination, which may impact the costs, timing or successful completion of a clinical trial. For example, in recent years the FDA has issued draft guidance and launched programs aiming to reform and modernize the dose optimization procedures used by clinical trial sponsors during the development of oncology drugs. Although these efforts have not yet resulted in any formal changes to the FDA's regulations or policies, changes in the FDA's thinking with respect to dose selection and optimization could require us to change the design of our planned or ongoing clinical trials or otherwise conduct additional preclinical, clinical or manufacturing studies beyond those we currently anticipate, which could increase our costs and/or delay the development of our product candidates.

As another example, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the EU Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the EU Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

Further, conducting clinical trials in foreign countries, as we may do for certain of our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the possibility that we could be required to conduct additional preclinical studies before initiating any clinical trials, the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with comparable foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Principal 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 a regulatory authority concludes that the financial relationship may have affected the interpretation of the clinical 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 the marketing application we submit. Any such delay or rejection could prevent or delay us from commercializing our current or future product candidates.

If any of our preclinical studies or clinical trials of our product candidates are delayed or terminated, the commercial prospects of our product candidates may be harmed, and our ability to ultimately generate revenues from any of these product candidates will be delayed or not realized at all. In addition, any delays in completing our clinical trials may increase our costs, slow down our product candidate development and regulatory approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business, financial condition, results of operations and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. If our product candidates and any future product candidates prove to be ineffective, unsafe or commercially unviable, our entire platform and approach would have little, if any, value, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

Furthermore, the results of preclinical studies and clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy despite having progressed through preclinical studies and initial clinical trials. Furthermore, for some of our programs, in the future we intend to conduct basket trials, which will be designed to include multiple clinically defined populations under one investigational protocol, although each population is enrolled and analyzed separately. A basket trial design could potentially decrease the time to study new populations by decreasing administrative burden, however, these trials may not provide opportunities for accelerated regulatory pathways, and do not overcome limitations to extrapolating data from the experience in one disease to other diseases, because safety and efficacy results in each indication are analyzed separately. Accordingly, clinical success in a basket trial, or any trial in one indication, may not predict success in another indication. In contrast, in the event of an adverse safety issue, clinical hold, or other adverse finding in one or more indications being tested, such event could adversely affect our trials in the other indications and may delay or prevent completion of the clinical trials. A number of companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials for similar indications that we are pursuing due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval of any products.

Synthetic lethality represents an emerging class of precision medicine targets, and negative perceptions of the efficacy, safety or tolerability of this class of targets, including any that we develop, could adversely affect our ability to conduct our business, advance our product candidates or obtain regulatory approvals.

Aside from PARP inhibitors, such as Lynparza, Rubraca, Zejula and Talzenna, no synthetic lethality small molecule inhibitor therapeutics have been approved to date by the FDA or other comparable regulators. AEs in future clinical trials of our product candidates or in clinical trials of others developing similar products and the resulting publicity, as well as any other AEs in the field of synthetic lethality, or other products that are perceived to be similar to synthetic lethality, such as those related to gene therapy or gene editing, could result in a decrease in the perceived benefit of one or more of our programs, increased regulatory scrutiny, decreased confidence by patients and CROs in our product candidates, and less demand for any product that we may develop. Our substantial pipeline of synthetic lethality small molecule inhibitor product candidates could result in a greater quantity of reportable AEs or other reportable negative clinical outcomes, manufacturing reportable events or material clinical events that could lead to clinical delays or holds by the FDA or applicable regulatory authority or other clinical delays, any of which could negatively impact the perception of one or more of our synthetic lethality programs, as well as our business as a whole. In addition, responses by U.S. federal, state or foreign governments to negative public perception may result in new legislation or regulations that could limit our ability to develop any product candidates or commercialize any approved products, obtain or maintain regulatory approval, or otherwise achieve profitability. More restrictive statutory regimes, government regulations, or negative public opinion would have an adverse effect on our business, financial condition, results of operations, and prospects, and may delay or impair the development of our product candidates and commercialization of any approved products or demand for any products we may develop.

Tissue-type agnostic basket trials are an emerging clinical approach that may result in delays in clinical development, additional regulatory requirements and delays in, or the prevention of, our ability to obtain regulatory approval or commercialize our product candidates.

We initiated a Phase 1/2 tissue-type agnostic basket trial with darovasertib in June 2019, and may also utilize a basket trial approach in clinical trials for other product candidates. Basket trials allow us to evaluate the safety and efficacy of a product candidate in a variety of tumor types with a specific molecular profile. We believe that this clinical approach provides many benefits, however, there are limited precedents, and as a result, there a number of inherent risks.

There is limited precedent for the FDA and foreign regulatory authorities to review and grant tissue-type agnostic approvals. Furthermore, as clinical trials increasingly use classification of tumors by molecular profiling, the FDA or other regulatory authority may change or issue guidance or adopt a policy that adversely affects requirements for basket trials. In the event that such guidance or policy has an effect on any of our protocols or trials, as the case may be, it may result in the delay of clinical development, or require us to conduct additional preclinical studies or clinical trials.

Even if we obtain a tissue-type agnostic approval for one or more of our product candidates, there is limited precedent for obtaining reimbursement. Third-party payors may reimburse at different levels across tumor tissue types and indicates, or not at all.

We may find it difficult to enroll patients in our clinical trials given the limited number of patients who have the diseases for which our product candidates are being developed. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our and our collaboration partners' ability to enroll a sufficient number of patients who remain in the clinical trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The enrollment of patients depends on many factors, including:

- the patient eligibility and exclusion criteria defined in the protocol;
- the size and nature of the patient population required for analysis of the clinical trial's primary endpoints;
- the proximity of patients to clinical trial sites;
- the design of the clinical trial;
- the risk that enrolled patients will not complete a clinical trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinical trial investigators' willingness to continue enrolling patients and patients' willingness to complete protocol assessments during any public health outbreak, epidemic or pandemic;
- clinicians' and patients' perceptions as to the safety of the product candidate;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new therapies that may be approved for the indications we are investigating as well as any drugs under development; and
- our ability to obtain and maintain patient consents.

We will be required to identify and enroll a sufficient number of patients for each of our clinical trials. Potential patients for any planned clinical trials may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for such trials. We also may encounter difficulties in identifying and enrolling patients with a stage of disease appropriate for our planned clinical trials and monitoring such patients adequately during and after treatment. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible patients to participate in the clinical trials required by the FDA or a comparable foreign regulatory authority. In addition, the process of finding and diagnosing patients may prove costly.

In addition, our clinical trials may compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. As a result of any public health outbreak, competition for potential patients in our trials may be further exacerbated as a result of any clinical site closures. Since the number of qualified clinical investigators is already limited, we may conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site.

Furthermore, certain conditions for which we plan to evaluate our current development candidates are rare diseases, such as metastatic uveal melanoma, with limited patient pools from which to draw for clinical trials. For example, one of our product candidates, darovasertib, is currently being evaluated in a Phase 1/2 basket trial that we initiated in June 2019 to evaluate darovasertib in solid tumors harboring GNAQ/GNA11 hotspot mutations in metastatic uveal melanoma. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as completion of required follow-up periods. The eligibility criteria of our clinical trials, once established, will further limit the pool of available trial participants.

In addition, our clinical trials may be affected by any public health outbreak, epidemic or pandemic. Clinical site initiation and patient enrollment may be delayed. For example, as a result of the COVID-19 pandemic, several of our sites halted new enrollment for several months in 2020 before resuming enrollment. Some patients may not be able or willing to comply with clinical trial protocols, and data collected may be incomplete, if quarantines impede patient movement or interrupt healthcare services. Similarly, the ability to recruit and retain patients, and principal investigators and site staff who, as healthcare providers, may have heightened exposure to infectious diseases, may be delayed or disrupted, which may adversely impact our clinical trial operations.

If patients are unwilling to participate in our clinical trials for any reason, including the existence of other approved therapies or concurrent clinical trials for similar patient populations, if they are unwilling to enroll in a clinical trial with a placebo-controlled design, or we otherwise have difficulty enrolling a sufficient number of patients, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of our product candidates may be delayed. Our inability to enroll a sufficient number of patients for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. In addition, we expect to rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will have limited influence over their actual performance.

We cannot assure you that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

Our product candidates or any future product candidates may be associated with undesirable side effects or AEs that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

As with most pharmaceutical products, use of our product candidates could be associated with side effects or AEs which can vary in severity from minor reactions to death and in frequency from infrequent to prevalent. Undesirable side effects or unacceptable toxicities caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or a comparable foreign regulatory authority. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of these or other side effects. Furthermore, certain of our product candidates may be co-administered with third-party approved or experimental therapies, such as darovasertib with crizotinib in the combination arms of our Phase 1/2 clinical trial or IDE397 with PRMT5 inhibitors in the combination arms of our Phase 1/2 clinical trial. These combinations may have additional side effects. The uncertainty resulting from the use of our product candidates in combination with other therapies may make it difficult to accurately predict side effects in future clinical trials.

To date, only three of our product candidates, IDE397, darovasertib, and IDE161 have been tested in clinical trials, and they have been observed to be generally well tolerated, with certain drug-related SAEs and AEs being reported for darovasertib, as monotherapy and in combination with crizotinib, for IDE397, and for IDE161.

If unacceptable side effects arise in the further development of darovasertib, including in combination with crizotinib, in the further development of IDE397, including in combination with PRMT5 inhibitors, in the further development of IDE161, or in the development of any of our other product candidates, we, the FDA or comparable foreign regulatory authorities, or the IRBs at the institutions in which the clinical trials are being conducted could suspend or terminate our clinical trials or the FDA or a comparable foreign regulatory authority could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete any of our clinical trials or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition, results of operations and prospects significantly.

In addition, even if we successfully advance our product candidates or any future product candidates into and through clinical trials, such trials will likely only include a limited number of patients and limited duration of exposure to our product candidates. As a result, we cannot be assured that adverse effects of our product candidates will not be uncovered when a significantly larger number of patients are exposed to the product candidate. Further, any clinical trials may not be sufficient to determine the effect and safety consequences of taking our product candidates over a multi-year period.

If any of our product candidates receives marketing approval and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;

- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a Medication Guide outlining the risks of such side effects for distribution to patients or similar risk management measures;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues to us, which would adversely affect our business, financial condition, results of operations and prospects. In addition, if one or more of our product candidates prove to be unsafe, our entire technology platform and pipeline could be affected, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to successfully develop molecular diagnostics for biomarkers that enable patient selection and/or that demonstrate drug-target interaction, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates.

A key component of our strategy includes the use of molecular diagnostics to guide patient selection and/or to confirm target engagement of our product candidates. In some cases, a diagnostic may be commercially available, for example, on a tumor-profiling panel. If not already commercially available, we may collaborate with diagnostic companies for the development of biomarkers associated with our product candidates. We may have difficulty in establishing or maintaining such development relationships, and we will face competition from other companies in establishing these collaborations.

There are also several risks associated with biomarker identification and validation. We, in collaboration with any diagnostic partners, may not be able to identify predictive biomarkers or pharmacodynamic biomarkers for one or more of our programs. We may not be able to validate potential biomarkers (e.g., certain genetic mutations) or their functional relevance preclinically in relevant *in vitro* or *in vivo* models. Data analytics and information from databases that we rely on for identifying or validating some of our biomarker-target relationships may not accurately reflect potential patient populations. Potential biomarkers, even if validated preclinically, may not be functionally effective or validated in human clinical trials.

If we, in collaboration with these parties, are unable to successfully develop companion diagnostics for our product candidates, or experience delays in doing so, the development of our product candidates may be adversely affected. The development of companion diagnostic products requires a significant investment of working capital, and may not result in any future income. This could require us to raise additional funds, which could dilute our current investors or impact our ability to continue our operations in the future.

There are also risks associated with diagnostics that are commercially available, including that we may not have access to reliable supply for such diagnostics.

The failure to obtain required regulatory approvals or certification for any companion diagnostic tests that we may pursue may prevent or delay approval of our product candidates. Moreover, the commercial success of any of our product candidates may be tied to the regulatory approval or certification, market acceptance and continued availability of a companion diagnostic.

The FDA regulates *in vitro* companion diagnostics as medical devices that will likely be subject to and require prospective validation in clinical trials in conjunction with the clinical trials for our product candidates, and which will require regulatory clearance or approval prior to commercialization. We plan to collaborate with third parties for the development, testing and manufacturing of these companion diagnostics, the application for and receipt of any required regulatory clearances or approvals, and the commercial supply of these companion diagnostics. Our third-party collaborators may fail to obtain the required regulatory clearances or approvals, which could prevent or delay approval of our product candidates. In addition, the commercial success of any of our product candidates may be tied to and dependent upon the receipt of required regulatory clearances or approvals of the companion diagnostic.

Even if a companion diagnostic is approved, we will rely on the continued ability of any third-party collaborator to make the companion diagnostic commercially available to us on reasonable terms in the relevant geographies. Furthermore, if commercial tumor profiling panels are not able to be updated to include additional tumor-associated genes, or if clinical oncologists do not incorporate molecular or genetic sequencing into their clinical practice, we may not be successful in developing or commercializing our existing product candidates or any future product candidates.

Further, approval, clearance or certification of companion diagnostics may be subject to further legislative or regulatory reforms notably in the EU. On May 25, 2017, the new In Vitro Medical Devices Regulation, or IVDR, entered into force. The IVDR repeals and replaces the EU In Vitro Diagnostic Medical Devices Directive. Unlike directives, which must be implemented into the national laws of the EU member states, regulations are directly applicable, i.e., without the need for adoption of EU member states laws implementing them, in all EU member states and are intended to eliminate current differences in the regulation of medical devices among EU member states. The IVDR, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU for in vitro diagnostic medical devices and ensure a high level of safety and health while supporting innovation. The IVDR became applicable on May 26, 2022. However, on October 14, 2021, the European Commission had proposed a "progressive" roll-out of the IVDR to prevent disruption in the supply of in vitro diagnostic medical devices. Therefore, the IVDR applies since May 26, 2022 but there is a tiered system extending the grace period for many in vitro diagnostic medical devices (depending on their risk classification) before they have to be fully compliant with the Regulation.

The regulation of companion diagnostics is subject to further requirements since the IVDR became applicable as it introduced a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue an EU certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a marketing authorization application for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent authorities or the EMA. These modifications may make it more difficult and costly for us to obtain regulatory clearances, approvals or certifications for our companion diagnostics or to manufacture, market or distribute our products after clearance, approval or certification is obtained.

Interim, "topline" and preliminary data from our clinical trials may differ materially from the final data.

From time to time, we may publicly disclose preliminary or "topline" data from our clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same clinical trials, or different conclusions or considerations may qualify such topline results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data is available. From time to time, we may also disclose interim data from our clinical trials. Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business, financial condition, results of operations and prospects.

Others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and the value of our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically a summary of extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or our business. If the topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, financial condition, operating results and prospects.

We may be unable to obtain regulatory approval for our product candidates or any future product candidates. The denial or delay of such approval would prevent or delay commercialization of our product candidates and adversely impact our business, financial condition, operating results and prospects.

The process of obtaining regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA or comparable foreign regulatory authorities have substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed. Neither we nor any collaborator or any future collaborator, is permitted to market any of our product candidates in the United States or abroad until we receive approval of an NDA from the FDA or similar regulatory approvals from comparable foreign regulatory authorities.

Prior to obtaining approval to commercialize a product candidate in the United States, we or our collaborators must demonstrate with substantial evidence from adequate and well-controlled clinical trials, and to the satisfaction of the FDA, that such product candidates are safe and effective for their intended uses. Foreign regulatory authorities may require a similar demonstration before we can obtain approval to commercialize a product candidate abroad. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA or comparable foreign regulatory authorities. The FDA or a comparable foreign regulatory authority, as the case may be, may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or may object to elements of our clinical development program.

The FDA or a comparable foreign regulatory authority can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or implementation of our clinical trials;
- negative or ambiguous results from our clinical trials, or results may not meet the level of statistical significance required by the FDA or a comparable foreign regulatory agency for approval;
- serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;
- we are unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA's or the applicable comparable foreign regulatory agency's non-approval of the formulation, labeling or specifications of our product candidates or any of our future product candidates;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- such authorities could question the integrity of data obtained in our current or future clinical trials, for example, due to missed protocol procedures;
- such authorities may not agree that the data collected from clinical trials of our product candidates are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and such authorities may impose requirements for additional preclinical studies or clinical trials;
- such authorities may disagree regarding the formulation, labeling and/or the specifications of our product candidates;
- such authorities may only approve indications that are significantly more limited than what we apply for and/or with other significant restrictions on distribution and use;

- such authorities may find deficiencies in the manufacturing processes or facilities of our third-party manufacturers with which we or any of our collaborators or any potential future collaborators, contract for clinical and commercial supplies; and
- the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our collaborators' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our collaborators or any potential future collaborators, from commercializing any products.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or comparable foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Even if we eventually complete clinical trials and receive approval of an NDA or foreign marketing application for a product, the FDA or a comparable foreign regulatory authority may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, and/or the implementation of a REMS, which may be required to ensure safe use of the drug after approval. The FDA or a comparable foreign regulatory authority also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or a comparable foreign regulatory authority may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

We may develop our product candidates and future product candidates in combination with other therapies, and safety or supply issues with combination-use products may delay or prevent development and approval of our product candidates.

We may develop our product candidates in combination with one or more cancer therapies, both approved and unapproved. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product candidates or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our product candidates for use in combination with other drugs or for indications other than cancer. Similarly, if the therapies we use in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA or similar regulatory authorities outside of the United States may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially.

We may also evaluate our product candidates in combination with one or more cancer therapies that have not yet been approved for marketing by the FDA or a similar regulatory authority outside of the United States. We may be unable to effectively identify and collaborate with third parties for the evaluation of our product candidates in combination with their therapies. We will not be able to market and sell any product candidate we develop in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval. The regulations prohibiting the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other foreign government agencies. In addition, there are additional risks similar to the ones described for our products currently in development and clinical trials that result from the fact that such cancer therapies are unapproved, such as the potential for serious adverse effects, delay in their clinical trials and lack of FDA or comparable foreign regulatory authorities approval.

If the FDA or a similar regulatory authority outside of the United States does not approve these other drugs or revokes approval of, or if safety, efficacy, manufacturing, or supply issues arise with, the drugs we choose to evaluate in combination with any product candidate we develop, we may be unable to obtain approval of or market such product.

Although we may apply for orphan drug designation for our product candidates, we may not receive the designation or we may be unable to obtain the benefits associated with such designation, including the potential for marketing exclusivity

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. In the United States, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding, tax credits for certain clinical trial costs and user-fee waivers. If a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug and indication for seven years, except in limited circumstances.

In the EU, the European Commission grants orphan designation on the basis of the EMA's Committee for Orphan Medicinal Products opinion. A medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment, of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. In the EU, orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Moreover, upon grant of a marketing authorization and assuming the requirement for orphan designation are also met at the time the marketing authorization is granted, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed Pediatric Investigation Plan, or PIP.

Although we may apply for orphan drug designation for our product candidates, we may not receive the designation we apply for. Even if we received orphan drug designation for one or more of our product candidates, which we have received for darovasertib in uveal melanoma, there is no guarantee that we will obtain approval or orphan drug exclusivity for the product. Even if we obtain approval and orphan drug exclusivity for any of our product candidates, that exclusivity may not effectively protect the product candidate from competition because different therapies can be approved for the same condition and the same therapy could be approved for different conditions. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to provide greater safety, greater effectiveness or a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. In the EU, during the exclusivity period, marketing authorizations may be granted to a similar medicinal product with the same orphan indication if: (i) the applicant can establish that the second medicinal product, although similar to the orphan medicinal product already authorized is safer, more effective or otherwise clinically superior to the orphan medicinal product already authorized; (ii) the marketing authorization holder for the orphan medicinal product grants its consent; or (iii) if the marketing authorization holder of the orphan medicinal product is unable to supply sufficient quantities of product. The European exclusivity period can be reduced to six years, if, at the end of the fifth year a drug no longer meets the criteria for orphan drug designation (i.e. the prevalence of the condition has increased above the orphan designation threshold or it is judged that the product is sufficiently profitable so as not to justify maintenance of market exclusivity). Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. While we may seek additional orphan drug designations for applicable indications for our current and any future product candidates, we may never receive such designations. Even if we do receive such designations, there is no guarantee that we will enjoy the benefits of those designations.

We may seek and fail to obtain fast track or breakthrough therapy designations for our current or future product candidates. Even if we are successful, these programs may not lead to a faster development or regulatory review process, and they do not guarantee we will receive approval for any product candidate.

If a product is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, the product sponsor may apply for fast track designation. The sponsor of a fast track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the product candidate may be eligible for priority review. A fast track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted. The FDA has broad discretion whether or not to grant fast track designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Although the FDA has granted fast track designation to darovasertib in combination with crizotinib for treatment of adult patients with MUM and to IDE161 for treatment of adult patients with breast cancer or ovarian cancer and we may seek additional designation for other product candidates in the future, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may rescind the fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

We may also seek breakthrough therapy designation for any product candidate that we develop. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA may also be eligible for priority review. Like fast track designation, breakthrough therapy designation is within the discretion of the FDA. Accordingly, even if we believe a product candidate we develop meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs developed under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if a product candidate we develop qualifies as a breakthrough therapy, the FDA may later decide that the drug no longer meets the conditions for qualification and rescind the designation.

We may attempt to secure approval from the FDA through the use of the accelerated approval pathway. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw any accelerated approval we have obtained.

We may in the future seek accelerated approval for our one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit.

The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit or are not completed in a timely manner, the FDA may withdraw its approval of the drug on an expedited basis. In addition, in December 2022, President Biden signed an omnibus appropriations bill to fund the U.S. government through fiscal year 2023 which included the Food and Drug Omnibus Reform Act of 2022, or FDORA. Among other things, the legislation introduced reforms intended to expand the FDA's ability to regulate products receiving accelerated approval, including by increasing the FDA's oversight over the conduct of confirmatory trials; however, the ultimate impact of these reforms remains unclear.

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

We face significant competition in an environment of rapid technological and scientific change, and our failure to effectively compete may prevent us from achieving significant market penetration. Most of our competitors have significantly greater resources than we do and we may not be able to successfully compete.

The biotechnology and pharmaceutical industries in particular are characterized by rapidly advancing technologies, intense competition and a strong emphasis on developing proprietary therapeutics. We compete with a variety of multinational biopharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing or will likely develop product candidates and processes competitive with our product candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We believe that a significant number of product candidates are currently under development, and may become commercially available in the future, for the treatment of diseases and other conditions for which we may try to develop product candidates. 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. We believe that while our precision medicine target and biomarker discovery platform and our scientific and technical know-how give us a competitive advantage in this space, competition from many sources remains. Our competitors include larger and better funded biopharmaceutical, biotechnological and oncology therapeutics companies, as well as universities and other research institutions.

Our commercial opportunity and success will be reduced or eliminated if competing products emerge that are safer, more effective, or less expensive than the therapeutics we develop. Our competitors may 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.

For darovasertib, we are not aware of other companies actively developing clinical-stage therapeutics directed to PKC as a target for solid tumors. MingSight is developing a PKC beta inhibitor in chronic lymphocytic leukemia, or CLL, and diabetic macular edema, both in Phase 1 studies. Varian Biopharmaceuticals is advancing a preclinical-stage atypical PCK iota inhibitor, including as a dermatologic gel formulation for potential topical treatment of Basal Cell Carcinoma, or BCC. Exscientia is developing a PKC theta inhibitor in inflammatory diseases in Phase 1 studies. Varsity Pharma is developing a PKC inhibitor in CLL. We are aware of other companies that are conducting research and development of potential therapies for primary UM or for MUM based on other targets and approaches. For example, Aura Biosciences is developing AU-011 a virus-like drug conjugate (VDC) as local treatment for early-stage choroidal melanoma. Immunocore is developing and commercializing Tebentafusp, also known under its branded name as Kimmtrak for the treatment of adult patients with HLA-A*02:01-positive unresectable or metastatic uveal melanoma. Novartis is developing DYP688, an antibody-drug-conjugate, or ADC, with a GNAQ-11 inhibitor payload in a Phase 1/2 clinical trial in MUM.

For IDE397, Servier Pharmaceuticals, LLC, or Servier, is evaluating a small molecule MAT2A inhibitor designated as S95035 in a Phase 1 trial and Insilico Medicine has a small molecule MAT2A inhibitor in IND-enabling studies.

For IDE161, we are not aware of any other clinical-stage therapies targeting PARG. Several companies are conducting preclinical research to develop PARG inhibitors, including Nodus Oncology, SynRx, 858 Therapeutics and Satya Pharma Innovations.

For GSK101 (IDE705), Artios Pharma is developing two clinical-stage therapies targeting Pol Theta, both in Phase 1/2 studies. Additionally, Repare Therapeutics and Breakpoint Therapeutics have Pol Theta inhibitors in IND-enabling studies.

For our preclinical pipeline of synthetic lethality therapeutics, potential competition includes established companies as well as earlier-stage emerging biotechnology companies. Multiple established companies have been involved with research and development in synthetic lethality, such as AstraZeneca (Lynparza), Pfizer (Talzenna), GSK (Zejula) and Roche. Additionally, several other early-stage companies, including 858 Therapeutics, Anticancer Bioscience, Artios, Breakpoint Therapeutics, FoRx Therapeutics, Repare Therapeutics, Ryvu Therapeutics, Tango, Vividion, Xpose, and Eikon Therapeutics.

Development decisions and data from clinical trials of our competitors may adversely impact clinical development of our product candidates, and may additionally or alternatively have a material adverse impact on our financial condition or business prospects.

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. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic, including branded generic, products. As a result, obtaining market acceptance of, and 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.

In some cases we may also develop diagnostics to enable relevant biomarker screening for clinical and commercial purposes in connection with our product candidates. If not already commercially available, we anticipate working in collaboration with diagnostic companies for this development, and we will face competition from other companies in establishing these collaborations. 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.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, coverage, reimbursement and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competing products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

We expect to expand our development and regulatory capabilities and potentially implement sales and distribution capabilities, and as a result, we will need to increase the size of our organization, and we may experience difficulties in managing growth.

As of December 31, 2023, we had 124 employees. We will need to continue to expand our managerial, operational, finance and other resources in order to manage our operations and clinical trials, continue our development activities, submit for regulatory approval and, if approved, commercialize our product candidates or any future product candidates. Our management and personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our growth strategy requires that we:

- manage our preclinical studies and clinical trials effectively;
- identify, recruit, retain, incentivize and integrate additional employees, including sales personnel;
- manage our internal development and operational efforts effectively while carrying out our contractual obligations to third parties; and
- continue to improve our operational, financial and management controls, reports systems and procedures.

There is no assurance that any of these increases in scale, expansion of personnel, equipment, software and computing capacities, or process enhancements will be successfully implemented, or that we will have adequate space in our laboratory facilities to accommodate such required expansion.

We currently have no sales organization. If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell any products effectively, if approved, or generate product revenue.

We currently do not have a marketing or sales organization. In order to commercialize any product, if approved, in the United States and foreign jurisdictions, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. In advance of any of our product candidates receiving regulatory approval, we expect to establish a sales organization with technical expertise and supporting distribution capabilities to commercialize each such product candidate, which will be expensive and time-consuming. We have no prior experience in the marketing, sale and distribution of pharmaceutical products, and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. Under our GSK Collaboration Agreement, GSK will be responsible for commercialization of any Pol Theta or WRN products. We may choose to collaborate with additional third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our product candidates. If we are not successful in commercializing products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

If we fail to attract and retain senior management and key scientific personnel, our business may be materially and adversely affected.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management, particularly our President and Chief Executive Officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals could delay or prevent the successful development of any products, initiation or completion of our planned clinical trials or the commercialization of our product candidates or any other product candidates.

Competition for qualified personnel in the biotechnology and biopharmaceutical fields is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and if we initiate commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all. In addition, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output.

Our employees and independent contractors, including principal investigators, consultants, collaborators, service providers and other vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations.

We are exposed to the risk that our employees and independent contractors, including principal investigators, consultants, collaborators, service providers and other vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or other unauthorized activities that violate: the laws and regulations of the FDA and other similar regulatory bodies, including those laws that require the reporting of true, complete and accurate information to such regulatory bodies; manufacturing standards; U.S. federal and state healthcare fraud and abuse laws, data privacy and security laws and other similar non-U.S. laws; or laws that require the true, complete and

accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third-parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our business, financial condition, results of operations and prospects.

Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product candidates and other hazardous compounds. We and any third-party manufacturers and suppliers we engage are subject to numerous federal, state and local environmental, health and safety laws, regulations and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination, which could cause an interruption of our research and development efforts, commercialization efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products.

Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. 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 and pollution insurance to cover us for certain biological or hazardous waste exposure and contamination situations, this insurance may not provide adequate coverage against potential liabilities. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We attempt to distribute our technology, biology, execution and financing risks across a range of therapeutic classes, disease states, programs and technologies. Due to the significant resources required for the development of our broad portfolio of programs, and depending on our ability to access capital, we must make certain risk assessments and prioritize development of certain product candidates. Moreover, we may expend our limited resources to pursue a particular product candidate and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Our organization is committed to a broad approach to precision medicine that seeks to maximize our integrated biomarker and small molecule drug discovery capabilities. Our current portfolio consists of multiple programs, extending across multiple classes of precision medicine, including direct targeting of oncogenic pathways and synthetic lethality. Together, these programs require significant capital investment. The directly targeted therapy programs are at various stages of preclinical and early clinical development, and our synthetic lethality programs are in the target identification, validation, lead optimization, and early clinical stages of development. We seek to maintain a process of prioritization and resource allocation to maintain an optimal balance between advancing and expanding our synthetic lethality and direct targeting programs. Because we have limited financial and managerial resources, we focus on specific product candidates, indications and discovery programs. As a result, we may forgo or delay pursuit of opportunities with other product candidates that could have had greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaborations, licenses and other similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Furthermore, as our programs progress, we or others may determine: that certain of our risk allocation decisions were incorrect or insufficient; that we made platform level technology mistakes; that individual programs or our approach to synthetic lethality or precision medicine in general has technology or biology risks that were unknown or underappreciated; that our choices on how to build our organizational infrastructure to drive our expansion will result in an inability to manufacture our products for clinical trials or otherwise impede our manufacturing capabilities; or that we have allocated resources in such a way that large investments are not recovered and capital allocation is not subject to rapid re-direction. All of these risks may relate to our current or future precision medicine programs or companion diagnostics, and in the event material decisions in any of these areas turn out to have been incorrect or under-optimized, we may experience a material adverse impact on our business, financial condition, results of operations and prospects.

Public health outbreaks, epidemics or pandemics (such as the COVID-19 pandemic) may materially and adversely affect our business and operations.

The COVID-19 pandemic previously adversely affected, and the COVID-19 pandemic or other actual or threatened public health outbreaks, epidemics, or pandemics may in the future adversely affect, among other things, our research and development efforts, clinical trial operations, manufacturing and supply chain operations, administrative personnel, third-party service providers, and business partners.

While the COVID-19 pandemic did not materially adversely affect our business operations during the twelve months ended December 31, 2023, economic and health conditions in the United States and across most of the globe continue to change rapidly and may materially affect us economically. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, a continuing widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 or a future public health outbreak could materially affect our business and the value of our common stock. The ultimate impact of the COVID-19 pandemic or a similar public health outbreak is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material adverse effect on our business, results of operations and financial condition.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain, or deploy key leadership and other personnel, or otherwise prevent products from being developed, approved, or commercialized in a timely manner or at all, which may adversely affect our business.

The ability of the FDA and other government agencies 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 FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, including a prolonged government shutdown, or such as the European Medicines Agency following its relocation to Amsterdam and resulting staff changes, may cause significant regulatory delays and, therefore, delay our efforts to seek approvals and adversely affect our business, financial condition, results of operations, or cash flows. For example, over the last several years, the U.S. government has shut down several times, and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities.

Additionally, in response to the COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations, any resurgence of the virus or emergence of new variants may lead to further inspectional or administrative delays. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA and other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters is located in the San Francisco Bay Area, which in the past has experienced both severe earthquakes and wildfires. We do not carry earthquake insurance. Earthquakes, wildfires or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters or other facilities, that damaged critical infrastructure, such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted 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 currently are limited and are unlikely to prove adequate 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, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, the third parties on which we depend, including suppliers, contract manufacturers and CROs are similarly vulnerable to natural disasters or other sudden, unforeseen and serious adverse events. If such an event were to affect our supply chain, manufacturing arrangements or interfere with a preclinical study or clinical trial, it could have a material adverse effect on our business.

We are currently operating in a period of economic uncertainty and capital markets disruption, which has been significantly impacted by geopolitical instability due to the ongoing military conflict between Russia and Ukraine. Our business, financial condition and results of operations may be materially adversely affected by any negative impact on the global economy and capital markets resulting from the conflict in Ukraine or any other geopolitical tensions.

U.S. and global markets are experiencing volatility and disruption following the escalation of geopolitical tensions and the ongoing military conflict between Russia and Ukraine. In February 2022, a military invasion of Ukraine by Russian troops was reported. Following the invasion, the U.S. and global financial markets experienced volatility, which has led to disruptions to trade, commerce, pricing stability, credit availability and supply chain continuity globally. In response to the invasion, the United States, United Kingdom and European Union, along with others, imposed significant new sanctions and export controls against Russia, Russian banks and certain Russian individuals and may implement additional sanctions or take further punitive actions in the future. The full economic and social impact of the sanctions imposed on Russia (as well as possible future punitive measures that may be implemented), as well as the counter measures imposed by Russia, in addition to the ongoing military conflict between Ukraine and Russia and related sanctions, which could conceivably expand into the

surrounding region, remains uncertain; however, both the conflict and related sanctions have resulted and could continue to result in disruptions to trade, commerce, pricing stability, credit availability and supply chain continuity in both Europe and globally, and has introduced significant uncertainty into global markets. Such risks and disruptions may negatively impact our supply chain, manufacturing arrangements, preclinical studies, clinical trials and our access to capital markets and ability to finance operations, which could have a materially adverse impact on our results of operations, financial condition and prospects.

Risks Related to Our Dependence on Third Parties

The commercial success of our partnered product candidates in our Pol Theta and WRN programs, which are part of the GSK Collaboration Agreement, will depend in large part on the development and marketing efforts of GSK. If GSK is unable to perform in accordance with the terms of the GSK Collaboration Agreement, our potential to generate future revenue from these programs would be significantly reduced and our business would be materially and adversely harmed.

We will have limited influence and/or control over GSK's approaches to development and commercialization of any Pol Theta or WRN products. While we will have the right to receive potential milestone, profit share and royalty streams payable as GSK or its sublicensees advance development of such Pol Theta or WRN products, we are likely to have limited ability to influence GSK's development and commercialization efforts. If GSK does not perform in the manner that we expect or fulfill its responsibilities in a timely manner, or at all, the clinical development, regulatory approval and commercialization efforts related to product candidates we have licensed to GSK could be delayed or terminated. Furthermore, GSK or its licensees may elect to devote greater resources to other programs that do not relate to us or our collaboration.

If we terminate the GSK Collaboration Agreement, or any program thereunder due to a material breach by GSK, we have the right to assume the responsibility at our own expense for the development of the applicable product candidates. Assumption of sole responsibility for further development will greatly increase our expenditures, and may mean we need to limit the size and scope of one or more of our programs, seek additional funding and/or choose to stop work altogether on one or more of the affected product candidates. This could result in a limited potential to generate future revenue from such product candidates, and our business could be materially and adversely affected.

We rely on third parties to conduct certain of our preclinical studies and all of our clinical trials and intend to rely on third parties in the conduct of all of our future clinical trials. If these third parties do not successfully carry out their contractual duties, fail to comply with applicable regulatory requirements or meet expected deadlines, it may delay or prevent us from seeking or obtaining regulatory approval or commercializing our current or future product candidates.

We currently do not have the ability to independently conduct preclinical studies that comply with the regulatory requirements known as good laboratory practice, or GLP, requirements. We also do not currently have the ability to independently conduct any clinical trials. The FDA and regulatory authorities in other jurisdictions require us to comply with regulations and standards, commonly referred to as GCP, requirements for conducting, monitoring, recording and reporting the results of clinical trials, in order to ensure that the data and results are scientifically credible and accurate and that the clinical trial patients are adequately informed of the potential risks of participating in clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct GLP-compliant preclinical studies and GCP-compliant clinical trials on our product candidates properly and on time. The third parties with whom we contract for execution of our GLP-compliant preclinical studies and our GCP-compliant clinical trials play a significant role in the conduct of these studies and trials and the subsequent collection and analysis of data. These third parties are not our employees and, except for restrictions imposed by our contracts with such third parties, we have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely on these third parties to conduct our GLP-compliant preclinical studies and GCP-compliant clinical trials, we remain responsible for ensuring that each of our GLP preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

Many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. Further, some of these agreements may also be terminated by such third parties on short notice, or under certain circumstances, including our insolvency. If the third parties conducting our preclinical studies or our clinical trials do not adequately perform their contractual duties or obligations, experience significant business challenges, disruptions or failures, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our protocols or to GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties. This could be difficult, costly or impossible, and our preclinical studies or clinical trials may need to be extended, delayed, terminated or repeated. As a result, we may not be able to obtain regulatory approval in a timely fashion, or at all, for the applicable product candidate, and our business, financial position, results of operations and prospects may be adversely affected.

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

We do not own or operate manufacturing facilities and have no plans to build our own clinical or commercial scale manufacturing capabilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and related raw materials for preclinical and clinical development, as well as for commercial manufacture of any future approved products. The facilities used by third-party manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, third-party manufacturers for compliance with cGMP requirements or similar applicable foreign requirements for manufacture of drug products. If these third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other comparable foreign regulatory authorities, including requirements related to the manufacturing of high potency compounds, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. These third-party manufacturers may be delayed in their manufacture or shipment of our product candidates due to public health outbreaks, heightened geopolitical conflict, increases in inflation and interest rates, or supply chain disruptions. For example, deterioration in the relationship between the United States and the PRC may impact international trade, government spending, regional stability and macroeconomic conditions. The impact of these potential developments, including any resulting sanctions, export controls or other restrictive actions that may be imposed against governmental or other entities in, for example, the PRC, may contribute to disruption of our PRC-based third-party suppliers and instability and volatility in the global markets, which in turn could adversely impact our operations and weaken our financial results. Additionally, our ability to audit these third-party manufacturers for compliance with cGMP requirements or similar foreign requirements (where applicable) and our specifications may be hindered or delayed due to a public health outbreak or geopolitical conditions.

In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. 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, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

In addition, we may be unable to establish or renew any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- failure of third-party manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of the manufacturing agreement by the third-party;
- failure to manufacture our product according to our specifications;
- failure to manufacture our product according to our schedule or at all;

- misappropriation of our proprietary information, including our trade secrets and know-how; and
- termination or nonrenewal of the agreement by the third-party at a time that is costly or inconvenient for us.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us, particularly if the COVID-19 pandemic, geopolitical conflict and macroeconomic concerns continue or worsen.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval, and any related remedial measures may be costly or time-consuming to implement. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials used in the manufacture of our product candidates. If our current third-party manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all.

We rely on, and in the future may rely on, third-party databases and collaborations with third parties to inform patient selection and drug target identification for our existing product candidates and any future product candidates and for the supply of biomarker companion diagnostics.

We are using bioinformatics, including data analytics, biostatistics, and computational biology, to identify new target and biomarker opportunities. As part of this approach, we interrogate public and proprietary databases comprising human tumor genetic information and specific cancer-target dependency networks. We rely on these databases and data analytics for identifying or validating some of our biomarker-target relationships and access to these databases may not continue to be available publicly or through a proprietary subscription on acceptable terms.

Many of our precision medicine targeted therapeutic product candidates also rely on the availability and use of commercially available tumor diagnostics panels or data on the prevalence of our target patient population to inform the patient selection and drug target identification for our product candidates. In cases where such biomarker diagnostic is not already commercially available, we expect to establish strategic collaborations for the clinical supply and development of companion diagnostics. If these diagnostics are not able to be developed, or if commercial tumor profiling panels are not able to be updated to include additional tumor-associated genes, or if clinical oncologists do not incorporate molecular or genetic sequencing into their clinical practice, we may not be successful in developing our existing product candidates or any future product candidates.

We depend on third-party suppliers for key materials required for the production of our product candidates, and the loss of these third-party suppliers or their inability to supply us with adequate materials could harm our business.

We rely on third-party suppliers for certain materials, such as starting reagents, required for the production of our product candidates and/or for certain materials and assays, such as diagnostics, for clinical and commercial use of our product candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors that are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Additionally, the facilities to manufacture our product candidates must be the subject of a satisfactory inspection before the FDA or other regulatory authorities approve an NDA or grant a marketing authorization for the product candidate manufactured at that facility. We will depend on these third-party manufacturing partners for compliance with the FDA's requirements for the manufacture of our finished products. If our manufacturers cannot successfully manufacture material that conforms to our specifications and the FDA's and other regulatory authorities' GMP requirements, our product candidates will not be approved or, if already approved, may be subject to recalls.

Furthermore, certain of the third-party suppliers on which we rely are based in the PRC. The evolving trade dispute between the PRC and the United States has resulted in the imposition of significant tariffs on certain imports from the PRC. Any deterioration of the relationship between the United States and the PRC, or the imposition of more stringent export controls or tariffs applicable to our suppliers in the PRC, could adversely affect our ability to obtain the raw materials required for the manufacture of our product candidates, and therefore adversely affect our business, financial condition, results of operations and prospects.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the possibility of a breach of the manufacturing agreements by the third parties because of factors beyond our control;
- the possibility of termination or nonrenewal of the agreements by the third parties before we are able to arrange for a qualified replacement third-party manufacturer; and
- the possibility that we may not be able to secure a manufacturer or manufacturing capacity in a timely manner and on satisfactory terms in order to meet our manufacturing needs.

Any of these factors could cause the delay of approval or commercialization of any products, cause us to incur higher costs or prevent us from commercializing any products successfully. Furthermore, if any of our product candidates are approved and contract manufacturers fail to deliver the required commercial quantities of finished product on a timely basis and at commercially reasonable prices, and we are unable to find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality and on a timely basis, we would likely be unable to meet demand for our products and could lose potential revenue. It may take several years to establish an alternative source of supply for our product candidates and to have any such new source approved by the FDA or any other relevant regulatory authority.

If we fail to comply with our obligations under any of our in-license agreements, we could lose license rights that are important to our business.

Our current in-license agreements or any future in-license agreements provide or may provide that we must use reasonable efforts to obtain regulatory approval for a product candidate using the licensed compound. The agreements further impose or may impose an obligation to make various milestone payments and royalty payments as well as other obligations on us. If we materially breach the terms of any in-license agreement and fail to cure such breach within the period allowed, then the licensor may terminate the license agreement. In addition, the licensor has or may have the right to terminate on our insolvency. If the agreement is terminated, then we will not be able to further develop or commercialize the licensed compound or any future related product candidates.

Furthermore, any dispute with the licensor may result in the delay or termination of the research, development or commercialization of the licensed compound or any future related product candidates, and may result in costly litigation or arbitration that diverts management attention and resources away from our day-to-day activities, which may adversely affect our business, financial condition, results of operations and prospects.

Our existing collaboration arrangements and any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our product candidates or diagnostics associated with such product candidates.

In the future, we may seek to enter into additional collaboration arrangements for the development or commercialization of certain of our product candidates or diagnostics for biomarkers associated with our product candidates. To the extent that we decide to enter into additional collaboration agreements in the future, we may face significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time-consuming to negotiate, document, implement and maintain and challenging to manage. We may not be successful in our efforts to prudently manage our existing collaborations or to enter new ones should we chose to do so. The terms of new collaborations or other arrangements that we may establish may not be favorable to us.

The success of our collaboration arrangements, including our GSK Collaboration Agreement, will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include risks that:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to their acquisition of competitive products or their internal development of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our current or future product candidates or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, which may result in a need for additional capital to pursue further development or commercialization of the applicable current or future product candidates;
- collaborators may own or co-own intellectual property covering products that result from our collaboration with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property;
- disputes may arise with respect to the ownership or inventorship of any intellectual property developed pursuant to our collaborations; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Risks Related to Commercialization of Our Product Candidates

Even if we receive regulatory approval for any product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions on marketing or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

If one of our product candidates is approved, it will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

For example, the FDA or similar foreign regulatory authorities may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time-consuming post-approval studies, post-market surveillance or clinical trials to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient

registries and other risk minimization tools. Similar requirements may apply in foreign jurisdictions. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, AE reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs or similar foreign requirements and GCP requirements for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our product candidates, including AEs of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- suspension or withdrawal of regulatory approval, restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or additional clinical trials;
- suspension of any of our ongoing clinical trials;
- fines, restitutions, disgorgement of profits or revenues, warning letters, untitled letters or holds on clinical trials;
- refusal by the FDA or comparable foreign regulatory authorities to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

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

In addition, if any of our product candidates is approved, our product labeling, advertising and promotion will be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. Similar requirements may apply in foreign jurisdictions. If we receive marketing approval for a product, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

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

The incidence and prevalence of our target patient populations are estimations. If the market opportunities for our product candidates are smaller than we estimate, our business, financial position, results of operations and prospects may be harmed.

We rely on various sources, including published literature and public or proprietary databases, to ascertain an estimate of the number of patients having particular genetic alterations, such as mutations, deletions or fusions, across various tissue-type specific indications. The determinable prevalence may vary depending on the source and quality of the underlying data and in some cases, insufficient data or poorly curated data may impact our ability to accurately estimate the prevalence of our target patient populations for each indication and in the aggregate across multiple indications both in the clinical trial setting, as well as in the commercial setting, if our product is approved. If the market opportunities for our product candidates are smaller than we estimate, our business, financial position, results of operations and prospects may be harmed. In addition, upon treatment with our product candidates, patients may have or develop resistance to our product candidates, reducing the addressable patient population and the duration of treatment.

Even if our product candidates or any future product candidate obtains regulatory approval, they may fail to achieve the broad degree of physician and patient adoption and use necessary for commercial success.

Even if our product candidates or any future product candidate receives FDA or other regulatory approvals, the commercial success of any product will depend significantly on the broad adoption and use of the resulting product by physicians and patients for approved indications. For a variety of reasons, including among other things, competitive factors, pricing or physician preference, reimbursement by insurers, the degree and rate of physician and patient adoption of any products, if approved, will depend on a number of factors, including:

- the clinical indications for which the product is approved and patient demand for approved products that treat those indications;
- the safety and efficacy of our product as compared to other available therapies;
- the availability of companion diagnostics for biomarkers associated with our product candidates or any other future product candidates;
- the time required for manufacture and release of our products;
- the availability of coverage and adequate reimbursement from managed care plans, private insurers, government payors (such as Medicare and Medicaid) and other third-party payors for any of our products that may be approved;
- acceptance by physicians, operators of hospitals and clinics and patients of the product as a safe and effective treatment;
- physician and patient willingness to adopt a new therapy over other available therapies for a particular indication;
- proper training and administration of our product candidates by physicians and medical staff;
- patient satisfaction with the results and administration of our product candidates and overall treatment experience, including, for example, the convenience of any dosing regimen;
- the cost of treatment with our product candidates in relation to alternative treatments and reimbursement levels, if any, and willingness to pay for the product, if approved, on the part of insurance companies and other third-party payors, physicians and patients;
- the prevalence and severity of side effects;
- limitations or warnings contained in the FDA-approved labeling for our products or similar foreign requirements;
- the willingness of physicians, operators of hospitals and clinics and patients to utilize or adopt our products as a solution;
- any FDA requirement for a REMS or similar foreign risk mitigation measures;
- the effectiveness of our sales, marketing and distribution efforts;
- adverse publicity about our products or favorable publicity about competitive products; and
- potential product liability claims.

We cannot assure you that our current or future product candidates, if approved, will achieve broad market acceptance among physicians and patients. Any failure by our product candidates that obtain regulatory approval to achieve market acceptance or commercial success would adversely affect our business, financial condition, results of operations and prospects.

The successful commercialization of any products will depend in part on the extent to which governmental authorities, private health insurers, managed care plans and other third-party payors provide coverage, adequate reimbursement levels and implement pricing policies favorable for any products. Failure to obtain or maintain coverage and adequate reimbursement for products, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The availability of coverage and adequacy of reimbursement by governmental healthcare programs, such as Medicare and Medicaid, private health insurers, managed care plans and other third-party payors are essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates that receive FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement by third-party payors for our products will have an effect on our ability to successfully commercialize our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication, or place products at certain formulary levels that result in lower reimbursement levels and higher cost-sharing obligation imposed on patients. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service. As a result, the coverage determination process will often require us to provide scientific and clinical support for the use of our products to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. We cannot be sure that coverage will be available for any product that we may develop. A decision by a third-party payor not to cover any of our product candidates could reduce physician utilization of our products once approved and adversely affect our business, financial condition, results of operations and prospects.

Assuming there is coverage for our products, if any, by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our products, pricing of other third-party therapeutics may limit the amount we will be able to charge for our products. These third-party payors may deny or revoke the reimbursement status of our products, if approved, or establish prices for our products at levels that are too low to enable us to realize an appropriate return on our investment. If reimbursement is not available, is decreased or eliminated in the future, or is available only at limited levels, we may not be able to successfully commercialize our products and may not be able to obtain a satisfactory financial return on our products.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries has and will continue to put pressure on the pricing and usage of our products, if any. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our products. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products, and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of any products.

We face an inherent risk of product liability as a result of the planned clinical trials of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranty. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of any products. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for any products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to clinical trial participants or patients;
- regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize any products.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of any products. Although we have obtained and intend to maintain product liability insurance covering our clinical trials, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient funds to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. If and when we obtain approval for marketing any of our product candidates, we intend to expand our insurance coverage to include the sale of such product candidate; however, we may be unable to obtain this liability insurance on commercially reasonable terms or at all.

Risks Related to Intellectual Property

Our success depends on our ability to obtain and maintain protection for our intellectual property and our proprietary technologies and to avoid infringing the rights of others.

Our commercial success depends in part on our ability to obtain and maintain patent, trademark, trade secret and other intellectual property protection for our product candidates and proprietary technologies as well as our ability to operate without infringing upon the proprietary rights of others.

We and our licensors have applied, and we intend to continue applying, for patents covering important aspects of our product candidates, proprietary technologies and their uses as we deem appropriate. However, the patent prosecution process is expensive, time-consuming and complex, and we may not be able to apply for patents on certain aspects of our current or future product candidates and proprietary technologies in a timely fashion, at a reasonable cost, in all jurisdictions, or at all. If we cannot adequately obtain, maintain and enforce our intellectual property rights and proprietary technology, competitors may be able to use our technologies or the goodwill we have acquired in the marketplace and erode or negate any competitive advantage we may have and our ability to compete, which could harm our business and ability to achieve profitability and/or cause us to incur significant expenses. Failure to obtain, maintain and/or enforce intellectual property rights necessary to our business and failure to protect, monitor and control the use of our intellectual property rights could negatively impact our

ability to compete and cause us to incur significant expenses. The intellectual property laws and other statutory and contractual arrangements in the United States and other jurisdictions we depend upon may not provide sufficient protection in the future to prevent the infringement, use, violation or misappropriation of our patents, trademarks, data, technology and other intellectual property rights and products by others, and may not provide an adequate remedy if our intellectual property rights are infringed, misappropriated or otherwise violated by others.

Our patent applications cannot be enforced against third parties practicing the inventions claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the invention as claimed. The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators or licensors will be successful in protecting our product candidates and proprietary technologies by obtaining and defending patents. These risks and uncertainties include the following:

- the United States Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other requirements during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained or licensed patents that will limit, interfere with or eliminate our ability to make, use and sell our product candidates;
- other parties may have designed or may design around our claims or developed technologies that may be related or competitive to our platform, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications, either by claiming the same methods or devices or by claiming subject matter that could dominate our patent position;
- any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any product candidates that we may develop;
- because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates and proprietary technologies;
- an interference proceeding can be provoked by a third-party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications for any application with an effective filing date before March 16, 2013;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

We rely in part on our portfolio of issued and pending patent applications in the United States and other countries to protect our intellectual property and competitive position. The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. It is possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. If we fail to timely file for patent protection in any jurisdiction, we may be precluded from doing so at a later date. And 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, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in any of our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Moreover, should we become a licensee of a third-party's patents or patent applications, depending on the terms of any future in-licenses to which we may become a party, we may not have the right to control the preparation, filing and prosecution of patent

applications, or to maintain or enforce the patents, covering technology in-licensed from third parties. Therefore, these patents and patent applications may not be prosecuted, maintained and/or enforced in a manner consistent with the best interests of our business. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products or services. Accordingly, we cannot provide any assurances about which of our patent applications will issue, the breadth of any resulting patent, whether any of the issued patents will be found to be infringed, invalid or unenforceable or will be threatened or challenged by third parties, that any of our issued patents have, or that any of our currently pending or future patent applications that mature into issued patents will include, claims with a scope sufficient to protect our products and services. The coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. We cannot offer any assurances that the breadth of our granted patents will be sufficient to stop a competitor from developing, manufacturing and commercializing a product or technologies in a non-infringing manner that would be competitive with one or more of our products or technologies, or otherwise provide us with any competitive advantage. Further, our patents or the patent rights that we license from others, may be challenged in the courts or patent offices in the United States and abroad. Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, *inter partes* review, nullification or derivation action or similar proceedings in court or before patent offices in the United States or foreign jurisdictions for a given period after allowance or grant, during which time third parties can raise objections against such patents. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, all of which could limit our ability to stop others from using or commercializing similar or identical product candidates, or limit the duration of the patent protection of our product candidates. In addition, defending such challenges in such proceedings may be costly. Further, there can be no assurance that we will have adequate resources to enforce our patents. Thus, any patents that we may own may not provide the anticipated level of, or any, protection against competitors. Furthermore, an adverse decision may result in a third-party receiving a patent right sought by us, which in turn could affect our ability to develop, manufacture or commercialize our products or technologies.

The degree of future protection for our patent rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates;
- any of our pending patent applications will issue as patents;
- any of the patents we own or license will be found to ultimately be valid and enforceable if subject to challenge;
- we were the first to make the inventions covered by each of our patents and pending applications;
- we were the first to file patent applications for these inventions;
- we will be able to successfully manufacture and commercialize our products on a substantial scale, if approved, before relevant patents we may have expire;
- any patents issued to us or our licensors will provide a basis for an exclusive market for any commercially viable products we may develop or will provide us with any competitive advantages;
- we will develop or in-license additional proprietary technologies that are patentable;
- the patents of others will not have an adverse effect on our business;
- others will not develop, manufacture and/or commercialize similar or alternative products or technologies that do not infringe our patents;
- our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; and
- our commercial activities or products will not infringe upon the patents of others.

Our ability to enforce patent rights also depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. Moreover, it may be difficult or impossible to obtain evidence of

infringement in a competitor's or potential competitor's product or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful. If we initiate lawsuits to protect or enforce our patents, or litigate against third-party claims, such proceedings would be expensive and would divert the attention of our management and technical personnel.

Where we obtain licenses from or collaborate with third parties, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties, or such activities, if controlled by us, may require the input of such third parties. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could have a material adverse impact on our competitive position, business, financial condition, results of operations and prospects.

Some of our patents and patent applications may in the future be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products, services and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us.

Furthermore, our owned and in-licensed intellectual property rights may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our owned and in-licensed patent rights and technology was funded in part by the U.S. government. As a result, the government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations, and prospects.

Further, we rely on a combination of contractual provisions, confidentiality procedures and patent, trademark, copyright, trade secret and other intellectual property laws to protect the proprietary aspects of our products, brands, technologies, trade secrets, know-how and data. These legal measures afford only limited protection, and competitors or others may gain access to or use our intellectual property rights and proprietary information. Our success will depend, in part, on preserving our trade secrets, maintaining the security of our data and know-how and obtaining, maintaining and enforcing other intellectual property rights. We may not be able to obtain, maintain and/or enforce our intellectual property or other proprietary rights necessary to our business or in a form that provides us with a competitive advantage.

If we fail to obtain sufficient patent or other intellectual property protection for our product candidates or proprietary technologies or if we lose any patent or other intellectual property protection for our product candidates or proprietary technologies, our business, financial condition, results of operations and prospects could be adversely affected.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation for patents covering our product candidates, our business may be materially harmed, and in any case, the terms of our patents may not be sufficient to effectively protect our product candidates and business.

Patents have a limited term. In most countries, including the United States, the expiration of a patent is generally 20 years after its first effective non-provisional filing date. However, depending upon the timing, duration and specifics of FDA marketing approval of darovasertib, IDE397, our other product candidates or any future product candidates, one or more of any U.S. patents we may be issued or have licensed may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments.

The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA-approved product as compensation for the patent term lost during the FDA regulatory review

process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, 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 competitive position, business, financial condition, results of operations, and prospects could be harmed, possibly materially.

If there are delays in obtaining regulatory approvals or other additional delays, the period of time during which we can market our product candidates under patent protection could be further reduced. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. Once the patent term has expired, we may be open to competition from similar or generic products. The launch of a generic version of one of our products in particular would be likely to result in an immediate and substantial reduction in the demand for that product, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process to maintain patent applications and issued patents. In addition, periodic maintenance fees, renewal fees, annuity fees and various other government fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent and/or applications and any patent rights we may obtain in the future. While an unintentional lapse of a patent or patent application can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance with these requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our products or services, we may not be able to stop a competitor from marketing products or services that are the same as or similar to our products or services, which would have a material adverse effect on our business, financial condition and results of operations. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by others, and the patent protection, prosecution and enforcement for some of our product candidates may be dependent on our licensors.

We currently are reliant upon licenses of certain intellectual property rights and proprietary technology from third parties that are important or necessary to the development of our proprietary technology, including technology related to our product candidates. For example, we rely on our exclusive license agreement with Novartis for the clinical development of darovasertib and our option and license agreement with CRT for the clinical development of PARG inhibitors. These licenses, and other licenses we may enter into in the future, may not provide adequate rights to use such intellectual property rights and proprietary technology in all relevant fields of use or in all territories in which we may wish to develop or commercialize technology and product candidates in the future. Licenses to additional third-party proprietary technology or intellectual property rights that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms. In that event, we may be required to expend significant time and resources to redesign our proprietary technology or product candidates or to develop or license replacement technology, which may not be feasible on a technical or commercial basis. If we are unable to do so, we may not be able to develop and commercialize technology and product candidates in fields of use and territories for which we are not granted rights pursuant to such licenses, which could harm our business, financial condition, results of operations and prospects significantly. Third-party patents may exist which might be enforced against our current or future product candidates, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

In some circumstances, we may not have the right to control the preparation, filing, prosecution and enforcement of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, some of our agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that our licensors or collaborators will prosecute, maintain, enforce and defend such intellectual property rights in a manner consistent with the best interests of our business, including by taking reasonable measures to protect the confidentiality of know-how and trade secrets, or by paying all applicable prosecution and maintenance fees related to intellectual property registrations for any of our product candidates. We also cannot be certain that our licensors have drafted or prosecuted the patents and patent applications licensed to us in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. This could cause us to lose rights in any applicable intellectual property that we in-license, and as a result our ability to develop and commercialize product candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products.

Our current licenses impose, and our future licenses likely will impose, various royalty payments, milestones, and other obligations on us. If we fail to comply with any of these obligations, we may be subject to liability, including the payment of damages, and the licensor may have the right to terminate the license. Termination by the licensor would cause us to lose valuable rights, and could prevent us from developing and commercializing our product candidates and proprietary technologies. Furthermore, if any current or future licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products similar or identical to our planned products. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in product candidates that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize product candidates, we may be unable to achieve or maintain profitability. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties (potentially including our competitors) to receive licenses to a portion of the intellectual property rights that are subject to our existing licenses. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

We may fail to comply with any of our obligations under existing or future agreements pursuant to which we license or have otherwise acquired intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business.

We are party to various agreements that we depend on to operate our business, including intellectual property rights relating to darovasertib, in particular, our agreement with Novartis. Our rights to use currently licensed intellectual property, or intellectual property to be licensed in the future, are or will be subject to the continuation of and our compliance with the terms of these agreements. These agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations which could lead to disputes, including but not limited to those regarding:

- the scope of rights granted under the license agreement;
- the extent to which our proprietary technology and product candidates infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us or our counterparties, alone or jointly;
- the scope and duration of our payment obligations;
- the priority of invention of patented technology;
- rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

The resolution of any contractual interpretation dispute that may arise, if unfavorable to us, could have a material adverse effect on our business, financial condition, results of operations and prospects. Such resolution could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, increase what we believe to be our financial or other obligations under the relevant agreement or decrease the third-party's financial or other obligations under the relevant agreement.

Furthermore, if disputes over intellectual property rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current license agreements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. If we fail to comply with our obligations under current or future license agreements, these agreements may be terminated or the scope of our rights under them may be reduced and we might be unable to develop, manufacture or market any product that is licensed under these agreements. We are generally also subject to all of the same risks with respect to protection of intellectual property that we may license as we are for intellectual property that we own, which are described herein. If we or any of our current or future licensors fail to adequately protect this intellectual property, our ability to commercialize product candidates could suffer.

We may become subject to third-party claims alleging infringement, misappropriation or violation of such third-party's patents or other intellectual property rights and/or third-party claims seeking to invalidate our patents, which could require us to spend significant time and money and, if successfully asserted against us, could delay or prevent us from developing, manufacturing and selling our products.

Our commercial success depends significantly on our ability to develop, manufacture or commercialize our products and product candidates without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. However, our research, development and commercialization activities may nonetheless be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Claims by third parties that we infringe their intellectual property rights may result in liability for damages or prevent or delay our developmental and commercialization efforts. We cannot assure you that our operations do not, or will not in the future, be found to infringe existing or future patents.

Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates or impair our competitive position. As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, reexaminations, *inter partes* review proceedings and post-grant review proceedings before the USPTO and/or corresponding foreign patent offices, and companies in the industry have used these proceedings to gain a competitive advantage. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. For example, we are aware of an international patent application published as PCT WO 2017/096165 A1. If a patent issues from such patent application with claims similar to those published, our ability to commercialize a product candidate for our MAT2A program may be adversely affected if we do not obtain a license under such patent.

Furthermore, 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 and can involve other factors such as expert opinion. Our analysis of these issues, including interpreting the relevance or the scope of claims in a patent or a pending application, determining applicability of such claims to our proprietary technologies or product candidates, predicting whether a third-party's pending patent application will issue with claims of relevant scope, and determining the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties.

Additionally, patent applications in the United States and elsewhere are typically published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain U.S. applications that will not be filed outside the United States can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product

candidates or the use of our product candidates. These applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to make, use or sell our products. As a result, we may be unaware of third-party patents that may be infringed by commercialization of darovasertib, IDE397 or our other product candidates, and cannot be certain that we were the first to file a patent application related to a product candidate or proprietary technology. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect. We may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of our product candidates.

Further, we may be required to indemnify future collaboration partners against claims of infringement, misappropriation, or other violations of intellectual property rights. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If a patent infringement suit were brought against us, we could be forced, including by court order to stop or delay development, manufacturing and/or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or in order to avoid potential claims, we may choose to seek, or be required to seek, a license from the third-party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on commercially reasonable terms, or at all, in which event our business would be materially and adversely affected. Even if we were able to obtain a license, we may be unable to maintain such licenses and the rights may be nonexclusive, which could give our competitors access to the same intellectual property.

Although no third-party has asserted a claim of patent infringement against us as of December 31, 2023, others may hold proprietary rights that could prevent darovasertib, IDE397, our other product candidates or any future product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidates or proprietary technologies could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe or attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be infringing, and require us to obtain a license to manufacture or market darovasertib, IDE397, our other product candidates or any future product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be time-consuming and a substantial diversion of management and employee resources from our business. Even if we believe such claims are without merit, we cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Even if such licenses are available, we could incur substantial costs related to royalty payments for licenses obtained from third parties, which could negatively affect our gross margins, and the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. In addition, we cannot be certain that we could redesign our product candidates or proprietary technologies to avoid infringement, if necessary, or on a cost-effective basis. If we were to challenge the validity of any such third-party U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. We will have similar burdens to overcome in foreign courts in order to successfully challenge a third-party claim of patent infringement. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing darovasertib, our other product candidates or any future product candidates, until the asserted patent expires or is held finally invalid or not infringed in a court of law. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity or the disclosure of confidential information, and the perceived value of our product candidates or intellectual property could be diminished correspondingly.

Additionally, our collaborators or any third parties with which we collaborate in the future, may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. Also, we may be obligated under our agreements with our collaborators, licensors, suppliers and others to indemnify and hold them harmless for damages arising from intellectual property infringement by us. Any of the foregoing could harm our competitive position, business, financial condition, results of operations, and prospects.

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

Third parties, including our competitors may currently, or in the future, infringe, misappropriate or otherwise violate our issued patents or other intellectual property rights or those of our licensors. To prevent infringement or unauthorized use, we may be required to file lawsuits or initiate other proceedings to protect or enforce our patents or other intellectual property rights, which can be expensive, time-consuming and unsuccessful. However, the steps we have taken, and are taking, to protect our proprietary rights may not be adequate to enforce our rights as against such infringement, misappropriation or violation of our intellectual property rights. In certain circumstances it may not be practicable or cost-effective for us to enforce our intellectual property rights fully, particularly in certain developing countries or where the initiation of a claim might harm our business relationships. We may also be hindered or prevented from enforcing our rights with respect to a government entity or instrumentality because of the doctrine of sovereign immunity. Our ability to enforce our patent or other intellectual property rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products or technologies. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or technologies. Thus, we may not be able to detect unauthorized use of, or take appropriate steps to enforce, our intellectual property rights. Any inability to meaningfully enforce our intellectual property rights could harm our ability to compete and reduce demand for our products and product candidates.

In addition, in a patent infringement proceeding, a court or administrative tribunal may decide that a patent we own or in-license is not valid, is unenforceable and/or is not infringed. If we or any of our collaborators or potential future collaborators, were to initiate legal proceedings against a third-party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. Similar mechanisms for challenging the validity and enforceability of a patent exist in foreign patent agencies. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and could result in the revocation, cancellation, or amendment of our patents or those of our licensors. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. A court may decide that a patent or other intellectual property right of ours is invalid or unenforceable, in whole or in part, construe the patent's claims or other intellectual property narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents or other intellectual property do not cover the technology in question. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we could lose at least part, and perhaps all, of the patent protection on an affected product candidate. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

Additionally, interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO, or equivalent actions brought in foreign jurisdictions, may be necessary to determine the priority of invention with respect to our patents or patent applications or those of our licensors. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. An unfavorable outcome could require us to cease using the covered technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. These and other uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. Any of the foregoing could harm our business, financial condition, results of operations and prospects. Even if our patents or other intellectual property rights are found to be valid and infringed, a court may refuse to grant injunctive relief against the infringer and instead grant us monetary damages and/or ongoing royalties. Such monetary compensation may be insufficient to adequately offset the damage to our business caused by the infringer's competition in the market. An adverse result in any litigation or administrative proceeding could put one or more of our patents or other intellectual property rights at risk of being invalidated or interpreted narrowly, which could adversely affect our competitive business position, financial condition and results of operations.

We may be subject to claims that we or our employees, consultants, advisors or other third parties have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

We may be subject to claims that our employees or consultants have wrongfully used for our benefit or disclosed to us confidential information of third parties. As is common in the biotechnology and biopharmaceutical industries, in addition to our employees, we engage the services of consultants, advisors and other third parties to assist us in the development of our product candidates. Many of these individuals, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or biopharmaceutical companies including our competitors or potential competitors. Some of these employees, consultants and contractors, may have executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment or engagement. Although we try to ensure that individuals working for or collaborating with us do not use the intellectual property rights, proprietary information or know-how of others in their work for us, and do not perform work for us that is in conflict with their obligations to another employer or any other entity, we may become subject to claims that we, our employees, consultants, advisors or other third parties have, inadvertently or otherwise, misappropriated the intellectual property, including know-how, trade secrets or other information proprietary to their former or current employers or clients. We may also be subject to claims that patents and applications we have filed to protect inventions of our employees, consultants, advisors or other third parties, even those related to one or more of our product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, which could adversely affect our competitive position, business, financial condition, results of operations, and prospects. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team.

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

We may also be subject to claims that our former employees, contractors or collaborators, or other third parties have an ownership interest in our current or future patents, patent applications, or other intellectual property rights, including as an inventor or co-inventor. We may be subject to ownership or inventorship disputes in the future arising, for example, from conflicting obligations of employees, consultants or others who were or are involved in developing our products or product candidates. Although it is our policy to require our employees and our personnel who may be involved in the development of intellectual property to execute agreements assigning such inventions, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. The assignment of intellectual property may not be self-executing and despite such agreement, such inventions may become assigned to third parties. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. We

may be subject to claims that former employees, consultants, advisors or other third parties have an ownership interest in our patents or other 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 rights, and other owners may be able to license their rights to other third parties, including our competitors. Such an outcome could have a material adverse effect on our business. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

In addition, we may face claims by third parties challenging ownership interest in or inventorship of intellectual property rights we regard as our own, based on claims that our agreements with employees, consultants, advisors or other third parties obligating them to assign intellectual property to us are ineffective or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such intellectual property. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against these and other claims challenging inventorship or ownership and it may be necessary or we may desire to obtain a license to such third-party's intellectual property rights to settle any such claim; however, there can be no assurance that we would be able to obtain such license on commercially reasonable terms, if at all. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. A court could prohibit us from using technologies, features or other intellectual property rights that are essential to our products or technologies, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of another person or entity, including another or former employers. An inability to incorporate technologies, features or other intellectual property rights that are important or essential to our products or product candidates could have a material adverse effect on our business, financial condition, results of operations, and competitive position, and may prevent us from developing, manufacturing and/or commercializing our products or technologies. In addition, we may lose valuable intellectual property rights or personnel. Such an outcome could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees. Any litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent sales representatives. A loss of key personnel or their work product could hamper or prevent our ability to develop, manufacture and/or commercialize our products or services, which could materially and adversely affect our business, financial condition and results of operations.

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

In addition to patent protection, we also rely on other intellectual property rights, including protection of copyright, trade secrets, know-how, technology and/or other proprietary information that is not patentable or that we elect not to patent. Trade secrets can be difficult to protect, and some courts are less willing or unwilling to protect trade secrets. To maintain the confidentiality of our trade secrets and proprietary information, we rely heavily on confidentiality agreements with third parties, and confidential information and invention assignment agreements with employees, consultants, advisors and appropriate third parties. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes and we may not enter into such agreements with all employees, consultants and third parties who have been involved in the development of our intellectual property rights. Although we generally require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, customer or third-party with authorized access. Our security measures may not prevent an employee, consultant, advisor or other third-party from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Therefore, we may not be able to prevent the unauthorized disclosure or use of our technical knowledge or other trade secrets by such employees, consultants, advisors or third parties, despite the existence generally of these confidentiality restrictions. These agreements may not provide meaningful protection against the unauthorized use or disclosure of our trade secrets, know-how or other proprietary information in the event the unwanted use is outside the scope of the provisions of the contracts or in the event of any unauthorized use, misappropriation, or disclosure of such trade secrets, know-how, or other proprietary information. There

can be no assurances that such employees, consultants, advisors or third parties will not breach their agreements with us, that we will have adequate remedies for any breach, or that our trade secrets will not otherwise become known or independently developed by third parties, including our competitors.

Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. We may not be able to obtain adequate remedies in the event of such unauthorized use. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time-consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any breach. Even though we use commonly accepted security measures, trade secret violations are often a matter of state law in the United States, and the criteria for protection of trade secrets can vary among different jurisdictions. If the steps we have taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of our products and provision of our services, we must, at times, share trade secrets with them. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position, business, financial condition, results of operations, and prospects would be harmed. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. The exposure of our trade secrets and other proprietary information would impair our competitive advantages and could have a material adverse effect on our business, financial condition and results of operations. In particular, a failure to protect our proprietary rights may allow competitors to copy our technology, which could adversely affect our pricing and market share. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

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

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

- others may be able to make precision medicines that are similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- the patents of others may harm our business;

- we may choose not to seek patent protection for some of our proprietary technology to maintain certain trade secrets or know-how, and a third-party may subsequently file a patent covering such trade secrets or know-how;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; and
- we may not develop additional proprietary technologies that are patentable;

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

Risks Related to Government Regulation

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

In the United States, the EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private payors. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- an increase to the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and an extension the rebate program to individuals enrolled in Medicaid managed care organizations;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, executive and congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the U.S. Supreme Court's decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, led to aggregate reductions of Medicare payments to providers. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022,

unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

The American Rescue Plan Act of 2021 was also signed into law, which eliminates the statutory Medicaid drug rebate cap, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

Moreover, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law, which among other things, includes prescription drug provisions that have significant implications for the pharmaceutical industry and beneficiaries, including extending enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025, allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the drug price negotiation program is currently subject to legal challenges. For that and other reasons, it is currently unclear how the IRA will be effectuated. The implementation of cost containment measures, including the prescription drug provisions under the IRA, as well as other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved. Complying with any new legislation and regulatory changes could be time-intensive and expensive, resulting in a material adverse effect on our business.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices. These reforms could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under any U.S. federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal civil and criminal false claims and civil monetary penalties laws, including the civil False Claims Act, which prohibit, among other things, including through civil whistleblower or qui tam actions, individuals or entities from knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. Pharmaceutical manufacturers can cause false claims to be presented to the U.S. federal government by engaging in impermissible marketing practices, such as the off-label promotion of a product for an indication for which it has not received FDA approval. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the Health Insurance Portability and Accountability Act, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, 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 U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation;
- the Federal Food Drug or Cosmetic Act, or FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (nurse practitioners, certified nurse anesthetists, physician assistants, clinical nurse specialists, anesthesiology assistants and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives;
- the U.S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U.S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office, and foreign political parties or officials thereof; and
- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. 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.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The regulatory environment surrounding information security, data collection and privacy is increasingly demanding. We are subject to numerous U.S. federal and state laws and non-U.S. regulations governing the protection of personal and confidential information of our clinical patients, clinical investigators, employees and vendors/business contacts, including in relation to medical records, credit card data and financial information. Outside the United States, an increasing number of laws, regulations, and industry standards apply to data privacy and security. For example, in Europe, European Union General Data Protection Regulation, or GDPR, went into effect in May 2018, implementing more stringent requirements in relation to our use of personal data. The GDPR applies to any company established in the European Economic Area, or EEA, as well as to those outside the EEA if they collect and use personal data in connection with the offering of goods or services to individuals in the EEA or the monitoring of their behavior. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the U.S., and the efficacy and longevity of current transfer mechanisms between the EU and the U.S. remains uncertain, and the efficacy and longevity of current transfer mechanisms between the EEA, and the United States remains uncertain. Case law from the Court of Justice of the European Union, or CJEU, states that reliance on the standard contractual clauses - a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism - alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case-by-case basis. On October 7, 2022, President Biden signed an Executive Order on 'Enhancing Safeguards for United States Intelligence Activities' which introduced new redress mechanisms and binding safeguards to address the concerns raised by the CJEU in relation to data transfers from the EEA to the United States and which formed the basis of the new EU-US Data Privacy Framework, or DPF, as released on December 13, 2022. The European Commission adopted its Adequacy Decision in relation to the DPF on July 10, 2023,

rendering the DPF effective as a GDPR transfer mechanism to U.S. entities self-certified under the DPF. The DPF also introduced a new redress mechanism for EU citizens which addresses a key concern in the previous CJEU judgments and may mean transfers under standard contractual clauses are less likely to be challenged in future. We currently rely on the EU standard contractual clauses and the UK Addendum to the EU standard contractual clauses, as relevant, to transfer personal data outside the EEA and the UK, including to the United States, with respect to both intragroup and third party transfers. We expect the existing legal complexity and uncertainty regarding international personal data transfers to continue. In particular, we expect the DPF Adequacy Decision to be challenged and international transfers to the United States and to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. As a result, we may have to make certain operational changes and we will have to implement revised standard contractual clauses and other relevant documentation for existing data transfers within required time frames.

Further, from January 1, 2021, companies have had to comply with the GDPR and also the UK data protection regime, which imposes separate but similar obligations to those under the GDPR. The UK GDPR mirrors the fines under the GDPR (e.g., fines up to the greater of €20 million (£17.5 million) or 4% of global turnover). On October 12, 2023, the UK Extension to the DPF came into effect (as approved by the UK Government), as a UK GDPR data transfer mechanism to U.S. entities self-certified under the UK Extension to the DPF. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

In the United States, HIPAA imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon "covered entities" (health plans, health care clearinghouses and certain health care providers), and their respective business associates, individuals or entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly regulated under HIPAA, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information.

In addition, certain states govern the privacy and security of health-related and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. By way of example, the California Consumer Privacy Act, or CCPA, went into effect on January 1, 2020, and imposes increased privacy and security obligations on entities handling certain personal information of consumers or households, and gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with data breach litigation. The CCPA may increase our compliance costs and potential liability. Further, the California Privacy Rights Act, or CPRA, generally went into effect on January 1, 2023, and significantly amends the CCPA. It imposes additional data protection obligations on covered companies doing business in California, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also created a new California data protection agency specifically tasked to enforce the law, which would likely result in increased regulatory scrutiny of California businesses in the areas of data protection and security. Additional compliance investment and potential business process changes may also be required. Similar laws have passed in other states and are continuing to be proposed at the state and federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

If any person, including any of our employees, clinical trial collaborators or those with whom we share such information, negligently disregards or intentionally breaches our established controls with respect to clinical subject, clinical investigator or employee data, or otherwise mismanages or misappropriates that data, we could be subject to significant monetary damages, regulatory enforcement actions, fines and/or criminal prosecution in one or more jurisdictions. In addition, a data breach could result in negative publicity which could damage our reputation and have an adverse effect on our business, financial condition or results of operations.

Risks Related to Our Common Stock

Our stock price may be volatile and you may not be able to resell shares of our common stock at or above the price you paid.

The trading price of our common stock could be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include those discussed in this "Risk Factors" section of this Annual Report on Form 10-K and others such as:

- results from, and any delays in, our clinical trials for darovasertib (IDE196), IDE397, IDE161, or any other future clinical development programs, including public misperception of the results of our clinical trials;
- announcements by academic or other third parties challenging the fundamental premises underlying our approach to treating cancer and/or biopharmaceutical product development;
- announcements of regulatory approval or disapproval of our current or any future product candidates;
- failure or discontinuation of any of our research and development programs;
- manufacturing setbacks or delays of or issues with the supply of the materials for our product candidates;
- announcements relating to, or results from, our GSK Collaboration Agreement;
- announcements relating to future licensing, collaboration or development agreements;
- delays in the commercialization of our current or any future product candidates;
- public misperception regarding the use of our therapies;
- acquisitions and sales of new products, technologies or businesses;
- quarterly variations in our results of operations or those of our future competitors;
- changes in earnings estimates or recommendations by securities analysts;
- announcements by us or our competitors of new products, significant contracts, commercial relationships, acquisitions or capital commitments;
- developments with respect to intellectual property rights;
- our commencement of, or involvement in, litigation;
- changes in financial estimates or guidance, including our ability to meet our future revenue and operating profit or loss estimates or guidance;
- major changes in our board of directors or management;
- new legislation in the United States relating to the sale or pricing of pharmaceuticals;
- FDA or other U.S. or comparable foreign regulatory actions affecting us or our industry;
- product liability claims or other litigation or public concern about the safety of our product candidates;
- market conditions in the biopharmaceutical and biotechnology sectors, particularly as a result of the volatility in the market caused by the COVID-19 pandemic, as well as adverse geopolitical and macroeconomic developments, such as the ongoing Ukraine-Russia conflict, the Israel-Hamas conflict, and related sanctions, instability in the global banking system, actual and anticipated changes in interest rates, economic inflation and the responses by central banking authorities to control such inflation; and
- general economic and geo-political conditions in the United States and abroad.

In addition, the stock markets in general, and the markets for biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility. In particular, the market prices of securities of smaller biotechnology have experienced dramatic fluctuations that often have been unrelated or disproportionate to the operating results of these companies. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. Furthermore, the trading price of our common stock may be adversely affected by third-parties trying to drive down the market price. Short sellers and others, some of whom post anonymously on social media, may be positioned to profit if our stock declines and their activities

can negatively affect our stock price. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business.

An active, liquid and orderly market for our common stock may not be maintained, and you may not be able to resell your common stock.

Prior to our initial public offering, or IPO, in May 2019, there was no public market for shares of our common stock. Our stock currently trades on the Nasdaq Global Select Market, but we can provide no assurance that we will be able to maintain an active trading market on the Nasdaq Global Select Market or any other exchange in the future. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses, applications, or technologies using our shares as consideration.

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

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of December 31, 2023, we have outstanding a total of 65.0 million shares of common stock, of which the holders of approximately 2.3 million shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock. In addition, as of December 31, 2023, approximately 11.4 million shares of common stock that are either subject to outstanding options or reserved for future issuance under our existing equity incentive plan will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

General Risks

Our information technology systems, or those of our collaborators, CROs or other contractors or consultants, may fail or suffer security breaches, which could adversely affect our business. Security breaches, loss of data or financial assets, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability.

We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information, preclinical and clinical trial data, health-related information and personal information, or collectively, Confidential Information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such Confidential Information, including both our own and that of third parties. We have established physical, electronic and organizational measures to safeguard and secure our systems to prevent a data compromise, and rely on commercially available systems, software, tools, and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our Confidential Information. Our internal information technology systems and infrastructure, and those of our current and any future collaborators, contractors and consultants and other third parties on which we rely, are vulnerable to attack, damage and interruption from computer viruses, malware (e.g. ransomware), malicious code, misconfigurations, "bugs" or other vulnerabilities, natural disasters, terrorism, war, telecommunication and electrical failures, hacking, cyberattacks or intrusions over the Internet, phishing attacks and other social engineering schemes, attachments to emails, human error, fraud, denial or degradation of service attacks, sophisticated nation-state and nation-state-supported actors, employee theft or misuse, persons inside our organization, or persons with access to systems inside our organization.

The risk of a security breach or disruption or data loss, particularly through cyberattacks or cyber-intrusion, including by computer hackers, foreign governments and cyber-terrorists, has generally increased as the number, level of persistence, intensity and sophistication of attempted attacks and intrusions from around the world have increased. Emerging and evolving cybersecurity threats such as the attack on SolarWinds and the Log4j vulnerability reported in December 2021 pose unique challenges and involve sophisticated threat actors. In addition, the pervasive use of mobile devices that access

Confidential Information increases the risk of data security breaches, which could lead to the loss of Confidential Information, including both our own and that of third parties. As a result of the continuing hybrid working environment, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities.

We rely on industry-accepted security measures and technology to securely maintain all confidential and proprietary information on our information systems. We have devoted and will continue to devote significant resources to the security of our information technology systems, but they may still be vulnerable to these threats. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. There can also be no assurance that our programs, and our future collaborators', contractors' and consultants' cybersecurity risk management programs and processes, including policies, controls or procedures, will be fully implemented, complied with or effective in protecting our systems, networks and Confidential Information.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Moreover, if a computer security breach affects our systems or results in the unauthorized release of personally identifiable information, our reputation could be materially damaged. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to applicable privacy and security laws. We would also be exposed to a risk of loss, including financial assets, litigation and potential liability and significant incident response, system restoration or remediation and future compliance costs, all of which could materially adversely affect our business, financial condition, results of operations and prospects. We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

If we engage in future acquisitions or strategic collaborations, it may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption or incurrence of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions, we may incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

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

Our programs may require the use of intellectual property rights held by third parties to which we do not have rights. In such a case, the growth of our business will depend in part on our ability to acquire, in-license or use these rights. However, we may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates on reasonable terms and conditions or at all.

The acquisition or licensing of intellectual property rights for pharmaceutical products is very competitive. If we seek to acquire or license additional intellectual property rights, we may 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 have more institutional experience and greater financial and other resources than we have. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities, 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. Furthermore, companies that perceive us to be a competitor may be unwilling to assign or license rights to us or may interfere with our acquisition or licensing of rights from others. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We have collaborated with U.S. academic institutions and may in the future collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have on reasonable terms, we may have to abandon development of that program and our competitive position, business, financial condition, results of operations, and prospects could suffer.

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

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects.

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

Our patent rights may be affected by developments or uncertainty in the United States' or other jurisdictions' patent statutes, patent case law, USPTO rules and regulations or the rules and regulations of other jurisdictions' patent offices.

There are a number of recent changes to U.S. patent laws that may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, on September 16, 2011, the Leahy-Smith America Invents Act, or Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first to file" system in which the first inventor to file a patent application is typically entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post-grant proceedings including opposition, derivation, reexamination, *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. In addition, the U.S. congress may pass additional patent reform legislation that is unfavorable to us.

The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future. Similarly, statutory or judicial changes to the patent laws of other countries may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents.

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

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

The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. For example, some foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, some countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

Further, on June 1, 2023, the European Union Patent Package (EU Patent Package) regulations were implemented with the goal of providing a single pan-European Unitary Patent and a new European Unified Patent Court (UPC) for litigation involving European patents. As a result, all European patents, including those issued prior to ratification of the EU Patent Package, now by default automatically fall under the jurisdiction of the UPC. It is uncertain how the UPC will impact granted European patents in the biotechnology and pharmaceutical industries. Our European patent applications, if issued, could be

challenged in the UPC. During the first seven years of the UPC's existence, the UPC legislation allows a patent owner to opt its European patents out of the jurisdiction of the UPC. We may decide to opt out our future European patents from the UPC, but doing so may preclude us from realizing the benefits of the UPC. Moreover, if we do not meet all of the formalities and requirements for opt-out under the UPC, our future European patent applications and patents could remain under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke our European patents, and allow for the possibility of a competitor to obtain pan-European injunction. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and product candidates and, resultantly, on our business, financial condition, prospects and results of operations.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We employ reputable professionals and rely on such third parties to help us comply with these requirements and effect payment of these fees with respect to the patents and patent applications that we own, and if we license intellectual property we may have to rely upon our licensors to comply with these requirements and effect payment of these fees with respect to any patents and patent applications that we license. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

If securities or industry analysts do not continue to publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

We incur significant costs as a result of operating as a public company, and our management devotes substantial time to new compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business.

We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Exchange Act and regulations regarding corporate governance practices. The listing requirements of the Nasdaq Global Select Market and the rules of the Securities and Exchange Commission, or SEC, require that we satisfy certain corporate governance requirements relating to director independence, filing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and make some activities more time-consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including D&O insurance, on acceptable terms.

As a public company, we are subject to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, and the related rules of the SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. Additionally, as a result of our ceasing to be an emerging growth company and being deemed a large accelerated filer as of January 1, 2024, commencing with this Annual Report on Form 10-K for the year ending December 31, 2023, our independent registered public accounting

firm is required to issue an opinion on the effectiveness of our internal control over financial reporting. We expect to incur significant expenses and devote substantial management effort toward ensuring compliance with the auditor attestation requirements of Section 404. Furthermore, we will also have to file a more expansive proxy statement and be subject to shorter filing deadlines, which will require additional time and expense as well. It may require significant resources and management oversight to maintain and, if necessary, improve our disclosure controls and procedures and internal control over financial reporting to meet this standard. As a result, management's attention may be diverted from other business concerns, which could adversely affect our business and operating results. To comply with these requirements, we may need to hire more employees in the future or engage outside consultants, which would increase our costs and expenses.

In order to provide the reports required by these rules, we must conduct reviews and testing of our internal controls. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal control over financial reporting, we may not detect errors on a timely basis and our audited financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. In order to report our results of operations and financial statements on an accurate and timely basis, we will depend on CROs and contract manufacturing organizations, or CMOs, to provide timely and accurate notice of their costs to us and on GSK to provide timely and accurate reports of cost sharing under the GSK Collaboration Agreement. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Global Select Market or other adverse consequences that would materially harm to our business.

If we are unable to maintain effective internal controls, our business, financial position, results of operations and prospects could be adversely affected.

As a public company, we are subject to reporting and other obligations under the Exchange Act, including Section 404, which require annual management assessments of the effectiveness of our internal control over financial reporting. As a result of our ceasing to be an emerging growth company and being deemed a "large accelerated filer" as of January 1, 2024, commencing with this Annual Report on Form 10-K for the year ending December 31, 2023, our independent registered public accounting firm will be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to Section 404.

The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act of 2002. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources, which we expect to further increase in 2024 when we are no longer be an emerging growth company and are deemed a large accelerated filer.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. 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 for external purposes in accordance with accounting principles generally accepted in the United States. Any failure to maintain effective internal controls could have an adverse effect on our business, financial position, and results of operations.

If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its stock ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post-change taxable income may be limited. As a result of such ownership changes, our ability to utilize certain NOLs and other tax attributes may be permanently limited if such attributes will expire unused. We have experienced ownership changes in the past, and we may experience ownership changes in the future due to subsequent shifts in our stock ownership (some of which may be outside our control). As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes to offset future taxable income.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent changes in control or changes in our management without the consent of our board of directors. These provisions include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our amended and restated bylaws without obtaining stockholder approval;
- the required approval of at least 66 2/3% of the shares entitled to vote at an election of directors to adopt, amend or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by our chief executive officer or president or by the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.
In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful;
- we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law;
- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification;
- we will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification;
- the rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons; and
- we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

If the costs of maintaining adequate D&O insurance coverage increase significantly in the future, our operating results could be materially adversely affected. Likewise, if any of our current D&O insurance coverage should become unavailable to us or become economically impractical, we may need to decrease our coverage limits or increase our self-insured retention or we may be unable to renew such insurance at all. If we incur liabilities that exceed our coverage or incur liabilities not covered by our insurance, we would have to self-fund any indemnification amounts owed to our directors and officers and employees in which case our results of operations and financial condition could be materially adversely affected. Additionally, a lack of D&O insurance may make it difficult for us to retain and attract talented and skilled directors and officers to serve our company, which could adversely affect our business.

Our amended and restated certificate of incorporation provides for an exclusive forum in the Court of Chancery of the State of Delaware and in the U.S. federal district courts for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any state law derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, any action to interpret, apply, enforce, or determine the validity of our amended and restated certificate of incorporation or amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees and result in increased costs for investors to bring a claim.

We do not intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We do not intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 1C. Cybersecurity.

Cybersecurity Risk Management and Strategy

We have developed and implemented a cybersecurity risk management program intended to protect the confidentiality, integrity, and availability of our critical systems and information. Our cybersecurity risk management program includes a cybersecurity incident response plan.

We design and assess our program based on the National Institute of Standards and Technology Cybersecurity Framework (NIST CSF). This does not imply that we meet any particular technical standards, specifications, or requirements, only that we use the NIST CSF as a guide to help us identify, assess, and manage cybersecurity risks relevant to our business.

Our cybersecurity risk management program is integrated into our overall enterprise risk management program, and shares common methodologies, reporting channels and governance processes that apply across the enterprise risk management program to other legal, compliance, strategic, operational, and financial risk areas.

Our cybersecurity risk management program includes:

- risk assessments designed to help identify material cybersecurity risks to our critical systems, information, products, services, and our broader enterprise information technology environment;
- a security team principally responsible for managing (1) our cybersecurity risk assessment processes, (2) our security controls, and (3) our response to cybersecurity incidents;
- a documented set of cybersecurity policies and procedures that specifies the manner in which security controls are implemented;
- the use of external service providers, where appropriate, to assess, test or otherwise assist with aspects of our security controls;
- cybersecurity awareness training of our employees, incident response personnel, and senior management;
- a cybersecurity incident response plan that includes procedures for responding to cybersecurity incidents; and
- a third-party risk management process for service providers, suppliers, and vendors who have access to our critical systems and information.

There can be no assurance that our cybersecurity risk management program and processes, including our policies, controls or procedures, will be fully implemented, complied with or effective in protecting our systems and information.

We have not identified risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have materially affected or are reasonably likely to materially affect us, including our operations, business strategy, results of operations, or financial condition. For more information, see the section titled “Risk Factor— Our information technology systems, or those of our collaborators, CROs or other contractors or consultants, may fail or suffer security breaches, which could adversely affect our business. Security breaches, loss of data or financial assets, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability.”

Cybersecurity Governance

Our board of directors considers cybersecurity risk as part of its risk oversight function and has delegated to the Audit Committee, or the Committee, oversight of cybersecurity, data privacy and other information technology risks. The Committee

oversees management's implementation of our cybersecurity risk management program. The Committee is composed of members of our board of directors with diverse expertise, including risk management, public accounting, biotechnology, chief executive officer roles, and multiple public company directorships, which has prepared them to oversee our cybersecurity risks.

The Committee receives quarterly reports from management on our cybersecurity risks. In addition, management updates the Committee, as necessary, regarding any material cybersecurity incidents, as well as any incidents with lesser impact potential.

The Committee reports to our full board of directors regarding its activities, including those related to cybersecurity. The full board of directors also receives briefings from management on our cybersecurity risk management program. Board members receive presentations on cybersecurity topics from our Senior Vice President ("SVP"), Head of Finance and Investor Relations, Chief Legal Officer, internal security staff and external experts as part of the board of directors' continuing education on topics that impact public companies.

Our management team, including our SVP, Head of Finance and Investor Relations and Chief Legal Officer, is responsible for assessing and managing our material risks from cybersecurity threats. The team has primary responsibility for our overall cybersecurity risk management program and supervises both our internal cybersecurity personnel and our retained external cybersecurity consultants. Our management team's experience includes monitoring the cybersecurity landscape for new risks and best practices, developing and executing cybersecurity strategies, overseeing related governance policies, testing compliance with applicable technical standards, remediating known risks and leading employee training programs.

Our management team supervises efforts to prevent, detect, mitigate, and remediate cybersecurity risks and incidents through various means, which may include briefings from internal security personnel; threat intelligence and other information obtained from governmental, public or private sources, including external consultants engaged by us; and alerts and reports produced by security tools deployed in the information technology environment.

Item 2. Properties

Our corporate headquarters is located in South San Francisco, California, where we lease and occupy approximately 29,600 square feet of office and laboratory space. The current term of our South San Francisco lease expires in July 2024, with an option to extend the term through July 2026.

In June 2023, we entered into a lease agreement for 43,966 square feet of space at 5000 Shoreline Court, South San Francisco, California. The lease term is expected to commence in June 2024 and the lease term is one hundred twenty months.

In November 2023, we additionally entered into a lease for an office located in San Diego, California, where we occupy approximately 5,700 square feet of office space. The lease commenced in December 2023 and expires in March 2028.

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

Item 3. Legal Proceedings

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

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our common stock trades on the Nasdaq Global Select Market under the symbol "IDYA."

Stockholders

As of February 16, 2024, we had 9 record holders of our common stock. Since many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Dividend Policy

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

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Sale of Unregistered Securities

None.

Use of Proceeds from the Sale of Registered Securities

Not applicable.

Issuer Purchases of Equity Securities

None.

Item 6. Reserved

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes included elsewhere in this report. This discussion and analysis and other parts of this report contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives, expectations, forecasts and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under the section titled "Risk Factors" and elsewhere in this report.

Overview

We are a precision medicine oncology company committed to the discovery and development of targeted therapeutics for patient populations selected using molecular diagnostics. Our approach integrates small molecule drug discovery with extensive capabilities in identifying and validating translational biomarkers to develop targeted therapies for select patient populations that are most likely to benefit from these targeted therapies. Our small molecule drug discovery expertise includes discovery and development of small molecule therapeutics. We are applying these capabilities to develop a robust pipeline in precision medicine oncology.

Our clinical pipeline includes four potential first-in-class clinical-stage product candidates – darovasertib (PKC), IDE397 (MAT2A), IDE161 (PARG) and GSK101 (Pol Theta Helicase). We own or control all commercial rights of the three most-advanced of these product candidates: darovasertib, IDE397 and IDE161. We are also advancing our Werner Helicase program for which we have selected a development candidate in collaboration with GlaxoSmithKline, or GSK and, subject to investigational new drug-, or IND-, enabling studies, are targeting an IND in 2024. We also have multiple earlier-stage preclinical programs. We have established selective, value-accretive collaborations with leading pharmaceutical companies to support our clinical development activities.

Darovasertib – PKC Inhibitor Clinical Candidate in Metastatic Uveal Melanoma and Primary Uveal Melanoma

Our most advanced clinical program is evaluating darovasertib, or IDE196 which we in-licensed from Novartis, a small molecule protein kinase C, or PKC, inhibitor, in uveal melanoma, or UM. We are evaluating darovasertib in combination with crizotinib in a potential registrational clinical trial in patients having MUM. We are also evaluating darovasertib as monotherapy in a Phase 2 clinical trial in primary UM. We are further evaluating darovasertib in combination with crizotinib in a Phase 2 clinical trial in patients with cutaneous melanoma.

We have initiated and achieved double-digit patient enrollment and have opened multiple clinical sites, including international sites, where we are recruiting patients for enrollment in a potential registration-enabling Phase 2/3 clinical trial, designated as IDE196-002, to evaluate darovasertib in combination with crizotinib, Pfizer's investigational cMET inhibitor, in patients having metastatic UM, or MUM, with human leukocyte antigen-, or HLA-A*02:01 negative, or HLA-A2(-), serotype, as part of a second Clinical Trial Collaboration and Supply Agreement, or Second Pfizer agreement, with Pfizer. We are targeting clinical program update(s) in 2024.

We are also planning to enroll additional HLA-A*02:01 positive, or HLA-A2(+), patients as an independent clinical strategy to address HLA-A2(+) MUM patients, in a clinical study. We are further evaluating darovasertib in combination with crizotinib in a Phase 2 expansion arm of IDE196-001 clinical trial in patients with cutaneous melanoma, alternatively referred to as skin melanoma.

We separately initiated and have achieved double-digit patient enrollment in our Phase 2 clinical trial, designated as IDE196-009, evaluating darovasertib as single-agent neoadjuvant and adjuvant therapy in patients having primary UM, with ongoing enrollment and multiple clinical sites open. We are targeting a clinical efficacy update in mid-year 2024 and regulatory guidance update in 2024.

We are also supporting evaluation of darovasertib as single-agent neoadjuvant and adjuvant therapy in primary UM in an ongoing investigator-sponsored clinical trial, or IST, captioned as "Neoadjuvant / Adjuvant trial of Darovasertib in Ocular Melanoma", or NADOM, and led by St. Vincent's Hospital in Sydney with the participation of Alfred Health and the Royal Victorian Eye and Ear Hospital in Melbourne. We are targeting a clinical efficacy update in mid-year 2024.

We own or control all commercial rights in our darovasertib program in uveal melanoma, including in MUM and in primary UM, subject to certain economic obligations pursuant to our exclusive, worldwide license to darovasertib with Novartis.

IDE397 – MAT2A Inhibitor Clinical Candidate in Tumors with MTAP Deletion

IDE397, our small molecule methionine adenosyltransferase 2a, or MAT2A, inhibitor, is being evaluated in a Phase 1/2 clinical trial. We are actively enrolling into the Phase 2 monotherapy expansion cohort in selected priority indications for patients having tumors with methylthioadenosine phosphorylase, or MTAP, gene deletion, including squamous non-small cell lung cancer, or NSCLC, bladder, gastric and esophageal cancers. We observed IDE397 monotherapy responses in multiple priority solid tumor types based on experience across several patients in the early phase of the Phase 2 dose expansion.

We are enrolling patients into a Phase 2 clinical trial designated as IDE397-001 to evaluate IDE397 for patients having certain tumors with MTAP gene deletion. We are proceeding with enrollment of MTAP-deletion patients into a monotherapy Phase 2 expansion cohort with an initial focus on high priority solid tumor types, including squamous NSCLC, bladder, esophageal and gastric cancers. In June 2023, we announced selection of a Phase 2 monotherapy expansion dose for IDE397 and in connection therewith, reported preliminary evidence of clinical activity as monotherapy.

In collaboration with Amgen as part of the Amgen Clinical Trial Collaboration and Supply Agreement, or Amgen CTCSA, we initiated patient enrollment in the Amgen-sponsored Phase 1/2 clinical trial evaluating IDE397 in combination with AMG 193, the Amgen investigational MTA-cooperative protein arginine methyltransferase 5, or PRMT5, inhibitor, in patients having tumors with MTAP deletion, or the IDE397/AMG 193 combination study. This potential first-in-class synthetic lethality combination targets mechanistically complementary nodes of the MTAP methylation pathway – MAT2A and PRMT5 and is supported by data demonstrating preclinical anti-tumor efficacy presented at the 2023 Annual Meeting of the American Association for Cancer Research, or AACR 2023. We are targeting the development of a joint publication strategy in 2024.

We are collaborating with Gilead to clinically evaluate IDE397 in combination with Trodelvy, the Gilead Trop-2 directed ADC, in patients having MTAP deletion bladder cancer, in an IDEAYA-sponsored clinical trial pursuant to the Gilead CSCSA. We anticipate enrolling the first patient in this clinical trial in mid-year 2024.

We own all right, title and interest in and to IDE397 and the MAT2A program, including all worldwide commercial rights thereto.

IDE161 – PARG Inhibitor Clinical Candidate in Tumors with Homologous Recombination Deficiency

We are evaluating IDE161, a small molecule inhibitor of PARG being evaluated in a Phase 1/2 clinical trial designated as IDE161-001 for patients having tumors with HRD and potentially other genetic and/or molecular signatures. PARG is a novel target in a clinically validated biological pathway. PARG functions as a regulator of DNA repair in the same biochemical pathway as PARP. PARG hydrolyzes poly (ADP-ribose), or PAR, chains that are polymerized by PARP enzymes, completing the PAR cycle. Small molecule inhibitors of PARG result in a dose dependent increase in cellular PAR after DNA damage. PARG is a mechanistically distinct target relative to PARP.

We are progressing with enrollment of patients having tumors with HRD into the Phase 1 expansion portion of the Phase 1/2 clinical trial in selected priority tumors. In parallel, we are also continuing with Phase 1 dose optimization to confirm a move-forward expansion dose for the planned Phase 2 portion of the clinical trial. We are targeting clinical program update(s) in 2024. We are also validating IDE161 combination opportunities preclinically and targeting identification of potential combination(s) in 2024.

We received Fast Track Designation from the U.S. Food and Drug Administration, or FDA for IDE161 for ovarian cancer and breast cancer indications, specifically for the treatment of (i) adult, pretreated, platinum-resistant advanced or metastatic ovarian cancer patients having tumors with BRCA1/2 mutations and (ii) adult, pretreated, advanced or metastatic hormone receptor positive, or HR+, Her2- and BRCA1/2 mutant breast cancer patients.

We own or control all commercial rights in our PARG program, subject to certain economic obligations pursuant to our exclusive, worldwide license to certain PARG inhibitors, including IDE161, with CRT and University of Manchester.

Pol Theta

GSK101 (IDE705), our Pol Theta Helicase inhibitor clinical development candidate, is a potential first-in-class small molecule inhibitor of the helicase domain of Polymerase Theta, or Pol Theta. GSK101 was discovered and evaluated in preclinical studies in collaboration with GSK. Pursuant to the GSK Collaboration Agreement, GSK holds a global, exclusive license to develop and commercialize Pol Theta products arising out of the Pol Theta program. GSK is leading clinical development for GSK101 and is responsible for all research and development costs for the Pol Theta program.

We are evaluating GSK101 in combination with niraparib, the GSK small molecule inhibitor of PARP for the treatment of patients having tumors with BRCA or other HR mutations, or HRD in a Phase 1 clinical trial. GSK has dosed the first patient in this trial.

GSK is leading clinical development of GSK101 pursuant to the GSK Collaboration Agreement. GSK is responsible for all research and development costs for the Pol Theta program.

We have the potential to receive an additional $10.0 million milestone payment upon initiation of Phase 1 clinical dose expansion. In August 2023, we achieved and earned a $7.0 million milestone based on acceptance of the IND by the FDA. An earlier preclinical development $3.0 million milestone payment from GSK was achieved in August 2022 in connection with ongoing IND-enabling studies to support evaluation of GSK101.

We have the potential to earn further aggregate later - stage development and regulatory milestones of up to $465 million. Upon commercialization, we will be eligible to receive up to $475 million of commercial milestones, and tiered royalties on global net sales of GSK101 – ranging from high single-digit to sub-teen double-digit percentages, subject to certain customary reductions.

WRN Program in Tumors with High Microsatellite Instability

We selected a Werner Helicase Inhibitor DC in collaboration with GSK. This Werner Helicase Inhibitor DC is targeting the helicase domain of the Werner, or WRN, protein, for patients having tumors with high microsatellite instability, or MSI. Subject to successful completion of ongoing IND-enabling studies, we are targeting an IND submission in 2024 to enable first-in-human clinical evaluation of Werner Helicase Inhibitor DC for patients having tumors with high MSI.

We are collaborating with GSK on the ongoing IND-enabling studies and, subject to IND submission and FDA allowance of clinical development, GSK will lead clinical development for the Werner Helicase program.

In October 2023, we earned a $3 million milestone in connection with IND-enabling studies, for which payment was received in November 2023. We have the potential to earn up to an additional $17 million aggregate milestone payments through early Phase 1 clinical studies, including $7.0 million upon IND clearance. We are also eligible to receive additional future aggregate total development milestones of up to $465 million. Upon commercialization, we will be eligible to receive up to $475 million of commercial milestones, 50% of U.S. net profits and tiered royalties on global non-U.S. net sales of the Werner Helicase Inhibitor DC – ranging from high single-digit to sub-teen double-digit percentages, subject to certain customary reductions.

Other Pipeline Programs (Defined Biomarkers)

We have initiated early preclinical research programs focused on pharmacological inhibition of several new targets, or NTs, for patients with solid tumors characterized by defined biomarkers based on genetic mutations and/or molecular signatures. We believe these research programs have the potential for discovery and development of first-in-class or unique-in-class or best-in-class therapeutics. We are targeting development candidate nominations in 2024 for multiple NTs, including a development candidate to treat MTAP-deletion solid tumors. We own or control all commercial rights in our next-generation programs.

New Target and Biomarker Discovery Platform

We have invested significantly and continue to invest in capabilities for identification and validation of new precision medicine targets and biomarkers for patient selection. For targets of interest, we advance our research to discover therapeutic drugs and to further qualify relevant biomarkers.

We own or control all commercial rights in programs directed to targets identified in on our new target and biomarker discovery platform.

Prospectus Supplement - At-the-Market Facility

Our Registration Statement on Form S-3, which was filed under the Securities Act of 1933, as amended (the "Securities Act"), and became effective as of June 10, 2020, lapsed in June 2023. The January 2021 Sales Agreement was automatically terminated concurrently therewith. As of the termination date of the January 2021 Sales Agreement, approximately $61.8 million of common stock remained available to be sold under the at-the-market facility associated therewith.

On June 26, 2023, we filed a new Registration Statement on Form S-3 (File No. 333- 272936) under the Securities Act as an automatic shelf registration statement as a "well-known seasoned issuer", as defined in Rule 405 under the Securities Act. On June 26, 2023, we also entered into a new Open Market Sales Agreement, or June 2023 Sales Agreement, with Jefferies LLC (Jefferies) relating to an at-the-market offering program under which we may offer and sell, from time to time at our sole discretion, shares of our common stock, par value $0.0001 per share, having aggregate gross proceeds of up to $250.0 million through Jefferies as sales agent.

During the year ended December 31, 2023, we sold an aggregate of 1,188,705 shares of our common stock through at-the-market offerings for aggregate net proceeds of $28.6 million, after deducting underwriting discounts and commissions and other offering expenses, at a weighted average sales price of approximately $25.30 per share under the at-the-market offering pursuant to the January 2021 Sales Agreement and June 2023 Sales Agreement with Jefferies as sales agent. As of December 31, 2023, approximately $222.5 million of common stock remained available to be sold under the June 2023 Sales Agreement with Jefferies as sales agent.

Subsequent to December 31, 2023, from January 1, 2024 through January 17, 2024, we sold an aggregate of 6,115,516 shares of our common stock for aggregate net proceeds of $215.9 million at a weighted average sales price of approximately $36.39 per share under the at-the-market offering pursuant to the June 2023 Sales Agreement with Jefferies as sales agent.

On January 19, 2024, we entered into a new Open Market Sales Agreement, or January 2024 Sales Agreement, with Jefferies relating to an at-the-market offering program under which we may offer and sell, from time to time at our sole discretion, shares of our common stock, par value $0.0001 per share, having aggregate gross proceeds of up to $350.0 million through Jefferies as sales agent.

On January 24, 2024, pursuant to the January Open Market Sales Agreement, we sold an aggregate of 3,119,866 shares of our common stock for aggregate net proceeds of $126.4 million at a weighted average sales price of approximately $41.50 per share under the at-the-market offering pursuant to the January 2024 Sales Agreement with Jefferies as sales agent. As of January 24, 2024, approximately $220.5 million of common stock remained available to be sold under the ATM facility.

We may cancel our at-the-market program at any time upon written notice, pursuant to its terms.

2023 October Public Offering and Sale of IDEAYA Common Stock

On October 27, 2023, the Company completed a further underwritten public follow-on offering. The offering consisted of 5,797,872 shares of our common stock at an offering price to the public of $23.50 per share, including 797,872 shares of common stock upon the exercise in full of the overallotment option by the underwriters, as well as pre-funded warrants to purchase 319,150 shares of common stock at a public offering price of $23.4999 per underlying share, in each case before underwriting discounts and commissions. Pursuant to the offering, we received aggregate gross proceeds of approximately $143.7 million, before deducting underwriting discounts and commissions and other offering expenses, resulting in net proceeds of approximately $134.6 million, after deducting underwriting discounts and commissions and other offering expenses.

2023 April Public Offering and Sale of IDEAYA Common Stock

On April 27, 2023, the Company completed an underwritten public follow-on offering. The offering consisted of 8,858,121 shares of our common stock at an offering price to the public of $18.50 per share, including 1,418,920 shares of common stock upon the exercise in full of the overallotment option by the underwriters, as well as pre-funded warrants to purchase 2,020,270 shares of common stock at a public offering price of $18.4999 per underlying share, in each case before underwriting discounts and commissions. Pursuant to the offering, we received aggregate gross proceeds of approximately $201.3 million, before deducting underwriting discounts and commissions and other offering expenses, resulting in net proceeds of approximately $188.7 million, after deducting underwriting discounts and commissions and other offering expenses.

2022 Public Offering and Sale of IDEAYA Common Stock

On September 19, 2022, the Company completed an underwritten public offering of 8,761,905 shares of our common stock at an offering price to the public of $10.50 per share, including 1,142,857 shares of common stock upon the exercise in full of the overallotment option by the underwriters, pursuant to which we received aggregate net proceeds of $86.1 million, after deducting underwriting discounts and commissions and other offering expenses.

Corporate Update

We do not have any products approved for sale and have not generated any product revenue since inception. We have funded our operations through December 31, 2023 primarily through the sale and issuance of common stock, pre-funded warrants, redeemable convertible preferred stock, and convertible promissory notes, including our initial public offering, or IPO, in May 2019, a follow-on underwritten public offering in June 2020, a direct private placement equity investment by Glaxo Group Limited, an affiliate of GSK, in June 2020, the sale and issuance of common stock under our at-the-market facility pursuant to the August 2020 and January 2021 Sales Agreements with Jefferies as sales agent, and through additional follow-on underwritten public offerings in July 2021, September 2022, April 2023 and October 2023. Additionally, we received a non-dilutive upfront cash payment of $100 million from GSK in connection with the GSK Collaboration Agreement in July 2020. As of December 31, 2023, GSK has made aggregate payments to us in the amount of $13.0 million for the achievement of certain development and regulatory milestones with respect to Pol Theta and WRN products.

Since our inception in June 2015, we have devoted substantially all of our resources to discovering and developing our product candidates. We have incurred significant operating losses to date and expect that our operating expenses will increase significantly as we advance our product candidates through preclinical and clinical development; seek regulatory approval, and prepare for, and, if approved, proceed to commercialization; acquire, discover, validate and develop additional product candidates; obtain, maintain, protect and enforce our intellectual property portfolio; and hire additional personnel. Certain program costs that contribute to our operating expenses have been and/or will be reimbursed by GSK pursuant to the GSK Collaboration Agreement, including 100% of costs we incur for research we perform in connection with the Pol Theta program and 80% of the aggregate program costs incurred by us and GSK for research each of us performs for the Werner Helicase program. We anticipate that payments which we may make to Amgen will also contribute to our operating expenses as they are reimbursed by us pursuant to the Amgen CTCSA, including 50% of external costs Amgen incurs in connection with the Amgen-sponsored and executed IDE397 / AMG 193 Combination Study. We anticipate that we will also incur costs in accordance with the Gilead CSCSA. Gilead will bear internal or external costs incurred in connection with its supply of Trodelvy. We will bear all internal and external costs and expenses associated with the conduct of the combination study. In addition, we expect to incur additional costs associated with operating as a public company.

Our net losses were $113.0 million and $58.7 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $348.4 million.

Our ability to generate product revenue will depend on the successful development, regulatory approval and eventual commercialization of one or more of our product candidates, ourselves, or for some programs, in collaboration with our strategic partners.

Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings, or other capital sources, including potential collaborations with other companies or other strategic transactions. Adequate funding may not be available to us on acceptable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of our product candidates.

As of December 31, 2023, we had cash, cash equivalents, and short-term and long-term marketable securities of $632.6 million.

We believe that our cash, cash equivalents, and short-term and long-term marketable securities will be sufficient to fund our planned operations for at least twelve months from the date of the issuance of our Annual Report on Form 10-K filed February 20, 2024.

These funds will support our efforts through potential achievement of multiple preclinical and clinical milestones across multiple programs.

Components of Operating Results

Collaboration Revenues

To date, we have not generated any revenue from product sales, and we do not expect to generate any revenue from product sales unless and until we are able to initiate a registrational clinical trial, obtain regulatory approval and commercialize one of our product candidates in the future. Our revenue consists exclusively of collaboration revenue under the GSK Collaboration Agreement, including amounts that are recognized related to previously received upfront payments and amounts due and payable to us for research and development services. The amount of revenue recognized related to the GSK Collaboration Agreement, including as related to the previously received upfront payment or to certain development milestone payments, may vary considerably by period and certain components thereof may generally decrease year-over-year as we satisfy remaining performance obligations, for example, relating to the Pol Theta and WRN R&D Services. As of December 31, 2023, we have fully recognized the contract liabilities related to the upfront payment and reimbursements for the research and development performance obligations under the GSK Collaboration Agreement. There are no remaining contract liabilities as of December 31, 2023 as we concluded all the research and development performance obligations under the GSK Collaboration Agreement. The future revenue recognition will be contingent on additional milestone earned, profit sharing and royalties on any net product sales under our collaborations. We expect that any revenue we recognize or generate under the GSK Collaboration Agreement will fluctuate from period to period due to period to period variability in milestone payments and other payments.

Operating Expenses

Research and Development Expenses

Substantially all of our research and development expenses consist of expenses incurred in connection with discovery and development of our product candidates. These expenses include certain payroll and personnel-related expenses, including salaries, employee benefit costs and stock-based compensation expenses for our research and product development employees, fees to third parties to conduct certain research and development activities on our behalf including fees to CMOs and CROs in support of manufacturing and clinical activity for darovasertib, IDE397, IDE161 and WRN, consulting costs, costs for laboratory supplies, costs for product licenses and allocated overhead, including rent, equipment, depreciation, information technology costs and utilities. We expense both internal and external research and development expenses as they are incurred.

We have entered into various agreements with CMOs and CROs. Our research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development provided, but not yet invoiced, are included in accrued liabilities on the balance sheet. If the actual timing of the performance of services or the level of effort varies from the original estimates, we will adjust the accrual accordingly. Payments made to CMOs and CROs under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets until the services are rendered.

Costs of certain activities, such as preclinical studies, are generally recognized based on an evaluation of the progress to completion of specific tasks. Nonrefundable payments made prior to the receipt of goods or services that will be used or rendered for future research and development activities are deferred and capitalized as prepaid expenses and other current assets on our balance sheet. The capitalized amounts are recognized as expense as the goods are delivered or the related services are performed.

We do not allocate our internal costs by product candidate, including internal costs, such as payroll and other personnel expenses, laboratory supplies and allocated overhead. With respect to internal costs, several of our departments support multiple product candidate research and development programs, and therefore the costs cannot be allocated to a particular product candidate or development program. The following table summarizes our external clinical development expenses by program:

	Year Ended December 31,	
	2023	2022
External clinical development expenses [1]:		
IDE397[2]	$ 11,985	$ 9,426
IDE196	25,829	13,433
IDE161	7,104	2,749
Personnel related and stock-based compensation	38,948	26,717
Other research and development expenses	45,642	37,211
Total research and development expenses	$ 129,508	$ 89,536

(1) External clinical development expenses include manufacturing and clinical trial costs. These expenses are primarily for services provided by external consultants, CMOs and CROs.

(2) IDE397 includes costs from Amgen Clinical Trial Collaboration and Supply Agreement

We are focusing substantially all of our resources on the development of our product candidates. We expect our research and development expenses to increase substantially during the next few years, as we seek to initiate and/or advance clinical trials for our product candidates, complete our clinical program, pursue regulatory approval of our product candidates and prepare for a possible commercial launch. Predicting the timing or the cost to complete our clinical program or validation of our commercial manufacturing and supply processes is difficult and delays may occur because of many factors, including factors outside of our control. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those that we currently anticipate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development. Furthermore, we are unable to predict when or if our product candidates will receive regulatory approval with any certainty.

General and Administrative Expenses

General and administrative expenses consist primarily of payroll and personnel-related expenses, including salaries, employee benefit costs and stock-based compensation expense, professional fees for legal, patent, consulting, accounting and tax services, allocated overhead, including rent, equipment, depreciation, information technology costs and utilities, and other general operating expenses not otherwise classified as research and development expenses.

We anticipate that our general and administrative expenses will increase, as a result of increased personnel costs, including salaries, benefits and stock-based compensation expense, patent costs for our product candidates, expanded infrastructure and higher consulting, legal and accounting services associated with maintaining compliance with our Nasdaq stock exchange listing and requirements of the Securities and Exchange Commission, or the SEC, investor relations costs and director and officer insurance policy premiums associated with being a public company.

Other Income (Expense)

Interest Income and Other Income (Expense), Net

Interest income and other income (expense), net consists primarily of interest income earned on our cash, cash equivalents and marketable securities.

Results of Operations

A discussion regarding our financial condition and results of operations for fiscal year 2023 compared to fiscal year 2022 is presented below. A discussion regarding our financial condition and results of operations for fiscal year 2022 compared to fiscal year 2021 can be found in "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K filed with the SEC on March 7, 2023.

Comparison of the Years Ended December 31, 2023 and December 31, 2022

The following table summarizes our results of operations for the periods indicated (in thousands):

	Year Ended December 31,			
	2023	2022	Change	% Change
Revenue				
Collaboration revenue	$ 23,385	$ 50,931	$ (27,546)	(54%)
Operating expenses				
Research and development	129,508	89,536	39,972	45%
General and administrative	28,306	23,897	4,409	18%
Total operating expenses	157,814	113,433	44,381	39%
Loss from operations	(134,429)	(62,502)	(71,927)	115%
Other income				
Interest income and other income (expense), net	21,468	3,847	17,621	458%
Net loss	$ (112,961)	$ (58,655)	$ (54,306)	93%

Collaboration Revenue

Collaboration revenue decreased by $27.5 million, or 54%, during the year ended December 31, 2023 compared to the year ended December 31, 2022. In July 2020, the GSK Collaboration Agreement became effective, and we started recognizing collaboration revenue, which consists of revenue from preclinical and Phase 1 monotherapy clinical research and

development services under the MAT2A program as well as preclinical research services and the related license under the Pol Theta and WRN programs. Revenue we recognize from satisfaction of performance obligations under the GSK Collaboration Agreement is impacted by our estimates of the remaining costs to complete our obligations, which may vary due to changes to prospective collaboration research budgets or changes to respective allocation of resources and in any case require significant judgment, and may cause fluctuation in the revenue recognized from period to period.

During 2023, the Company recognized $23.4 million in revenue resulting from the progress in WRN R&D services and the Pol Theta program's IND acceptance milestone achievement and WRN program's toxicology study initiation milestone achievement.

As of December 31, 2023, we have fully recognized the contract liabilities related to the upfront payment and reimbursements for the research and development performance obligations under the GSK Collaboration Agreement. There are no remaining contract liabilities as of December 31, 2023 as we concluded all the research and development performance obligations under the GSK Collaboration Agreement. The future revenue recognition will be contingent on additional milestones earned, profit sharing and royalties on any net product sales under our collaborations. We expect that any revenue we recognize or generate under the GSK Collaboration Agreement will fluctuate from period to period due to period to period variability in milestone payments and other payments.

Research and Development Expenses

Research and development expenses increased by $40.0 million, or 45%, during the year ended December 31, 2023 compared to the year ended December 31, 2022. The increase in research and development expenses was primarily due to increases of $24.5 million in fees paid to CROs, CMOs and consultants related to the advancement of our lead product candidates through preclinical and clinical studies, $12.3 million in personnel-related expenses, including salaries, benefits and stock-based compensation, primarily related to an increase in headcount to support our growth, and $3.2 million in costs for laboratory supplies, facilities, software and insurance premiums to support our research and development programs.

General and Administrative Expenses

General and administrative expenses increased by $4.4 million, or 18%, during the year ended December 31, 2023 compared to the year ended December 31, 2022. The increase in general and administrative expenses was primarily due to increases of $1.6 million for consulting and legal services and $3.5 million in personnel-related expenses, including salaries, benefits and stock-based compensation, related to an increase in headcount to support our growth, partially offset by a decrease in $0.1 million in software licenses and facility costs, and $0.6 million in directors and officer's insurance premiums.

Interest Income and Other Income (Expense), Net

Interest income increased by $17.6 million, or 458%, during the year ended December 31, 2023 compared to the year ended December 31, 2022, primarily due to higher investment balances and interest rates.

Liquidity and Capital Resources; Plan of Operations

Sources of Liquidity

We have funded our operations primarily through the sale and issuance of common stock, pre-funded warrants, redeemable convertible preferred stock, and convertible promissory notes, the up-front and milestone payment received from GSK. As of December 31, 2023, we had cash, cash equivalents and marketable securities of $632.6 million, consisting primarily of money market funds, U.S. government securities, commercial paper, and corporate bonds.

Material Cash Requirements

We have incurred net losses since our inception. For the years ended December 31, 2023 and December 31, 2022, we had net losses of $113.0 million and $58.7 million, respectively, and we expect to incur substantial additional losses in future periods. As of December 31, 2023, we had an accumulated deficit of $348.4 million. Based on our current business plan, we believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our planned operations for at least the next 12 months from the issuance date of this Annual Report on Form 10-K.

To date, we have not generated any product revenue. We do not expect to generate any meaningful product revenue unless and until we obtain regulatory approval of and commercialize any of our product candidates, and we do not know when, or if, it will occur. We expect to continue to incur significant losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates and begin to commercialize any approved products. We are subject to all of the risks typically related to the development of new product candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Moreover, we expect to incur additional costs associated with operating as a public company.

We will continue to require additional capital to develop our product candidates and fund operations for the foreseeable future. We may seek to raise capital through private or public equity or debt financings, collaboration or other arrangements with corporate sources, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategies. We anticipate that we will need to raise substantial additional capital, the requirements for which will depend on many factors, including:

- the scope, timing, rate of progress and costs of our drug discovery, preclinical development activities, laboratory testing and clinical trials for our product candidates;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing development and commercial manufacturing activities;
- the extent to which we acquire or in-license other product candidates and technologies;
- the cost, timing and outcome of regulatory review of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our product candidates;
- the costs associated with being a public company; and
- the cost and timing associated with commercializing our product candidates, if they receive marketing approval.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we will continue to require additional capital to meet operational needs and capital requirements associated with such operating plans. If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any future debt financing into which we enter may impose upon us additional covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, repurchase our common stock, make certain investments or engage in certain merger, consolidation or asset sale transactions. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders. If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license to others rights to our product candidates in certain territories or indications that we would prefer to develop and commercialize ourselves.

We lease our laboratory and office facilities in South San Francisco, California under operating leases with expiration dates in July 2024. In May 2018, we amended our South San Francisco facility lease agreement to expand the size of the original premises by adding approximately 7,340 rentable square feet of additional space. In September 2019, we further amended our South San Francisco facility lease agreement to expand the size of the premises by adding 5,588 rentable square feet of additional space. As of December 31, 2023, we expect to make the total lease payments of $1.6 million through July 2024.

In June 2023, we entered into a lease agreement for 43,966 square feet of space at 5000 Shoreline Court, South San Francisco, California. The lease term is expected to commence in June 2024 and the lease term is one hundred twenty months. In November 2023, we additionally entered into a lease for an office located in San Diego, California, where we occupy approximately 5,700 square feet of office space. The lease commenced in December 2023 and expires in March 2028.

We enter into contracts in the normal course of business with third-party contract organizations for preclinical and clinical studies and testing, manufacture and supply of our preclinical and clinical materials and providing other services and products for operating purposes. These contracts generally provide for termination following a certain period after notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

Pursuant to the GSK Collaboration Agreement, we will be responsible for 20% of global research and development costs for the WRN program. The cost-sharing percentages will be adjusted based on the actual ratio of U.S. to global profits for WRN products, as measured three and six years after global commercial launch thereof. We may opt out of 50% U.S. net profit share and corresponding development cost share for the WRN program.

In September 2018, we entered into a license agreement with Novartis to develop and commercialize Novartis' LXS196 (also known as IDE196), a Phase 1 PKC inhibitor, for the treatment of cancers having GNAQ and GNA11 mutations. We have renamed Novartis' LXS196 oncology as IDE196, and which has a non-proprietary name of darovasertib. We paid Novartis an upfront payment of $2.5 million and issued 263,615 shares of our Series B redeemable convertible preferred stock concurrently with the execution of the license agreement. Subject to completion of certain clinical and regulatory development milestones, we agreed to make milestone payments in the aggregate of up to $9.0 million, and subject to achievement of certain commercial sales milestones, we agreed to make milestone payments in the aggregate of up to $20.0 million. We also agreed to pay mid to high single-digit tiered royalty payments based on annual worldwide net sales of licensed products, payable on a licensed product-by-licensed product and country by country basis until the latest of the expiration of the last to expire exclusively licensed patent, the expiration of regulatory exclusivity, and the ten year anniversary of the first commercial sale of such product in such country. The royalty payments are subject to reductions for lack of patent coverage, loss of market exclusivity, and payment obligations for third-party licenses.

In March 2020, we entered into the Pfizer Agreement. Pursuant to the Pfizer Agreement, as amended in September 2020, April 2021, September 2021 and May 2023, Pfizer supplies us with their MEK inhibitor, binimetinib, and their cMET inhibitor, crizotinib, to evaluate combinations of darovasertib independently with each of the Pfizer compounds, in patients with tumors harboring activating GNAQ or GNA11 mutations. Under the Pfizer Agreement, we are the sponsor of the combination studies and will provide darovasertib and pay for the costs of the combination studies. Pfizer will provide binimetinib and crizotinib for use in the clinical trial at no cost to us. The Pfizer Agreement provides that we and Pfizer will jointly own clinical data generated from the clinical trial and will also jointly own inventions, if any, relating to the combined use of darovasertib and binimetinib, or independently, to the combined use of darovasertib and crizotinib. We and Pfizer have formed a joint development committee responsible for coordinating all regulatory and other activities under the agreement.

We have further expanded the scope of our relationship with Pfizer, entering into additional agreements to facilitate evaluation of darovasertib in combination with crizotinib in a potential registrational clinical trial in MUM and separately, in combination with crizotinib in other cMET-driven tumor indications.

In March 2022, we and Pfizer entered into the Second Pfizer Agreement pursuant to which we may, subject to FDA feedback and guidance, evaluate darovasertib and crizotinib as a combination therapy in MUM in a planned Phase 2/3 potential registration-enabling clinical trial. Pursuant to the Second Pfizer Agreement, we are the sponsor of the planned combination trial and we will provide darovasertib and pay for the costs of the combination trial; Pfizer will provide crizotinib for the planned combination trial at no cost to us for up to an agreed-upon number of MUM patients. We and Pfizer will jointly own clinical data from the planned combination trial and all inventions relating to the combined use of darovasertib and crizotinib. We and Pfizer have formed a joint development committee responsible for coordinating all regulatory and other activities under the Second Pfizer Agreement.

Separately, in March 2022, we and Pfizer also entered into the Third Pfizer Agreement pursuant to which we may, subject to preclinical validation and FDA feedback and guidance, evaluate darovasertib and crizotinib, as a combination therapy in cMET-driven tumors such as NSCLC and/or HCC in a Phase 1 clinical trial. Pursuant to the Third Pfizer Agreement, we are the sponsor of the planned combination trial, and we will provide darovasertib and pay for the costs of the combination trial; Pfizer will provide crizotinib for the planned combination trial at no cost to us. We and Pfizer will jointly own clinical data from the planned combination trial and all inventions relating to the combined use of darovasertib and crizotinib. We and Pfizer had formed a joint development committee responsible for coordinating all regulatory and other activities under the Third Pfizer Agreement.

In May 2023, we continued our relationship with Pfizer by entering into Amendment No. 4 to the Pfizer Agreement relating to the supply of crizotinib in support of this Phase 2 clinical trial, pursuant to which Pfizer will continue to provide us with an additional defined quantity of crizotinib at no cost.

We also expanded our relationship with Pfizer in May 2023 under an Amendment No. 1 to the Second Pfizer Agreement to support the Phase 2/3 registrational trial to evaluate darovasertib and crizotinib as a combination therapy in MUM. Under the as-amended Second Pfizer Agreement, Pfizer will provide us with a first defined quantity of crizotinib at no cost, as well as an additional second defined quantity of crizotinib at a lump-sum cost. Under Amendment No. 1 to the Second Pfizer Agreement, we also terminated the Third Pfizer Agreement.

In January 2022, we exercised our option for an exclusive worldwide license rights covering a broad class of PARG inhibitors from Cancer Research Technology Ltd. (CRT) and the University of Manchester, and in connection therewith, paid a one-time option exercise fee of £250,000. Certain of the clinical and regulatory milestones are related to and may be due and payable by us if certain milestones are achieved in connection with the IDE161-001 Phase 1/2 clinical trial. We will be obligated to make future milestone payments to CRT aggregating up to £18.75 million upon the achievement of specific development and regulatory approval events for development of a PARG inhibitor in oncologic diseases, including an aggregate of up to £1.5 million and up to £2.25 million for the achievement of certain Phase 2 and Phase 3 development milestones, respectively, in each case as relating to first (e.g., a breast cancer) and second (e.g., ovarian cancer) tumor histologies.

In April 2023, we incurred an obligation to pay milestone payments in an aggregate amount of £750,000 to CRT based upon the achievement of certain milestones relating to first and second tumor histologies in connection with the Phase 1 portion of the Phase 1/2 clinical trial in oncologic diseases.

Following our exercise of the option, if we sublicense certain intellectual property developed under the agreement or Cancer Research UK background patents specifically relating to PARG, we will also have an obligation to pay to Cancer Research UK low double digit percentage of sublicense revenue we receive, if any. If the agreement is terminated due to our material breach, then we are eligible to receive a percentage of sublicensing revenue that Cancer Research UK receives for licensing intellectual property.

In July 2022, we entered into the Amgen CTCSA to clinically evaluate IDE397 in combination with AMG 193 in patients having MTAP-null solid tumors, in a Phase 1/2 clinical trial. Under the mutually non-exclusive Amgen CTCSA, we will provide IDE397 drug supply to Amgen, who will be the sponsor of the Phase 1 clinical combination trial evaluating IDE397 and AMG 193. Each party will pay for fifty percent (50%) of the external third-party costs of the combination study. Each party will be responsible for its own internal costs and expenses in support of the combination study. We and Amgen will jointly oversee clinical development of the combination therapy through a Joint Oversight Committee responsible for coordinating all regulatory and other activities under the Amgen CTCSA. The parties will jointly own collaboration data and combination-related intellectual property, if any, arising from the combination clinical trial. We and Amgen each retain commercial rights to our respective compounds, including with respect to use as a monotherapy agent or combination agent.

In November 2023, we entered into the Gilead CSCSA with Gilead to clinically evaluate IDE397 in combination with Trodelvy (sacituzumab-govitecan-hziy), a Trop-2 directed ADC, in patients having MTAP-deletion bladder cancer, in a Phase 1 clinical trial. Under the mutually non-exclusive Gilead CSCSA, we will receive Trodelvy drug supply from Gilead and will sponsor the Phase 1 clinical combination trial evaluating ID397 and Trodelvy. Gilead will bear internal or external costs incurred in connection with its supply of Trodelvy. We will bear all internal and external costs and expenses associated with the conduct of the combination study. We and Gilead will jointly oversee clinical development of the combination therapy through a Joint Steering Committee responsible for coordinating all regulatory and other activities under the Gilead CSCSA. We and Gilead each retain commercial rights to our respective compounds, including with respect to use as a monotherapy agent or combination agent.

Adequate additional funding may not be available to us on acceptable terms or at all. See the section of this Annual Report on Form 10-K titled “Part I, Item 1A. – Risk Factors” for additional risks associated with our substantial capital requirements.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Summary Statement of Cash Flows

The following table sets forth the primary sources and uses of cash, cash equivalents, and restricted cash for each of the periods presented below (in thousands):

	Year Ended December 31,	
	2023	2022
Net cash (used in) provided by:		
Operating activities	$ (115,224)	$ (87,175)
Investing activities	(158,456)	(33,404)
Financing activities	362,717	97,165
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 89,037	$ (23,414)

Cash Flows from Operating Activities

Net cash used in operating activities was $115.2 million for the year ended December 31, 2023. Cash used in operating activities was primarily due to the use of funds in our operations to develop our product candidates resulting in a net loss of $113.0 million, adjusted for net non-cash charges of $10.9 million and changes in net operating assets and liabilities of $13.2 million. Our non-cash charges consisted of $18.5 million in stock-based compensation, and $2.5 million in depreciation and amortization of right of use asset of $1.5 million, partially offset by $11.6 million accretion of discounts on marketable securities. The net change in our operating assets and liabilities consisted primarily of decreases of $13.8 million in contract liabilities due to revenue recognized under the GSK Collaboration Agreement, $2.0 million in prepaid and other assets, and $1.9 million in lease liabilities, partially offset by $1.6 million accrued and other liabilities due to CRO fees in support of research and manufacturing activities, $2.6 million in accounts payable, and $0.2 million in accounts receivable from GSK for estimated program costs under the GSK Collaboration Agreement.

Net cash used in operating activities was $87.2 million for the year ended December 31, 2022. Cash used in operating activities was primarily due to the use of funds in our operations to develop our product candidates resulting in a net loss of $58.7 million, adjusted for net non-cash charges of $14.4 million and changes in net operating assets and liabilities of $43.0 million. Our non-cash charges consisted of $11.6 million in stock-based compensation, and $2.1 million in depreciation, and $1.4 million of amortization of right of use asset, partially offset by $0.7 million accretion of discounts on marketable securities. The net change in our operating assets and liabilities consisted primarily of decreases of $46.5 million in contract liabilities due to revenue recognized under the GSK Collaboration Agreement, $2.1 million in prepaid and other assets, and $1.7 million in lease liabilities, partially offset by $4.6 million accrued and other liabilities due to CRO fees in support of research and manufacturing activities, $1.9 million in accounts payable, and $0.9 million in accounts receivable from GSK for estimated program costs under the GSK Collaboration Agreement.

Cash Flows from Investing Activities

Net cash used in investing activities was $158.5 million for the year ended December 31, 2023, which consisted primarily of $596.0 million used to purchase marketable securities and $2.4 million used to purchase property and equipment, partially offset by $439.9 million provided by maturities of marketable securities.

Net cash used in investing activities was $33.4 million for the year ended December 31, 2022, which consisted primarily of $255.8 million used to purchase marketable securities and $3.4 million used to purchase property and equipment, partially offset by $225.8 million provided by maturities of marketable securities.

Cash Flows from Financing Activities

Net cash provided by financing activities was $362.7 million for the year ended December 31, 2023, which consisted primarily of $281.2 million of net proceeds from our follow-on offering, $42.2 million of proceeds from issuance of pre-funded warrants, $28.6 million of proceeds from ATM offering, $9.6 million of proceeds from exercise of common stock options, and $1.2 million of proceeds from ESPP purchase.

Net cash provided by financing activities was $97.2 million for the year ended December 31, 2022, which consisted primarily of $86.1 million of net proceeds from our follow-on offering, $8.8 million of proceeds from ATM offering, $1.4 million of proceeds from exercise of common stock options, and $0.8 million of proceeds from ESPP purchase.

Critical Accounting Policies and Estimates

Our financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported revenue recognized and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates. For more detail on our critical accounting policies, refer to Note 2 to the financial statements appearing elsewhere in this Annual Report on Form 10-K.

Revenue Recognition

Licenses of intellectual property: If a license to our intellectual property is determined to be distinct from the other promised goods or services identified in an arrangement, we recognize revenue from non-refundable, upfront fees allocated to the license at the point in time when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other goods or services, we utilize 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 toward satisfying the performance obligation for purposes of recognizing revenue from non-refundable, upfront fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of progress and related revenue recognition.

Customer options for additional goods or services: If a contract contains customer options that allow the customer to acquire additional goods or services, including a license to our intellectual property, the goods and services underlying the customer options are evaluated to determine whether they are deemed to represent a material right. In determining whether the customer option has a material right, we assess whether there is an option to acquire additional goods or services at a discount. If the customer option is determined not to represent a material right, the option is not considered to be a performance obligation. If the customer option is determined to represent a material right, the material right is recognized as a separate performance obligation. We allocate the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until the option is exercised.

Milestone payments: At the inception of each arrangement or amendment that includes development, regulatory or commercial milestone payments, we evaluate whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price. ASC 606 prescribes two methods to use when estimating the amount of variable consideration: the expected value method and the most likely amount method. Under the expected value method, an entity considers the sum of probability-weighted amounts in a range of possible consideration amounts. Under the most likely amount method, an entity considers the single most likely amount in a range of possible consideration amounts. Whichever method is used, it should be consistently applied throughout the life of the contract; however, it is not necessary for us to use the same approach for all contracts. If it is probable that a significant revenue reversal would not occur when the uncertainty associated with the milestone is resolved, the associated milestone value is included in the transaction price. Milestone payments that are highly susceptible to factors outside our influence, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. If there is more than one performance obligation, the transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis. We recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability or achievement of each milestone and any related constraint, and if necessary, adjust our estimates 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.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license deemed to be the predominant item to which the royalties relate, we recognize 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).

Upfront payments and fees are recorded as contract liabilities upon receipt or when due and may require deferral of revenue recognition to a future period until we perform our obligations under these arrangements. Amounts payable to us are recorded as accounts receivable when our right to consideration is unconditional. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

Contractual cost sharing payments received from a customer or collaboration partner are accounted for as variable consideration. We include an expected value in the transaction price. Contractual cost sharing payments made to a customer or collaboration partner are accounted for as a reduction to the transaction price if such payments are not related to distinct goods or services received from the customer or collaboration partner.

Contracts may be amended to account for changes in contract specifications and requirements. Contract modifications exist when the amendment either creates new, or changes existing, enforceable rights and obligations. When contract modifications create new performance obligations and the increase in consideration approximates the standalone selling price for goods and services related to such new performance obligations as adjusted for specific facts and circumstances of the contract, the modification is accounted for as a separate contract. If a contract modification is not accounted for as a separate contract, we account for the promised goods or services not yet transferred at the date of the contract modification (the remaining promised goods or services) prospectively, as if it were a termination of the existing contract and the creation of a new contract, if the remaining goods or services are distinct from the goods or services transferred on or before the date of the contract modification. We account for a contract modification as if it were a part of the existing contract if the remaining goods or services are not distinct and, therefore, form part of a single performance obligation that is partially satisfied at the date of the contract modification. In such case the effect that the contract modification has on the transaction price, and on the entity's measure of progress toward complete satisfaction of the performance obligation, is recognized as an adjustment to revenue (either as an increase in or a reduction of revenue) at the date of the contract modification (the adjustment to revenue is made on a cumulative catch-up basis).

Upfront payment contract liabilities resulting from our license and collaboration agreements do not represent a financing component as the payment is not financing the transfer of goods and services, and the technology underlying the licenses granted reflects research and development expenses already incurred by us. As such, we do not adjust our revenues for the effects of a significant financing component.

Determination of the estimate of standalone selling price (SSP)

Prior to entering into the GSK Collaboration Agreement, we have never entered into a similar collaboration agreement nor have ever recognized any revenue, and the SSP of performance obligations identified in the GSK Collaboration Agreement is not directly observable. Accordingly, we developed an estimate of the SSP of each performance obligation based on the information known to us on the Effective Date and on input from an independent third-party valuation firm.

We applied the income approach as a primary methodology to determine the SSP of each performance obligation. Specifically, based on our early stage of development and other relevant factors, we determined to use the following methodologies:

(1) Preclinical and Phase 1 Monotherapy clinical research and development services under the MAT2A program (MAT2A R&D Services) – the expected costs of satisfying the performance obligation, adjusted for probabilities of technical success where appropriate;

(2) Preclinical research services and the related license to IDEAYA-owned technology under the Pol Theta program (Pol Theta R&D Services) – a combination of risk-adjusted net present value analysis and the expected costs of satisfying the performance obligation, adjusted for probabilities of technical success where appropriate;

(3) Preclinical research services and the related license to IDEAYA-owned technology under the WRN program (WRN R&D Services) – a combination of risk-adjusted net present value analysis and the expected costs of satisfying the performance obligation, adjusted for probabilities of technical success where appropriate;

(4) The Option – risk-adjusted net present value analysis;

(5) Material right associated with the option to license to IDEAYA-owned technology under the MAT2A program to the extent necessary for preclinical activities in preparation for the MAT2A Combination Trial (Preclinical MAT2A License) – the expected costs of satisfying the performance obligation; and,

(6) Material right associated with the supply of MAT2A product for the MAT2A Combination Trial (MAT2A Supply) – the expected costs of satisfying the performance obligation.

The assumptions used to determine the SSP of each performance obligation are based on numerous objective and subjective factors, combined with management judgment, including:

- projected preclinical and clinical research and development expenses;
- the probability of technical success for the development, regulatory approval and commercialization of our product candidates;
- projected cash flow during development and commercialization periods;
- discount rates based on cost of capital;
- the probability of exercise of the Option; and,
- the projected manufacturing cost and overhead expense for IDE 397.

We considered reasonably available data points, market conditions and entity-specific factors in estimating the SSP of performance obligations. However, some of these assumptions are specific to us and are not directly observable. We also applied our own judgment as management in determining these assumptions. Accordingly, these assumptions are subject to uncertainty, and changing methodology and/or assumption could materially impact the estimate of the SSP of performance obligations, and as a result, an amount of subsequent revenue recognition and/or its timing.

Determination of the timing of satisfaction of performance obligations

We recognize revenue from the MAT2A R&D Services, Pol Theta R&D Services and WRN R&D Services over time, as GSK simultaneously receives and consumes the benefits provided by our performance as we perform. We measure our progress toward complete satisfaction of the MAT2A R&D Services, Pol Theta R&D Services and WRN R&D Services based on the costs incurred as a percentage of the estimated total costs to be incurred to complete the performance obligations.

The estimated total costs to be incurred to complete the MAT2A R&D Services, Pol Theta R&D Services and WRN R&D Services may evolve and be updated throughout the performance period with the consultation with GSK through the joint development committee. The change in the estimated total costs and/or the timing of completion may materially impact an amount of subsequent revenue recognition and/or its timing. MAT2A R&D Services and Pol Theta R&D Services are completed. The expected timing of completing the WRN R&D Services may be updated.

JOBS Act Accounting Election

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an "emerging growth company" which we were until December 31, 2023 to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. As of June 30, 2023, the aggregate market value of the voting and non-voting common equity held by non-affiliates was $1.3 billion, and we are deemed a large accelerated filer as of January 1, 2024, commencing with this Annual Report on Form 10-K for the year ending December 31, 2023. As a result, we are ceased to be an emerging growth company as of December 31, 2023.

Recent Accounting Pronouncements

See the section titled "Summary of Significant Accounting Policies—Recent Accounting Pronouncements" in Note 2 to our financial statements included elsewhere in this Annual Report on Form 10-K for additional information.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Sensitivity

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates or exchange rates. As of December 31, 2023, we had cash equivalents and marketable securities of $632.6 million, consisting of interest-bearing money market funds, investments in U.S. government securities, commercial paper, and corporate bonds, for which the fair value would be affected by changes in the general level of U.S. interest rates. Even if the fair value of certain government securities, commercial paper, and corporate bonds is affected by changes in U.S. interest rates, the principal of such instruments will be due to us upon maturity.

While we are seeing, and expect to continue to see, record inflation and elevated interest rates due to geopolitical and macroeconomic events, such as the ongoing Ukraine-Russia conflict and related sanctions, the Israel-Hamas conflict, and the banking sector volatility, we do not believe that inflation, interest rate changes or exchange rate fluctuations have had a significant impact on our results of operations for any periods presented herein.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15 of Part IV 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

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial and accounting officer, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible disclosure controls and procedures.

Our management, with the participation of our principal executive officer and principal financial and accounting officer, evaluated the effectiveness of our disclosure controls and procedures at the end of the period covered by this Annual Report on Form 10-K. Based upon such evaluation, our principal executive officer and principal financial and accounting officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

Changes in Internal Control Over Financial Reporting

There were no changes in the Company's internal control over financial reporting that occurred during the quarter ended December 31, 2023 that have materially affected, or are reasonably likely to materially effect, the Company's internal control over financial reporting.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act). Under the supervision of and with the participation of our principal executive officer and principal financial and accounting officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2023 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in "Internal Control—Integrated Framework" (2013). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2023.

The effectiveness of our internal control over financial reporting as of December 31, 2023 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report, which is included under "Item 8. Financial Statements and Supplementary Data" of this Annual Report.

Item 9B. Other Information

Trading Plans

During the three months ended December 31, 2023, our Section 16 officers and directors adopted or terminated contracts, instructions or written plans for the purchase or sale of our securities as noted below:

			Trading Arrangement			
Name and Title	**Action**	**Date**	**Rule 10b5-1***	**Non-Rule 10b5-1****	**Total Shares to be Sold**	**Expiration Date**
Yujiro S. Hata President and Chief Executive Officer	Adopt	December 22, 2023	X		175,000	November 14, 2024
* Intended to satisfy the affirmative defense of Rule 10b5-1(c) ** Not intended to satisfy the affirmative defense of Rule 10b5-1(c)						

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

Part III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item will be contained in our definitive proxy statement to be filed with the SEC in connection with the Annual Meeting of Stockholders within 120 days after December 31, 2023, or the Proxy Statement, and is incorporated in this Annual Report on Form 10-K by reference.

Item 11. Executive Compensation.

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

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

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

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

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

Part IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this report:

(1) FINANCIAL STATEMENTS

The following documents are included on pages F-1 through F-27 attached hereto and are filed as part of this Annual Report on Form 10-K.

(2) FINANCIAL STATEMENT SCHEDULES

All schedules to the financial statements are omitted as the required information is either inapplicable or presented in the financial statements.

(3) EXHIBITS

The exhibits listed in the accompanying Exhibit Index are filed as part of, or incorporated by reference into, this report.

Exhibit Index

(a) Exhibits.

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	Amended and Restated Certificate of Incorporation.	8-K	5/28/2019	3.1	
3.2	Amended and Restated Bylaws.	8-K	5/28/2019	3.2	
4.1	Reference is made to Exhibits 3.1 through 3.2.				
4.2	Form of Common Stock Certificate.	S-1/A	5/13/2019	4.2	
4.3	Description of Common Stock.				X
4.4	Form of April 2023 Pre-funded Warrant	8-K	4/27/2023	4.1	
4.5	Form of October 2023 Pre-funded Warrant	8-K	10/27/2023	4.1	
10.1†	License Agreement by and between IDEAYA Biosciences, Inc. and Novartis International Pharmaceutical, Inc. dated as of September 19, 2018.	S-1	4/26/2019	10.1	
10.2(a)†	Evaluation, Option and License Agreement by and among IDEAYA Biosciences, Inc., Cancer Research Technology Ltd. and University of Manchester dated as of April 28, 2017.	S-1	4/26/2019	10.2(a)	
10.2(b)	Amendment #1 to Evaluation, Option and License Agreement by and among IDEAYA Biosciences, Inc., Cancer Research Technology Ltd. and University of Manchester dated as of April 24, 2019.	S-1	4/26/2019	10.2(b)	
10.2(c)	Amendment #2 to Evaluation, Option and License Agreement by and among IDEAYA Biosciences, Inc., Cancer Research Technology Ltd. and University of Manchester dated as of March 3, 2020.	10-K	3/24/2020	10.2(c)	
10.3(a)#	2019 Incentive Award Plan.	S-1/A	5/13/2019	10.5(a)	
10.3(b)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2019 Incentive Award Plan.	S-1/A	5/13/2019	10.5(b)	
10.3(c)#	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2019 Incentive Award Plan.	S-1/A	5/13/2019	10.5(c)	
10.3(d)#	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2019 Incentive Award Plan.	S-1/A	5/13/2019	10.5(d)	
10.4#	Employee Stock Purchase Plan.	S-1/A	5/13/2019	10.6	
10.5(a)#	2015 Equity Incentive Plan, as amended.	S-1	4/26/2019	10.4(a)	
10.5(b)#	Form of Stock Option Agreement under the 2015 Equity Incentive Plan.	S-1	4/26/2019	10.4(b)	
10.5(c)#	Form of Early Exercise Stock Option Agreement under the 2015 Equity Incentive Plan.	S-1	4/26/2019	10.4(c)	

10.5(d)#	Form of Stock Purchase Right Grant Notice and Restricted Stock Purchase Agreement under 2015 Equity Incentive Plan.	S-1	4/26/2019	10.4(d)	
10.6#	2023 Employment Inducement Award Plan	S-8	3/7/2023	99.3(a)	
10.7#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2023 Employment Inducement Award Plan	S-8	3/7/2023	99.3(b)	
10.8#	Employment Agreement by and between IDEAYA Biosciences, Inc. and Yujiro Hata.	S-1/A	5/13/2019	10.7(b)	
10.9#	Amended and Restated Employment Agreement by and between IDEAYA Biosciences, Inc. and Michael White.	10-Q	11/15/2021	10.2	
10.10#	Amended and Restated Employment Agreement by and between IDEAYA Biosciences, Inc. and Jason Throne.	10-K	3/23/2021	10.9	
10.11#	Employment Agreement by and between IDEAYA Biosciences, Inc. and Darrin Beaupre.	10-K	3/7/2023	10.10	
10.12#	Amended and Restated Employment Agreement, dated as of July 1, 2023 by and between IDEAYA Biosciences, Inc. and Andres Ruiz Briseno	10-Q	8/10/2023	10.5	
10.13#	Non-Employee Director Compensation Program.				X
10.14	Form of Indemnification Agreement for Directors and Officers.	S-1/A	5/13/2019	10.14	
10.15	Lease Agreement by and between IDEAYA Biosciences, Inc. and ARE-SAN FRANCISCO NO. 17, LLC dated as of August 26, 2016.	S-1	4/26/2019	10.15	
10.16	Letter Agreement Amendment to Lease Agreement by and between IDEAYA Biosciences, Inc. and ARE-SAN FRANCISCO NO. 17, LLC dated as of January 27, 2017.	S-1	4/26/2019	10.16	
10.17	First Amendment to Lease Agreement by and between IDEAYA Biosciences, Inc. and ARE-SAN FRANCISCO NO. 17, LLC dated as of May 31, 2018.	S-1	4/26/2019	10.17	
10.18	Second Amendment to Lease Agreement by and between IDEAYA Biosciences, Inc. and ARE-SAN FRANCISCO NO. 17, LLC dated as of September 30, 2019.	10-Q	11/13/2019	10.11	
10.19(a)†	Clinical Trial Collaboration and Supply Agreement by and between IDEAYA Biosciences, Inc. and Pfizer Inc. dated as of March 11, 2020.	10-Q	5/12/2020	10.4	
10.19(b)†	Amendment No. 1 to Clinical Trial Collaboration and Supply Agreement by and between Pfizer Inc. and IDEAYA Biosciences, Inc. dated as of September 23, 2020.	10-Q	11/12/2020	10.1	

10.19(c)†	Amendment No. 2 to Clinical Trial Collaboration and Supply Agreement by and between Pfizer Inc. and IDEAYA Biosciences, Inc. dated as of April 8, 2021.	10-Q	5/10/2021	10.1	
10.19(d)†	Amendment No. 3 to Clinical Trial Collaboration and Supply Agreement by and between Pfizer Inc. and IDEAYA Biosciences, Inc. dated as of August 9, 2021.	10-Q	11/15/2021	10.1	
10.19(e)†	Amendment No. 4 to Clinical Trial Collaboration and Supply Agreement by and between Pfizer Inc. and IDEAYA Biosciences, Inc. dated as of May 12, 2023	10-Q	8/10/2023	10.1	
10.20(a)†	Collaboration, Option and License Agreement by and between GlaxoSmithKline Intellectual Property (No. 4) Limited and IDEAYA Biosciences, Inc. dated as of June 15, 2020.	10-Q	8/12/2020	10.3	
10.20(b)	Amendment No. 1 to Collaboration, Option and License Agreement by and between GlaxoSmithKline Intellectual Property (No. 4) Limited and IDEAYA Biosciences, Inc. dated as of October 23, 2020.	10-K	3/18/2022	10.18	
10.20(c)†	Amendment No. 2. to Collaboration, Option and License Agreement by and between GlaxoSmithKline Intellectual Property (No. 4) Limited and IDEAYA Biosciences, Inc. dated as of January 31, 2022.	10-Q	5/10/2022	10.3	
10.21(a)†	Clinical Trial Collaboration and Supply Agreement by and between Pfizer Inc. and IDEAYA Biosciences, Inc. dated as of March 9, 2022.	10-Q	5/10/2022	10.1	
10.21(b)†	Amendment No. 1 to Clinical Trial Collaboration and Supply Agreement by and between Pfizer Inc. and IDEAYA Biosciences, Inc. dated as of May 12, 2023	10-Q	8/10/2023	10.2	
10.22†	Clinical Trial Collaboration and Supply Agreement by and between Amgen Inc. and IDEAYA Biosciences, Inc. dated as of July 26, 2022.	10-Q	11/8/2022	10.1	
10.23†	Clinical Trial Collaboration and Supply Agreement by and between Gilead Sciences, Inc. and IDEAYA Biosciences, Inc. dated as of November 29, 2023				X
10.24	Lease Agreement by and between DW LSP 5000 Shoreline, LLC and IDEAYA Biosciences, Inc. dated as of June 1, 2023.	10-Q	8/10/2023	10.3	
10.25	Office Lease Agreement by and between AAT TORREY 13-14, LLC and IDEAYA Biosciences, Inc. dated as of November 14, 2023				X
23.1	Consent of Independent Registered Public Accounting Firm.				X
24.1	Power of Attorney (included on signature page to this Annual Report on Form 10-K).				X

31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
32.1*	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
97	Policy for Recovery of Erroneously Awarded Compensation.	X
101.INS	Inline XBRL Instance Document	X
101.SCH	Inline XBRL Taxonomy Extension Schema with Embedded Linkbase Documents	X
104	Cover Page Interactive Data File (embedded with the Inline XBRL document)	X

† Certain information in this exhibit has been excluded pursuant to Regulation S-K, Item 601(b)(10).
# Indicates management contract or compensatory plan.
* The certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K is not deemed filed with the SEC and is not to be incorporated by reference into any filing of IDEAYA Biosciences, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary.

None.

INDEX TO THE FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of IDEAYA Biosciences, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying balance sheets of IDEAYA Biosciences, Inc. (the "Company") as of December 31, 2023 and 2022, and the related statements of operations and comprehensive loss, of stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2023, including the related notes (collectively referred to as the "financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2023, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2023 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2023, based on criteria established in *Internal Control - Integrated Framework*(2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's financial statements and on the Company's internal control over financial reporting 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 audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the financial statements 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. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's 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 for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued Research and Development Expenses Related to Contract Research Organizations

As described in Notes 2 and 4 to the financial statements, the Company has entered into various agreements with contract research organizations (CROs). The Company's accrued research and development expenses as of December 31, 2023 was $10.7 million, of which a portion relates to open agreements with CROs. The Company's research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development provided, but not yet invoiced, are included in accrued liabilities on the balance sheet. If the actual timing of the performance of services or the level of effort varies from the original estimates, management will adjust the accrual accordingly. Management's process involves reviewing open contracts and purchase orders, communicating with applicable personnel to identify services that have been performed, and estimating the level of service performed and the associated costs incurred based on vendor estimates for the services when the Company has not yet been invoiced or otherwise notified of actual costs.

The principal consideration for our determination that performing procedures relating to accrued research and development expenses related to CROs is a critical audit matter is a high degree of auditor effort in performing procedures related to the Company's accrued research and development expenses related to CROs.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the financial statements. These procedures included testing the effectiveness of controls relating to accrued research and development expenses, including controls related open agreements with CROs. These procedures also included, among others, testing research and development expenses related to CROs, on a sample basis, by obtaining and inspecting source documents, such as underlying agreements with CROs, purchase orders, invoices received, and information received from certain third party service providers.

/s/ PricewaterhouseCoopers LLP
San Jose, California
February 20, 2024

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

IDEAYA Biosciences, Inc.
Balance Sheets
(in thousands, except share and per share amounts)

	December 31,	
	2023	**2022**
Assets		
Current assets		
Cash and cash equivalents	$ 157,018	$ 68,632
Short-term marketable securities	368,096	296,197
Accounts receivable	18	211
Prepaid expenses and other current assets	7,500	5,414
Total current assets	532,632	370,454
Restricted cash	757	106
Long-term marketable securities	107,492	8,317
Property and equipment, net	6,164	6,509
Right-of-use assets	2,246	2,484
Other non-current assets	25	99
Total assets	$ 649,316	$ 387,969
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 6,598	$ 4,280
Accrued liabilities	18,756	16,999
Contract liability	—	8,568
Operating lease liabilities, current	1,747	1,871
Total current liabilities	27,101	31,718
Long-term contract liability	—	5,185
Long-term operating lease liabilities	1,125	1,611
Total liabilities	28,226	38,514
Commitments and contingencies (Note 6)		
Stockholders' equity		
Preferred stock, $0.0001 par value, 10,000,000 shares authorized as of December 31, 2023 and December 31, 2022; no shares issued and outstanding as of December 31, 2023 and December 31, 2022	—	—
Common stock, $0.0001 par value, 300,000,000 shares authorized as of December 31, 2023 and December 31, 2022; 65,039,369 and 48,193,179 shares issued and outstanding as of December 31, 2023 and December 31, 2022	7	5
Additional paid-in capital	968,885	587,724
Accumulated other comprehensive income (loss)	562	(2,871)
Accumulated deficit	(348,364)	(235,403)
Total stockholders' equity	621,090	349,455
Total liabilities and stockholders' equity	$ 649,316	$ 387,969

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

IDEAYA Biosciences, Inc.
Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2023	**2022**	**2021**
Collaboration revenue	$ 23,385	$ 50,931	$ 27,941
Total revenue	23,385	50,931	27,941
Operating expenses			
Research and development	129,508	89,536	58,158
General and administrative	28,306	23,897	20,051
Total operating expenses	157,814	113,433	78,209
Loss from operations	(134,429)	(62,502)	(50,268)
Other income			
Interest income and other income (expense), net	21,468	3,847	506
Net loss	(112,961)	(58,655)	(49,762)
Unrealized gains (losses) on marketable securities	3,433	(2,159)	(719)
Comprehensive loss	$ (109,528)	$ (60,814)	$ (50,481)
Net loss per common share, basic and diluted	$ (1.96)	$ (1.42)	$ (1.41)
Weighted-average number of common shares outstanding used in computing net loss per share, basic and diluted	57,519,929	41,444,696	35,252,443

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

IDEAYA Biosciences, Inc.
Statements of Stockholders' Equity
(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balances as of January 1, 2021	29,537,216	$ 3	$ 325,250	$ 7	$ (126,986)	$ 198,274
Issuance of common stock upon follow-on public offering, net of issuance costs	5,333,333	1	85,989	—	—	85,990
Issuance of common stock related to at-the-market offering program, net of issuance costs	3,407,872	—	57,263	—	—	57,263
Issuance of common stock upon exercise of stock options	211,900	—	1,510	—	—	1,510
Employee stock purchase plan (ESPP) purchase	50,037	—	697	—	—	697
Repurchase of unvested restricted stock	(7,313)	—	—	—	—	—
Vesting of early exercised common stock options and restricted stock	—	—	24	—	—	24
Stock-based compensation	—	—	8,237	—	—	8,237
Other comprehensive loss	—	—	—	(719)	—	(719)
Net loss	—	—	—	—	(49,762)	(49,762)
Balances as of December 31, 2021	38,533,045	4	478,970	(712)	(176,748)	301,514
Issuance of common stock upon follow-on public offering, net of issuance costs	8,761,905	1	86,080	—	—	86,081
Issuance of common stock related to at-the-market offering program, net of issuance costs	601,844	—	8,842	—	—	8,842
Issuance of common stock upon exercise of stock options	214,643	—	1,448	—	—	1,448
Employee stock purchase plan (ESPP) purchase	81,742	—	755	—	—	755
Stock-based compensation	—	—	11,629	—	—	11,629
Other comprehensive loss	—	—	—	(2,159)	—	(2,159)
Net loss	—	—	—	—	(58,655)	(58,655)
Balances as of December 31, 2022	48,193,179	5	587,724	(2,871)	(235,403)	349,455
Issuance of common stock upon follow-on public offering, net of issuance costs	14,655,993	2	281,120	—	—	281,122
Issuance of pre-funded warrants for the purchase of common stock	—	—	42,182	—	—	42,182
Issuance of common stock related to at-the-market offering program, net of issuance costs	1,188,705	—	28,598	—	—	28,598
Issuance of common stock upon exercise of stock options	931,012	—	9,559	—	—	9,559
Employee stock purchase plan (ESPP) purchase	70,480	—	1,213	—	—	1,213
Stock-based compensation	—	—	18,489	—	—	18,489
Other comprehensive gain	—	—	—	3,433	—	3,433
Net loss	—	—	—	—	(112,961)	(112,961)
Balances as of December 31, 2023	65,039,369	$ 7	$ 968,885	$ 562	$ (348,364)	$ 621,090

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

IDEAYA Biosciences, Inc.
Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2023	**2022**	**2021**
Cash flows from operating activities			
Net loss	$ (112,961)	$ (58,655)	$ (49,762)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization	2,476	2,101	1,725
Net amortization (accretion) of premiums (discounts) on marketable securities	(11,553)	(695)	1,834
Stock-based compensation	18,489	11,629	8,237
Amortization of right of use assets	1,532	1,414	1,307
Changes in assets and liabilities			
Accounts receivable	193	892	774
Prepaid expenses and other assets	(2,045)	(2,119)	(189)
Accounts payable	2,635	1,864	1,166
Accrued and other liabilities	1,635	4,572	4,212
Contract liabilities	(13,753)	(46,479)	(23,541)
Lease liabilities	(1,872)	(1,699)	(1,542)
Net cash used in operating activities	(115,224)	(87,175)	(55,779)
Cash flows from investing activities			
Purchases of property and equipment, net	(2,368)	(3,443)	(2,644)
Purchases of marketable securities	(595,980)	(255,808)	(314,996)
Maturities of marketable securities	439,892	225,847	243,956
Sales of marketable securities	-	-	4,018
Net cash used in investing activities	(158,456)	(33,404)	(69,666)
Cash flows from financing activities			
Proceeds from issuance of common stock in public offering, net of issuance costs	281,165	86,105	85,990
Proceeds from issuances of pre-funded warrants	42,182	—	—
Proceeds from issuance of common stock related to at-the-market offering program, net of issuance costs	28,598	8,857	57,263
Proceeds from exercise of common stock options, net of repurchases	9,559	1,448	1,504
Proceeds from ESPP purchases	1,213	755	697
Net cash provided by financing activities	362,717	97,165	145,454
Net increase (decrease) in cash, cash equivalents and restricted cash	89,037	(23,414)	20,009
Cash, cash equivalents and restricted cash			
Cash, cash equivalents and restricted cash, at beginning of period	68,738	92,152	72,143
Cash, cash equivalents and restricted cash, at end of period	$ 157,775	$ 68,738	$ 92,152
Reconciliation of cash, cash equivalents and restricted cash			
Cash and cash equivalents	$ 157,018	$ 68,632	$ 92,046
Restricted cash	$ 757	$ 106	$ 106
Cash, cash equivalents and restricted cash	$ 157,775	$ 68,738	$ 92,152
Supplemental disclosure of cash flow information:			
Cash paid for income taxes	$ —	$ —	$ 4
Cash paid for interest	$ 69	$ 60	$ 71
Supplemental non-cash investing and financing activities:			
Vesting of early exercised options and restricted stock	$ —	$ —	$ 24
Purchases of property and equipment in accounts payable and accrued liabilities	$ 147	$ 384	$ 92
Right-of-use asset obtained in exchange for a new operating lease liability	$ 1,294	$ —	$ —
Unpaid offering costs	$ 43	$ 39	$ —

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

1. Organization

Description of the Business

IDEAYA Biosciences, Inc. (the "Company") is a synthetic lethality-focused precision medicine oncology company committed to the discovery and development of targeted therapeutics for patient populations selected using molecular diagnostics. The Company is headquartered in South San Francisco, California and was incorporated in the State of Delaware in June 2015. To date, the Company has been primarily engaged in business planning, research, development, recruiting and raising capital.

Follow-On Offering

On September 19, 2022, we completed an underwritten public offering of 8,761,905 shares of our common stock at an offering price to the public of $10.50 per share, including 1,142,857 shares of common stock upon the exercise in full of the overallotment option by the underwriters, pursuant to which we received aggregate net proceeds of $86.1 million, after deducting underwriting discounts and commissions and other offering expenses.

On April 27, 2023, the Company completed an underwritten public follow-on offering. The offering consisted of 8,858,121 shares of our common stock at an offering price to the public of $18.50 per share, including 1,418,920 shares of common stock upon the exercise in full of the overallotment option by the underwriters, as well as pre-funded warrants to purchase 2,020,270 shares of common stock at a public offering price of $18.4999 per underlying share, in each case before underwriting discounts and commissions. Pursuant to the offering, we received aggregate gross proceeds of approximately $201.3 million, before deducting underwriting discounts and commissions and other offering expenses, resulting in net proceeds of approximately $188.7 million, after deducting underwriting discounts and commissions and other offering expenses.

On October 27, 2023, the Company completed a further underwritten public follow-on offering. The offering consisted of 5,797,872 shares of our common stock at an offering price to the public of $23.50 per share, including 797,872 shares of common stock upon the exercise in full of the overallotment option by the underwriters, as well as pre-funded warrants to purchase 319,150 shares of common stock at a public offering price of $23.4999 per underlying share, in each case before underwriting discounts and commissions. Pursuant to the offering, we received aggregate gross proceeds of approximately $143.7 million, before deducting underwriting discounts and commissions and other offering expenses, resulting in net proceeds of approximately $134.6 million, after deducting underwriting discounts and commissions and other offering expenses.

At-the-Market Offering

Our Registration Statement on Form S-3, which was filed under the Securities Act, and became effective as of June 10, 2020, lapsed in June 2023. The January 2021 Sales Agreement was automatically terminated concurrently therewith. As of the termination date of the January 2021 Sales Agreement, approximately $61.8 million of common stock remained available to be sold under the at-the-market facility associated therewith.

On June 26, 2023, we filed a new Registration Statement on Form S-3 (File No. 333- 272936) under the Securities Act as an automatic shelf registration statement as a "well-known seasoned issuer", as defined in Rule 405 under the Securities Act. On June 26, 2023, we also entered into a new Open Market Sales Agreement, or June 2023 Sales Agreement, with Jefferies LLC ("Jefferies") relating to an at-the-market offering program under which we may offer and sell, from time to time at our sole discretion, shares of our common stock, par value $0.0001 per share, having aggregate gross proceeds of up to $250.0 million through Jefferies as sales agent.

During the year ended December 31, 2023, we sold an aggregate of 1,188,705 shares of our common stock through at-the-market offerings for aggregate net proceeds of $28.6 million, after deducting underwriting discounts and commissions and other offering expenses, at a weighted average sales price of approximately $25.30 per share under the at-the-market offering pursuant to the January 2021 Sales Agreement and June 2023 Sales Agreement with Jefferies as sales agent. As of December 31, 2023, approximately $222.5 million of common stock remained available to be sold under the June 2023 Sales Agreement with Jefferies as sales agent.

We may cancel our at-the-market program at any time upon written notice, pursuant to its terms.

Liquidity

The Company has incurred significant losses and negative cash flows from operations in all periods since inception and had an accumulated deficit of $348.4 million as of December 31, 2023.

The Company has historically financed its operations primarily through the sale of convertible notes, redeemable convertible preferred stock and common stock, pre-funded warrants, and payments received from its collaboration arrangement.

To date, none of the Company's product candidates have been approved for sale, and the Company has not generated any revenue from commercial products since inception. Management expects operating losses to continue and increase for the foreseeable future, as the Company progresses into clinical development activities for its lead product candidates. The Company's prospects are subject to risks, expenses and uncertainties frequently encountered by companies in the biotechnology industry as discussed under Risks and Uncertainties in Note 2. While the Company has been able to raise multiple rounds of financing, there can be no assurance that in the event the Company requires additional financing, such financing will be available on terms which are favorable or at all. Failure to generate sufficient cash flows from operations, raise additional capital or reduce certain discretionary spending would have a material adverse effect on the Company's ability to achieve its intended business objectives.

As of December 31, 2023, the Company had cash, cash equivalents and marketable securities of $632.6 million. Management believes that the Company's current cash, cash equivalents and marketable securities will be sufficient to fund its planned operations for at least 12 months from the date of the issuance of these financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

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

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. Such estimates include useful lives of property and equipment, determination of the discount rate for operating leases, accruals for research and development activities, revenue recognition, stock-based compensation, and income taxes. On an ongoing basis, management reviews these estimates and assumptions. Changes in facts and circumstances may alter such estimates and actual results could differ from those estimates.

Segments

The Company operates and manages its business as one operating and reportable segment, which is the business of research and development for oncology-focused precision medicine. The Company's chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance. All of the Company's long-lived assets are located in the United States.

Risks and Uncertainties

The Company operates in a dynamic and highly competitive industry and is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, protection of proprietary technology, dependence on key personnel, contract manufacturers, contract research organizations and collaboration partners, compliance with government regulations and the need to obtain additional financing to fund operations. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical studies and clinical trials and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance and reporting. The Company believes that changes in any of the following areas could have a material adverse effect on the Company's future financial position, results of operations, or cash flows: ability to obtain future financing; advances and trends in new technologies and industry standards; results of clinical trials and collaboration activities; regulatory approval and market acceptance of the Company's products; development of sales channels; certain strategic relationships; litigation or claims against the Company based on intellectual property, patent, product, regulatory, or other factors; and the Company's ability to attract and retain employees necessary to support its growth.

Products developed by the Company require approvals from the U.S. Food and Drug Administration ("FDA") or other international regulatory agencies prior to commercial sales. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained or maintained, that the products will receive the necessary approvals, or that any approved products will be commercially viable. If the Company was denied approval, approval was delayed or the Company was unable to maintain approval, 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 generate revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from other pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees, consultants and other third parties.

The Company has expended and will continue to expend substantial funds to complete the research, development and clinical testing of product candidates. The Company also will be required to expend additional funds to establish commercial-scale manufacturing arrangements and to provide for the marketing and distribution of products that receive regulatory approval. The Company may require additional funds to commercialize its products. The Company is unable to entirely fund these efforts with its current financial resources. If adequate funds are unavailable on a timely basis from operations or additional sources of financing, the Company may have to delay, reduce the scope of or eliminate one or more of its research or development programs which would materially and adversely affect its business, financial condition and operations.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents and marketable securities. Substantially all the Company's cash is held by two financial institutions that management believes are of high credit quality. Such deposits may, at times, exceed federally insured limits.

The Company's investment policy addresses credit ratings, diversification, and maturity dates. The Company invests its cash equivalents and marketable securities in money market funds, U.S. government securities, commercial paper, and corporate bonds. The Company limits its credit risk associated with cash equivalents and marketable securities by placing them with banks and institutions it believes are creditworthy and in highly rated investments and, by policy, limits the amount of credit exposure with any one commercial issuer. The Company has not experienced any credit losses on its deposits of cash, cash equivalents or marketable securities.

Cash Equivalents

Cash equivalents that are readily convertible to cash are stated at cost, which approximates fair value. The Company considers all highly liquid investments purchased with an original or remaining maturity of three months or less at the date of purchase to be cash equivalents.

Restricted Cash

Restricted cash as of December 31, 2023 and December 31, 2022 consisted of cash balances held as security in connection with the Company's facility lease agreements in South San Francisco, California and San Diego, California. The balances are classified as long-term assets on the Company's balance sheet.

Marketable Securities

Marketable securities are investments in marketable securities with maturities greater than three months at the time of purchase. The Company determines the appropriate classification of its investments in marketable securities at the time of purchase and reevaluates such designation at each balance sheet date. The Company has classified and accounted for its marketable securities as available-for-sale. After consideration of the Company's risk versus reward objectives and liquidity requirements, the Company may sell these securities prior to their stated maturities. The Company classifies highly liquid securities with maturities beyond 12 months as long-term marketable securities in the balance sheet. These securities are carried at fair value as determined based upon quoted market prices or pricing models for similar securities. Unrealized gains and losses, if any, are excluded from earnings and are reported as a component of accumulated other comprehensive income (loss). The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income and other income (expense), net on the statements of operations and comprehensive loss. Realized gains and losses, if any, on available-for-sale securities are included in interest income and other income (expense), net. The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

Fair Value of Financial Instruments

The carrying amounts of the Company's certain financial instruments, including cash equivalents, accounts receivable, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities and market interest rates if applicable. Refer to Note 3 for details on the fair value of marketable securities.

Property and Equipment, Net

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, which is generally between three and five years. Leasehold improvements are stated at cost and amortized over the shorter of the useful lives of the assets or the lease term. Maintenance and repairs are charged to expense as incurred. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the balance sheet and any resulting gain or loss is reflected in the statements of operations and comprehensive loss in the period realized.

Impairment of Long-Lived Assets

The Company reviews property and equipment for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset or asset group may not be recoverable. Recoverability is measured by comparison of the carrying amount of the asset or asset group to the future net cash flows which the asset or asset group is expected to generate. If such asset or asset group is considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset or asset group exceeds the fair value of the asset or asset group. There have been no such impairments of long-lived assets for the years ended December 31, 2023 and December 31, 2022.

Leases

The Company determines if an arrangement is a lease, or contains a lease, at its inception. Operating leases are included in right-of-use ("ROU") assets, lease liabilities, and long-term lease liabilities on the Company's balance sheet.

ROU assets and lease liabilities are recognized based on the present value of the future lease payments over the lease term at commencement date. As most of the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of future payments. The ROU asset also includes any lease payments made to the lessor at or before the commencement date, minus lease incentives received, and initial direct costs incurred. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Lease expense for lease payments is recognized on a straight-line basis over the lease term. The Company combines lease and nonlease components.

Cloud Computing Arrangements

The Company capitalizes certain implementation costs incurred under a cloud computing arrangement that is a service contract. Costs incurred during the application development stage related to the implementation of the hosting arrangement are capitalized and included within prepaid expenses and other current assets, and other non-current assets on the accompanying balance sheets. Amortization of capitalized implementation costs is recognized on a straight-line basis over the term of the associated hosting arrangement when it is ready for its intended use. Costs related to preliminary project activities and post-implementation activities are expensed as incurred.

Revenue Recognition

The Company follows Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation.

The Company applies the five-step model to contracts when (1) parties have approved the contract and are committed to performing respective obligations, (2) the Company can identify each party's rights regarding the goods or services to be transferred, (3) the Company can identify the payment terms for the goods or services to be transferred, (4) the contract has commercial substance, and (5) it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, the Company assesses the goods or services promised within each contract and determines the performance obligations by assessing whether each promised good or service is distinct. Goods or services that are not distinct are bundled with other goods or services in the contract until a bundle of goods or services that is distinct is created. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligations when (or as) the performance obligations are satisfied. The Company constrains its estimate of the transaction price up to the amount (the "variable consideration constraint") that a significant reversal of recognized revenue is not probable.

Licenses of intellectual property: If a license to the Company's intellectual property is determined to be distinct from the other promised goods or services identified in an arrangement, the Company recognizes revenue from non-refundable, upfront fees allocated to the license at the point in time when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other goods or services, the Company applies 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 toward satisfying the performance obligation for purposes of recognizing revenue from non-refundable, upfront fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of progress and related revenue recognition.

Customer options for additional goods or services: If a contract contains customer options that allow the customer to acquire additional goods or services, including a license to the Company's intellectual property, the goods and services underlying the customer options are evaluated to determine whether they are deemed to represent a material right. In determining whether the customer option has a material right, the Company assesses whether there is an option to acquire additional goods or services at a discount. If the customer option is determined not to represent a material right, the option is not considered to be a performance obligation. If the customer option is determined to represent a material right, the material right is recognized as a separate performance obligation. The Company allocates the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until the option is exercised.

Milestone payments: At the inception of each arrangement or amendment that includes development, regulatory or commercial milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price. ASC 606 prescribes two methods to use when estimating the amount of variable consideration: the expected value method and the most likely amount method. Under the expected value method, an entity considers the sum of probability-weighted amounts in a range of possible consideration amounts. Under the most likely amount method, an entity considers the single most likely amount in a range of possible consideration amounts. The Company uses the expected value method to estimate the amount of variable consideration related to the reimbursement of Pol Theta and WRN program costs which is consistently applied throughout the life of the contract: however, it is not necessary for the Company to use the same approach for all contracts. If it is probable that a significant revenue reversal would not occur when the uncertainty associated with the milestone is resolved, the associated milestone value is included in the transaction price. Milestone payments that are highly susceptible to factors outside the Company's influence, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. If there is more than one performance obligation, the transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis. The Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability or achievement of each milestone and any related constraint, and if necessary, adjusts its estimates 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.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license 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).

Upfront payments and fees are recorded as contract liabilities upon receipt or when due and may require deferral of revenue recognition to a future period until the Company performs its obligations under these arrangements. Amounts payable to the Company are recorded as accounts receivable when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

Contractual cost sharing payments received from a customer or collaboration partner are accounted for as variable consideration. The Company includes an expected value in the transaction price. Contractual cost sharing payments made to a customer or collaboration partner are accounted for as a reduction to the transaction price if such payments are not related to distinct goods or services received from the customer or collaboration partner.

Contracts may be amended to account for changes in contract specifications and requirements. Contract modifications exist when the amendment either creates new, or changes existing, enforceable rights and obligations. When contract modifications create new performance obligations and the increase in consideration approximates the standalone selling price for goods and services related to such new performance obligations as adjusted for specific facts and circumstances of the contract, the modification is accounted for as a separate contract. If a contract modification is not accounted for as a separate contract, the Company accounts for the promised goods or services not yet transferred at the date of the contract modification (the remaining promised goods or services) prospectively, as if it were a termination of the existing contract and the creation of a new contract, if the remaining goods or services are distinct from the goods or services transferred on or before the date of the contract modification. The Company accounts for a contract modification as if it were a part of the existing contract if the remaining goods or services are not distinct and, therefore, form part of a single performance obligation that is partially satisfied at the date of the contract modification. In such case, the effect that the contract modification has on the transaction price, and on the entity's measure of progress toward complete satisfaction of the performance obligation, is recognized as an adjustment to revenue (either as an increase in or a reduction of revenue) at the date of the contract modification (the adjustment to revenue is made on a cumulative catch-up basis).

Upfront payment contract liabilities resulting from the Company's license and collaboration agreements do not represent a financing component as the payment is not financing the transfer of goods and services, and the technology underlying the licenses granted reflects research and development expenses already incurred by the Company. As such, the Company does not adjust its revenues for the effects of a significant financing component. Amounts received prior to satisfying the revenue recognition criteria are recorded as contract liability in the Company's balance sheets. If the related performance obligation is expected to be satisfied within the next twelve (12) months, this will be classified and included within current contract liability.

Research and Development Expenses

Research and development expenses consist of compensation costs, employee benefit costs, costs for contract manufacturing organizations ("CMOs"), costs for contract research organizations ("CROs"), costs for clinical trials, costs for sponsored research, consulting costs, costs for laboratory supplies, costs for product licenses, facility-related expenses and depreciation. All research and development costs are charged to research and development expenses as incurred and included within the statements of operations and comprehensive loss. 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 also 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.

Accrued Research and Development Expenses

The Company has entered into various agreements with CMOs and CROs. The Company's research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development provided, but not yet invoiced, are included in accrued liabilities on the balance sheet. 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. Payments made to CMOs and CROs under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets until the services are rendered. Management's process involves reviewing open contracts and purchase orders, communicating with applicable personnel to identify services that have been performed, and estimating the level of service performed and the associated costs incurred based on vendor estimates for the services when the Company has not yet been invoiced or otherwise notified of actual costs.

Stock-Based Compensation

The Company accounts for stock-based compensation arrangements with employees and non-employees in accordance with ASC 718, *Stock Compensation.* The Company accounts for stock-based compensation arrangements using a fair value method which requires the recognition of compensation expense related to all stock-based awards. The fair value method requires the Company to estimate the fair value of stock option awards on the date of grant using an option pricing model. The Company uses the Black-Scholes option pricing model to determine the fair value of options granted, which is expensed on a straight-line basis over the vesting period. Generally, the stock options granted by the Company to its employees have a 10-year term and vest over a 4-year period with 1-year cliff vesting.

Income Taxes

The Company accounts for income taxes using the asset and liability method whereby deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that are currently in effect unless such rate is expected to be different when the deferred item reverses. Valuation allowances are established where necessary to reduce deferred tax assets to the amounts expected to be realized. Deferred tax assets and liabilities are classified as noncurrent on the balance sheet.

The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. Recognized income tax positions are measured at the largest amount that has a greater than 50% likelihood of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. The Company records interest and penalties related to unrecognized tax benefits in interest expense and other expense, respectively.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' equity that are excluded from net loss, primarily unrealized gains and losses from the Company's marketable securities.

Net Loss per Share Attributable to Common Stockholders

Basic net loss per common share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common stock outstanding during the period, without consideration of potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common stock and potentially dilutive securities outstanding for the period. Pre-funded warrants are included in the calculation of basic and diluted earnings per share. For purposes of the diluted net loss per share calculation, stock options, restricted stock and restricted stock that is subject to repurchase at the original purchase price are considered to be potentially dilutive securities. The Company considers the shares issued upon the early exercise of stock options subject to repurchase to be participating securities, because holders of such shares have non-forfeitable dividend rights in the event a dividend is paid on common stock. The holders of early exercised shares subject to repurchase do not have a contractual obligation to share in the Company's losses. As such, the net loss was attributed entirely to common stockholders. Because the Company has reported a net loss for all periods presented, diluted net loss per common share is the same as basic net loss per common share for those periods.

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB") under its accounting standard codifications ("ASC") or other standard setting bodies and adopted by the Company as of the specified effective date, unless otherwise discussed below.

New Accounting Pronouncements Adopted

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments,* which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss model. It also eliminates the concept of other-than-temporary impairment and requires credit losses related to available-for-sale debt securities to be recorded through an allowance for credit losses rather than as a reduction in the amortized cost basis of the securities. These changes will result in earlier recognition of credit losses. For public business entities, this ASU is effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. The FASB subsequently issued supplemental guidance to ASC 326 within ASU 2019-05, *Financial Instruments—Credit Losses (Topic 326): Targeted Transition Relief*, ASU 2019-10, *Financial Instruments—Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842)* and ASU 2019-11, *Codification Improvements to Topic 326, Financial Instruments—Credit Losses*. ASU 2019-05 provides an option to irrevocably elect the fair value option for certain financial assets previously measured at amortized cost basis. ASU 2019-10 extended the effectiveness of Topic 326 for smaller reporting companies until fiscal years beginning after December 15, 2022. As of January 1, 2024, the Company is no longer a smaller reporting company. The Company adopted this ASU on January 1, 2023, and evaluated the impact of the adoption of the ASU. It did not result in a material impact on the Company's financial statements and related disclosures.

New Accounting Pronouncements Issued, Not yet Adopted

On October 2023, the FASB issued ASU 2023-06, Disclosure Improvements: Codification Amendments in Response to the SEC's Disclosure Update and Simplification Initiative, which modifies the disclosure or presentation requirements related to variety of FASB Accounting Standard Codification topics. The effective date for each amendment will be the date on which the SEC's removal of that related disclosure from Regulation S-X or Regulation S-K is effective. If by June 30, 2027, the SEC has not removed the applicable requirement from Regulation S-X or Regulation S-K, the pending content of the associated amendment will be removed from the Codification and will not become effective for any entities. We are currently evaluating the effect of adopting this ASU.

On December 14, 2023, the FASB issued ASU 2023-09, Improvements to Income Tax Disclosures, which amends the guidance in ASC 740, Income Taxes. The ASU is intended to improve the transparency of income tax disclosures by requiring (1) consistent categories and greater disaggregation of information in the rate reconciliation and (2) income taxes paid disaggregated by jurisdiction. It also includes certain other amendments to improve the effectiveness of income tax disclosures. The ASU's amendments are effective for public business entities for annual periods beginning after December 15, 2024. Entities are permitted to early adopt the standard "for annual financial statements that have not yet been issued or made available for issuance." Adoption is either prospectively or retrospectively, the Company will adopt this ASU on a prospective basis. The Company is currently evaluating the impact of the ASU but does not expect any material impacts upon adoption.

3. Fair Value Measurement and Marketable Securities

The Company applies fair value accounting for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, a three-tier fair value hierarchy has been established, which prioritizes the inputs used in measuring fair value as follows:

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

Level 2—Observable inputs other than Level 1 prices such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3—Unobservable inputs which reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

In determining fair value, the Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible as well as considers counterparty credit risk in its assessment of fair value.

As of December 31, 2023, financial assets measured and recorded at fair value are as follows (in thousands):

		December 31, 2023			
		Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Assets					
U.S. government securities[1]	Level 2	$ 412,679	$ 591	$ (135)	$ 413,135
Corporate bonds	Level 2	53,983	197	(32)	54,148
Commercial paper[2]	Level 2	126,601	—	(58)	126,543
Marketable securities		593,263	788	(225)	593,826
Money market funds[3]	Level 1	38,300	—	—	38,300
Total fair value of assets		$ 631,563	$ 788	$ (225)	$ 632,126

(1) $37.8 million was included in cash and cash equivalents on the balance sheet due to securities with purchase dates within 90 days of maturity dates

(2) $80.4 million was included in cash and cash equivalents on the balance sheet due to securities with purchase dates within 90 days of maturity dates

(3) Included in cash and cash equivalents on the balance sheet

As of December 31, 2022, financial assets measured and recognized at fair value are as follows (in thousands):

		December 31, 2022			
		Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Assets					
U.S. government securities	Level 2	$ 146,030	$ —	$ (2,291)	$ 143,739
Corporate bonds	Level 2	86,546	—	(580)	85,966
Commercial paper[1]	Level 2	78,797	—	—	78,797
Marketable securities		311,373	—	(2,871)	308,502
Money market funds[2]	Level 1	64,153	—	—	64,153
Total fair value of assets		$ 375,526	$ —	$ (2,871)	$ 372,655

(1) $4.0 million was included in cash and cash equivalents on the balance sheet due to securities with purchase dates within 90 days of maturity dates

(2) Included in cash and cash equivalents on the balance sheet

As of December 31, 2023 and December 31, 2022, all marketable securities had a remaining maturity of less than two years. There were no financial liabilities measured and recognized at fair value as of December 31, 2023 and December 31, 2022.

The Company considers available evidence in evaluating potential other-than-temporary impairments of its marketable securities, including the duration and extent to which fair value is less than cost, and the Company's ability and intent to hold the investment. As of December 31, 2023 and December 31, 2022, the Company held certain securities in an unrealized loss position. These unrealized losses were considered to be temporary as the Company expects to recover the entire amortized cost basis on the securities in unrealized loss positions based on the creditworthiness of the underlying issuer, and the Company neither intends to sell these securities nor considers it more likely than not that the Company would be required to sell any such security before its anticipated recovery. As a result, the Company did not consider any of these investments to be other-than-temporarily impaired at December 31, 2023 and December 31, 2022.

4. Balance Sheet Components

Property and Equipment, Net

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

	Useful Life (In Years)	As of December 31,	
		2023	2022
Laboratory equipment	5	$ 11,455	$ 9,743
Computer equipment	3	261	261
Software	3	231	231
Leasehold improvements	Shorter of useful life or lease term	3,321	3,321
Furniture and fixtures	5	507	506
Total property and equipment		15,775	14,062
Less: Accumulated depreciation and amortization		(9,611)	(7,553)
Property and equipment, net		$ 6,164	$ 6,509

Depreciation and amortization expense was $2.5 million, $2.1 million and $1.7 million for the years ended December 31, 2023, December 31, 2022 and December 31, 2021, respectively.

Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	As of December 31,	
	2023	2022
Accrued research and development expenses	$ 10,676	$ 11,146
Accrued salaries and benefits	6,974	5,248
Legal and professional fees	959	513
Other	147	92
Accrued liabilities	$ 18,756	$ 16,999

5. Operating Leases

The Company leases its laboratory and office facilities in South San Francisco for approximately 29,000 square feet with an expiration date in July 2024.

In June 2023, we entered into a lease agreement for approximately 44,000 square feet of space at 5000 Shoreline Court, South San Francisco, California. The estimated commencement date is June 2024 and the lease term is one hundred twenty months. The Company has the option to extend the lease term for two consecutive five-year periods.

In November 2023, we entered into a lease agreement for approximately 5,700 square feet of space at 11710 El Camino Real, San Diego, California for corporate office space. The lease commenced in December 2023 and expires in March 2028. We have an option to renew the lease for 3 years. The Company recorded a right-of-use asset and lease liability related to the lease upon its commencement date in December 2023. As of December 31, 2023, the balances of the right-of-use asset and the lease liability were $1.3 million each.

Future minimum lease payments under operating leases included on the Company's balance sheet are as follows:

(in thousands)	As of December 31, 2023
2024	1,897
2025	387
2026	398
2027	410
2028	106
Total future minimum lease payments	3,198
Less: imputed interest	(326)
Total operating lease liabilities	2,872

The following table summarizes other information about the Company's operating leases:

	As of December 31,	
	2023	2022
Weighted-average remaining lease term	2.4	1.6
Weighted-average discount rate	8.0%	6.9%

Operating lease costs were $1.7 million for each of the years ended December 31, 2023, 2022 and 2021. Variable lease costs were $1.4 million, $1.0 million, and $1.0 million for the years ended December 31, 2023, 2022, and 2021, respectively. Variable lease costs represent additional costs incurred, related to administration, maintenance and property tax costs incurred, which are billed based on both usage and as a percentage of the Company's share of total square footage.

During the years ended December 31, 2023, 2022 and 2021, cash paid for amounts included in the measurement of lease liabilities and included within cash used in operating activities in the statement of cash flows was $2.0 million, $2.0 million and $1.9 million, respectively.

6. Commitments and Contingencies

Contingencies

From time to time, the Company may be involved in litigation related to claims that arise in the ordinary course of its business activities. The Company accrues for these matters when it is probable that future expenditures will be made and these expenditures can be reasonably estimated. As of December 31, 2023, the Company does not believe that any such matters, individually or in the aggregate, will have a material adverse effect on the Company's financial position, results of operations or cash flows.

Indemnification

The Company enters into standard indemnification arrangements in the ordinary course of business with vendors, clinical trial sites and other parties. Pursuant to these arrangements, the Company indemnifies, holds harmless and agrees to reimburse the indemnified parties for losses suffered or incurred by the indemnified party. The term of these indemnification agreements is generally perpetual any time after the execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these arrangements is not determinable. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements. Accordingly, the Company has not recorded a liability related to such indemnification agreements as of December 31, 2023.

7. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2023, December 31, 2022 and December 31, 2021. The Company has incurred net operating losses only in the United States since its inception. The Company has not reflected any benefit of such net operating loss carryforwards in the financial statements.

The provision for income taxes differs from the amount expected by applying the federal statutory rate to the loss before taxes as follows:

	Year Ended December 31,		
	2023	2022	2021
Federal statutory income tax rate	21.0%	21.0%	21.0%
State income taxes	1.3%	1.9%	0.7%
Change in valuation allowance	(29.1%)	(23.4%)	(25.2%)
Stock Based Compensation	0.7%	(1.2%)	(0.2%)
Research tax credits	8.3%	4.4%	3.8%
Other permanent differences	(0.1%)	(0.1%)	(0.1%)
Section 162(m) Limitation	(2.1%)	(2.6%)	0.0%
Provision for income taxes	0.0%	0.0%	0.0%

The tax effects of temporary differences and carryforwards of the deferred tax assets are presented below (in thousands):

	As of December 31,	
	2023	2022
Deferred tax assets:		
Net operating loss carryforwards	$ 34,717	$ 31,777
Research and development credit carryforwards	19,997	9,454
Lease liability	610	739
Intangible assets	1,096	1,166
Stock-based compensation	2,593	1,713
Accruals and reserves	1,257	1,666
Deferred revenue	-	2,881
Capitalized research & development expenditures	36,267	15,134
Gross deferred tax assets	96,537	64,530
Less: Valuation allowance	(95,888)	(63,761)
Deferred tax assets, net of valuation allowance	649	769
Deferred tax liabilities:		
Right-of-use assets	(477)	(527)
Property and equipment	(172)	(242)
Net deferred tax assets	$ —	$ —

The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

ASC 740 requires that the tax benefit of net operating losses, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is "more likely than not." Realization of the future tax benefits is dependent on the Company's ability to generate sufficient taxable income within the carryforward period. Because of the Company's recent history of operating losses, management believes that recognition of the deferred tax assets arising from the above-mentioned future tax benefits is currently not likely to be realized and, accordingly, has provided a valuation allowance.

As of December 31, 2023, the Company had net operating loss carryforwards of $135.3 million available to reduce future taxable income, if any, for federal income tax purposes. As of December 31, 2023, the Company had net operating loss carryforwards of $89.6 million available to reduce future taxable income, if any, for state income tax purposes. If not utilized, the federal carryforwards of $11.6 million and the state carryforwards of $89.6 million will begin to expire in 2037 and 2036, respectively. The federal net operating loss carryforwards of $123.7 million arising after December 31, 2017 do not expire.

The Company also had federal and state research and development credit carryforwards of $12.0 million and $6.4 million, respectively. The Company also had Orphan Drug Credits, or ODC, related to the orphan drug designation of darovasertib in 2022, of $6.3 million. The federal credits will expire starting in 2037 if not utilized, and the state research credit can be carried forward indefinitely.

The Tax Reform Act of 1986 limits the use of net operating loss carryforwards in certain situations where changes occur in the stock ownership of a company. The annual limitation may result in the expiration of net operating losses and credits before utilization. The Company performed a Section 382 analysis through December 31, 2023. The Company has not experienced ownership changes in the current year. Subsequent ownership changes may affect the limitation in future years.

Related to unrecognized tax benefits noted below, the Company accrued no penalties or interest during the years ended December 31, 2023, December 31, 2022 and December 31, 2021. The Company does not expect its unrecognized tax benefit balance to change materially over the next 12 months.

The Company had $3.8 million and $2.0 million of unrecognized tax benefits as of December 31, 2023 and December 31, 2022, respectively.

The following table summarizes the activity related to the Company's unrecognized tax benefits (in thousands).

Balance as of January 1, 2022	$	1,304
Increase related to prior year tax positions		51
Increase related to current year tax positions		607
Balance as of December 31, 2022	$	1,962
Increase related to prior year tax positions		372
Increase related to current year tax positions		1,488
Balance as of December 31, 2023	$	3,822

The Company files income tax returns in the U.S. federal jurisdiction and in the state of Arizona, California, New Jersey, Wisconsin, North Carolina and Pennsylvania. For jurisdictions in which tax filings have been filed, all tax years remain open for examination by the federal and state authorities for three and four years, respectively, from the date of utilization of any net operating losses or credits.

The Inflation Reduction Act was signed into law on August 16, 2022, and contained several tax provisions to curb inflation by reducing the deficit, lowering prescription drug prices, investing into domestic energy production while promoting clean energy, and introduced the topic of corporate alternative minimum tax on applicable corporations. There is no impact to the Company's current tax provision.

In accordance with the 2017 Tax Act, research and experimental (R&E) expenses under Internal Revenue Code Section 174 are required to be capitalized beginning in 2022. R&E expenses are required to be amortized over a period of 5 years for domestic expenses and 15 years for foreign expenses. The Company has reflected this in its current tax provision.

The Company is under audit in California for tax years 2020-2021.

8. Common Stock

As of December 31, 2023 and December 31, 2022, the Company's certificate of incorporation authorized the Company to issue 300,000,000 shares of common stock at a par value of $0.0001 per share. Each share of common stock is entitled to one vote. The holders of common stock are also entitled to receive dividends whenever funds are legally available and when declared by the Company's board of directors. As of December 31, 2023, no dividends have been declared to date.

On October 27, 2023, the Company completed a further underwritten public follow-on offering. The offering consisted of 5,797,872 shares of our common stock at an offering price to the public of $23.50 per share, including 797,872 shares of common stock upon the exercise in full of the overallotment option by the underwriters, as well as pre-funded warrants to purchase 319,150 shares of common stock at a public offering price of $23.4999 per underlying share, in each case before underwriting discounts and commissions. Pursuant to the offering, we received aggregate gross proceeds of approximately $143.7 million, before deducting underwriting discounts and commissions and other offering expenses, resulting in net proceeds of approximately $134.6 million, after deducting underwriting discounts and commissions and other offering expenses.

On April 27, 2023, the Company completed an underwritten public follow-on offering. The offering consisted of 8,858,121 shares of our common stock at an offering price to the public of $18.50 per share, including 1,418,920 shares of common stock upon the exercise in full of the overallotment option by the underwriters, as well as pre-funded warrants to purchase 2,020,270 shares of common stock at a public offering price of $18.4999 per underlying share, in each case before underwriting discounts and commissions. Pursuant to the offering, we received aggregate gross proceeds of approximately $201.3 million, before deducting underwriting discounts and commissions and other offering expenses, resulting in net proceeds of approximately $188.7 million, after deducting underwriting discounts and commissions and other offering expenses.

As of December 31, 2023, the following aggregate warrants to purchase shares of the Company's common stock were issued and outstanding:

Issue Date	Expiration Date	Exercise Price per Share	Number of Shares subject to Outstanding Warrants
April 27, 2023	None	$0.0001	2,020,270
October 27, 2023	None	$0.0001	319,150

The Warrants are classified as a component of Stockholders' Equity within Additional Paid-in-Capital. The Warrants are equity classified because they are freestanding financial instruments that are legally detachable and separately exercisable from the equity instruments, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, are indexed to the Company's common stock and meet the equity classification criteria. The Warrants will not expire until they are fully exercised. As of December 31, 2023, no shares underlying the Warrants had been exercised.

The Company had reserved common stock for future issuance as follows:

	As of December 31,	
	2023	2022
Exercise of outstanding options under the 2015, 2019 and 2023 Plans	6,269,975	5,097,263
Shares available for grant under the 2019 Plan	964,622	664,919
Shares available for grant under the 2023 Inducement Plan	524,300	—
Shares available under the Employee Stock Purchase Plan	1,317,974	906,523
Pre-funded warrants issued and outstanding	2,339,420	—
Total	11,416,291	6,668,705

9. Stock-Based Compensation

2023 Inducement Plan

On February 24, 2023, the Company adopted the IDEAYA Biosciences, Inc. 2023 Employment Inducement Award Plan (the "2023 Inducement Plan"), pursuant to which the Company reserved 1,000,000 shares of its common stock to be used exclusively for grants of awards to individuals who were not previously employees or directors of the Company as an inducement material to the individual's entry into employment with the Company within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The 2023 Inducement Plan was approved by the Company's board of directors without stockholder approval in accordance with such rule. Options granted under the 2023 Inducement Plan have a term of 10 years and generally vest over a 4-year period with 1-year cliff vesting.

As of December 31, 2023, the number of shares available for issuance under the 2023 Inducement Plan was 524,300.

2019 Incentive Award Plan

In May 2019, the Company's board of directors adopted and the Company's stockholders approved the 2019 Incentive Award Plan (the "2019 Plan"), under which the Company may grant cash and equity-based incentive awards to the Company's employees, consultants and directors. Following the effectiveness of the 2019 Plan, the Company will not make any further grants under the 2015 Equity Incentive Plan (the "2015 Plan"). However, the 2015 Plan continues to govern the terms and conditions of the outstanding awards granted under it. Shares of common stock subject to awards granted under the 2015 Plan that are forfeited or lapse unexercised and which following the effective date of the 2019 Plan are not issued under the 2015 Plan will be available for issuance under the 2019 Plan.

Options granted under the 2019 Plan may be either incentive stock options ("ISOs") or nonqualified stock options ("NSOs"). ISOs may be granted only to Company employees (including officers and directors who are also employees). NSOs may be granted to Company employees and consultants.

The 2019 Plan is subject to an annual increase on the first day of each year beginning in 2020 and ending in 2029, equal to the lesser of 4% of the shares outstanding on the last day of the immediately preceding fiscal year, and such small number of shares as determined by the Company's board of directors. Options granted under the 2019 Plan have a term of 10 years (or five years if granted to a 10% stockholder) and generally vest over a 4-year period with 1-year cliff vesting.

As of December 31, 2023, the number of shares available for issuance under the 2019 Plan was 964,622.

2015 Equity Incentive Plan

In 2015, the Company established its 2015 Plan which provides for the granting of stock options to employees and consultants of the Company. Options granted under the 2015 Plan may be either ISOs or NSOs.

2019 Employee Stock Purchase Plan

In May 2019, the Company's board of directors adopted and the Company's stockholders approved the 2019 Employee Stock Purchase Plan (the "ESPP"). The ESPP provides eligible employees with the opportunity to acquire an ownership interest in the Company through periodic payroll deductions up to 15% of eligible compensation. The offering period is determined by the Company in its discretion but may not exceed 27 months. The per-share purchase price on the applicable exercise date for an offering period is equal to the lesser of 85% of the fair market value of the common stock at either the first business day or last business day of the offering period, provided that no more than 4,000 shares of common stock may be purchased by any one employee during each offering period.

The ESPP is intended to constitute an "employee stock purchase plan" under Section 423(b) of the Internal Revenue Code of 1986, as amended. A total of 195,000 shares of common stock were initially reserved for issuance under the ESPP, subject to an annual increase on January 1 of each year, beginning on January 1, 2020, equal to the lesser of 1% of the shares outstanding on the last day of the immediately preceding fiscal year and such number of shares as may be determined by the Company's board of directors, provided, however, that no more than 2,500,000 shares may be issued under the ESPP.

As of December 31, 2023, the number of shares available for issuance under the ESPP was 1,317,974. For the years ended December 31, 2023 and December 31, 2022, the Company recorded $0.6 million and $0.4 million, respectively, of compensation expense related to employee participation in the ESPP.

Stock-Based Compensation Expense

Total stock-based compensation expense recorded related to awards granted to employees and non-employees was as follows (in thousands):

	Year Ended December 31,		
	2023	2022	2021
Research and development	$ 10,826	$ 6,050	$ 3,492
General and administrative	7,663	5,579	4,745
Total stock-based compensation expense	$ 18,489	$ 11,629	$ 8,237

Stock Options

Activity under the Company's 2015 and 2019 Plans and 2023 Inducement Plan is set forth below:

	Outstanding Options			
	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Balance, January 1, 2023	5,097,263	$ 12.93	7.84	$ 29.58
Options granted	2,694,871	$ 18.95		
Options exercised	(931,012)	$ 10.27		
Options canceled	(591,147)	$ 16.93		
Balance, December 31, 2023	6,269,975	$ 15.53	7.82	$ 128.49
Exercisable as of December 31, 2023	2,612,605	$ 12.21	6.39	$ 62.22
Vested and expected to vest as of December 31, 2023	6,269,975	$ 15.53	7.82	$ 128.49

The weighted-average grant-date fair value of options granted during the years ended December 31, 2023 and December 31, 2022 was $13.98 and $10.10 per share, respectively. The aggregate intrinsic value of options exercised for the years ended December 31, 2023 and December 31, 2022 was $16.9 million and $1.8 million, respectively. Intrinsic values are calculated as the difference between the exercise price of the underlying options and the fair value of the common stock on the date of exercise.

As of December 31, 2023 and December 31, 2022, the total unrecognized stock-based compensation expense for stock options was $41.1 million and $28.0 million, respectively, which is expected to be recognized over a weighted-average period of 2.59 years and 2.65 years, respectively.

Black-Scholes Assumptions

The fair values of options were calculated using the assumptions set forth below:

	Year Ended December 31,		
	2023	2022	2021
Expected term	6.1 years	6.1 years	5.5 - 6.1 years
Expected volatility	81.76% - 86.90%	86.76% - 89.88%	90.0% - 103.6%
Risk-free interest rate	3.56% - 4.83%	1.62% - 4.05%	0.6% - 1.4%
Dividend yield	0%	0%	0%

Expected term. The expected term represents the weighted-average period the stock options are expected to remain outstanding and is based on the options' vesting terms, contractual terms and industry peers, as the Company does not have sufficient historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior.

Expected Volatility. The expected volatility is based on the Company's historical stock price volatility. The historical stock price volatility is calculated based on a period of time commensurate with the expected term assumption for each grant.

Risk-Free Interest Rate. The risk-free rate assumption is based on U.S. Treasury instruments whose term was consistent with the expected term of the Company's stock options.

Expected Dividend Rate. The Company has not paid and does not anticipate paying any dividends in the near future. Accordingly, the Company has estimated the dividend yield to be zero.

The Company accounts for forfeitures as they occur.

Fair Value of Common Stock

The fair value of the Company's common stock is determined based on its market price on the date of grant.

10. Significant Agreements

GSK Collaboration, Option and License Agreement

In June 2020, we entered into the GSK Collaboration Agreement, with GSK, pursuant to which we and GSK have entered into a collaboration for its synthetic lethality programs targeting MAT2A, Pol Theta and Werner Helicase. On July 27, 2020, ("the Effective Date"), we and GSK received Hart-Scott-Rodino Antitrust Improvements Act clearance, or HSR Clearance, and the GSK Collaboration Agreement became effective. Pursuant to the GSK Collaboration Agreement, GSK paid the Company $100.0 million on July 31, 2020.

Pursuant to the Agreement, GSK paid the Company $100.0 million on July 31, 2020. As of December 31, 2023, GSK has made aggregate payments in the amount of $13.0 million for the achievement of certain development and regulatory milestones with respect to Pol Theta and WRN products.

GSK Collaboration - MAT2A Program

Under the MAT2A program, we led research and development through early clinical development stage, and GSK had an exclusive option to obtain an exclusive license to continue development of and commercialize MAT2A products arising out of the MAT2A program, or the Option. We delivered an Option data package resulting from our conduct of a dose escalation portion of a MAT2A Phase 1 monotherapy clinical trial pursuant to the GSK Collaboration Agreement, following which the Option was exercisable within a specified time period.

In January 2022, GSK waived its rights under the GSK Collaboration Agreement to initiate, or request that we initiate, prior to GSK's exercise of the Option, a Phase 1 combination clinical trial for a MAT2A product and GSK's Type I PRMT inhibitor (GSK3368715) product, or the MAT2A Combination Trial. Accordingly, we have no further obligation under the GSK Collaboration Agreement to supply MAT2A product for the MAT2A Combination Trial at its own cost. Our obligation to supply the MAT2A compound for the MAT2A Combination Study was deemed a material right under the GSK Collaboration Agreement.

In August 2022, we received notice from GSK waiving its rights to exercise its Option, or the MAT2A Option Waiver, pursuant to the GSK Collaboration Agreement. As such, we retain and fully own all right, title and interest in and to IDE397 and the MAT2A program, including all worldwide commercial rights thereto. We will be responsible for the costs of further research and clinical development activities that we conduct for the MAT2A program following the MAT2A Option Waiver.

GSK Collaboration - Pol Theta Program

Pursuant to the GSK Collaboration Agreement, GSK holds a global, exclusive license to develop and commercialize Pol Theta products arising out of the Pol Theta program. We and GSK collaborated on preclinical research for the Pol Theta program, and GSK is leading clinical development for the Pol Theta program. GSK is responsible for all research and development costs for the Pol Theta program.

We will be eligible to receive total development and regulatory milestones of up to $485 million, with respect to each Pol Theta product, including as applicable, for multiple Pol Theta products that target certain alternative protein domains or are based on alternative modalities. Additionally, we will be eligible to receive up to $475 million of commercial milestones with respect to the Pol Theta product. We are also entitled to receive tiered royalties on global net sales of Pol Theta products by GSK, its affiliates and their sublicensees ranging from high single digit to sub-teen double digit percentages, subject to certain customary reductions.

In June 2022, we announced the nomination of a Pol Theta Helicase Inhibitor DC and in August 2022, announced the achievement of an initial preclinical development milestone in connection with ongoing IND-enabling studies to support evaluation of Pol Theta Helicase Inhibitor DC, triggering a $3.0 million milestone payment, which we received in October 2022.

An IND was submitted and was cleared by the FDA in August 2023 to enable clinical evaluation in combination with niraparib, triggering a $7.0 million milestone payment.

We have the potential to achieve an additional $10.0 million development milestone upon initiation of Phase 1 clinical dose expansion, as well as potential further aggregate late-stage development and regulatory milestones of up to $465 million. We are also entitled to receive tiered royalties on global net sales of Pol Theta products by GSK, its affiliates and their sublicensees ranging from high single digit to sub-teen double digit percentages, subject to certain customary reductions.

GSK Collaboration - Werner Helicase Program

Pursuant to the GSK Collaboration Agreement, GSK holds a global, exclusive license to develop and commercialize WRN products arising out of the WRN program. We and GSK are collaborating on ongoing preclinical research for the WRN program, and GSK will lead clinical development for the WRN program, with IDEAYA responsible for 20% and GSK responsible for 80% of such global research and development costs. The cost-sharing percentages will be adjusted based on the actual ratio of U.S. to global profits for WRN products, as measured three and six years after global commercial launch thereof.

We will be eligible to receive total development milestones of up to $485.0 million, with respect to each WRN product, including as applicable, for multiple WRN products that are based on alternative modalities. Additionally, we will be eligible to receive up to $475 million of commercial milestones with respect to each WRN product. We will be entitled to receive 50% of U.S. net profits and tiered royalties on global non-U.S. net sales of WRN products by GSK, its affiliates and their sublicensees ranging from high single digit to sub-teen double digit percentages, subject to certain customary reductions. We will have a right to opt-out of the 50% U.S. net profit share and corresponding research and development cost share for the WRN program, and would be eligible to receive tiered royalties on U.S. net sales of WRN products by GSK, its affiliates and their sublicensees at the same royalty rates as for global non-U.S. net sales thereafter, with economic adjustments based on the stage of the WRN program at the time of opt-out.

In October 2023, we earned a $3.0 million milestone from GSK in connection with IND-enabling studies for the Werner Helicase Inhibitor DC.

GSK Collaboration - General

Under the terms of the GSK Collaboration Agreement, subject to certain exceptions, we and GSK will not, directly or through third parties, develop or commercialize other products whose primary and intended mechanism of action is the modulation of WRN or Pol Theta for an agreed upon period of time. We and GSK have formed a joint steering committee, joint development committees, and joint commercialization committees responsible for coordinating all activities under the GSK Collaboration Agreement. Ownership of intellectual property developed under the GSK Collaboration Agreement is allocated between or shared by the parties depending on development and subject matter.

GSK's royalty obligations continue with respect to each country and each product until the later of (i) the date on which such product is no longer covered by certain intellectual property rights in such country and (ii) the 10th anniversary of the first commercial sale of such product in such country.

Each party has the right to sublicense its rights under the GSK Collaboration Agreement subject to certain conditions.

The GSK Collaboration Agreement will continue in effect on a product-by-product and country-by-country basis until the expiration of the obligation to make payments under the GSK Collaboration Agreement with respect to such product in each country, unless earlier terminated by either party pursuant to its terms. Either party may terminate the GSK Collaboration Agreement for the other party's insolvency or certain uncured breaches. We may terminate the GSK Collaboration Agreement if GSK or any of its sublicensees or affiliates challenge certain patents of ours. GSK may terminate the GSK Collaboration Agreement in its entirety or on a target-by-target basis upon 90-day notice to us.

Pfizer Clinical Trial Collaboration and Supply Agreements

In March 2020, we entered into the Pfizer Agreement. Pursuant to the Pfizer Agreement, as amended in September 2020, April 2021, September 2021 and May 2023, Pfizer supplies us with their MEK inhibitor, binimetinib, and their cMET inhibitor, crizotinib, to evaluate combinations of darovasertib independently with each of the Pfizer compounds, in patients with tumors harboring activating GNAQ or GNA11 mutations. Under the Pfizer Agreement, we are the sponsor of the combination studies and will provide darovasertib and pay for the costs of the combination studies. Pfizer will provide binimetinib and crizotinib for use in the clinical trial at no cost to us. The Pfizer Agreement provides that we and Pfizer will jointly own clinical data generated from the clinical trial and will also jointly own inventions, if any, relating to the combined use of darovasertib and binimetinib, or independently, to the combined use of darovasertib and crizotinib. We and Pfizer have formed a joint development committee responsible for coordinating all regulatory and other activities under the agreement.

In March 2022, we and Pfizer entered into the Second Pfizer Agreement pursuant to which we may, subject to FDA feedback and guidance, evaluate darovasertib and crizotinib as a combination therapy in MUM in a planned Phase 2/3 potential registration-enabling clinical trial. Pursuant to the Second Pfizer Agreement, we are the sponsor of the planned combination trial and we will provide darovasertib and pay for the costs of the combination trial; Pfizer will provide crizotinib for the planned combination trial at no cost to us for up to an agreed-upon number of MUM patients. We and Pfizer will jointly own clinical data from the planned combination trial and all inventions relating to the combined use of darovasertib and crizotinib. We and Pfizer have formed a joint development committee responsible for coordinating all regulatory and other activities under the Second Pfizer Agreement.

Separately, in March 2022, we and Pfizer also entered into the Third Pfizer Agreement pursuant to which we may, subject to preclinical validation and FDA feedback and guidance, evaluate darovasertib and crizotinib, as a combination therapy in cMET-driven tumors such as NSCLC and/or HCC in a Phase 1 clinical trial. Pursuant to the Third Pfizer Agreement, we are the sponsor of the planned combination trial, and we will provide darovasertib and pay for the costs of the combination trial; Pfizer will provide crizotinib for the planned combination trial at no cost to us. We and Pfizer will jointly own clinical data from the planned combination trial and all inventions relating to the combined use of darovasertib and crizotinib. We and Pfizer had formed a joint development committee responsible for coordinating all regulatory and other activities under the Third Pfizer Agreement.

In May 2023, we continued our relationship with Pfizer by entering into Amendment No. 4 to the Pfizer Agreement relating to the supply of crizotinib in support of this Phase 2 clinical trial, pursuant to which Pfizer will continue to provide us with an additional defined quantity of crizotinib at no cost.

We also expanded our relationship with Pfizer in May 2023 under an Amendment No. 1 to the Second Pfizer Agreement to support the Phase 2/3 registrational trial to evaluate darovasertib and crizotinib as a combination therapy in MUM. Under the as-amended Second Pfizer Agreement, Pfizer will provide us with a first defined quantity of crizotinib at no cost, as well as an additional second defined quantity of crizotinib at a lump-sum cost. Under Amendment No. 1 to the Second Pfizer Agreement, we also terminated the Third Pfizer Agreement.

Novartis License Agreement

In September 2018, we entered into a license agreement with Novartis International Pharmaceuticals Ltd. ("Novartis") to develop and commercialize Novartis' LXS196 (also known as IDE196), a Phase 1 protein kinase C ("PKC") inhibitor, for the treatment of cancers having GNAQ and GNA11 mutations. We have renamed Novartis' LXS196 oncology as IDE196, and which has a non-proprietary name of darovasertib. Under the license agreement, the Company is liable to make contingent development and sales-based milestone payments of up to $29.0 million and mid to high single-digit royalty payments based on net sales of the licensed products. Because the achievement of these milestones had not occurred or was not considered probable as of December 31, 2023, such contingencies have not been recorded in the Company's financial statements.

Amgen Clinical Trial Collaboration and Supply Agreement

In July 2022, we entered into the Amgen CTCSA to clinically evaluate IDE397 in combination with AMG 193 in patients having MTAP-null solid tumors, in a Phase 1/2 clinical trial. Under the mutually non-exclusive Amgen CTCSA, we will provide IDE397 drug supply to Amgen, who will be the sponsor of the Phase 1 clinical combination trial evaluating IDE397 and AMG 193. Each party will pay for fifty percent (50%) of the external third-party costs of the combination study. Each party will be responsible for its own internal costs and expenses in support of the combination study. We and Amgen will jointly oversee clinical development of the combination therapy through a Joint Oversight Committee responsible for coordinating all regulatory and other activities under the Amgen CTCSA. The parties will jointly own collaboration data and combination-related intellectual property, if any, arising from the combination clinical trial. We and Amgen each retain commercial rights to our respective compounds, including with respect to use as a monotherapy agent or combination agent.

Gilead Clinical Trial Collaboration and Supply Agreement

In November 2023, the Company entered into the Gilead CSCSA with Gilead to clinically evaluate IDE397 in combination with Trodelvy, the Gilead Trop-2 directed ADC, in patients having MTAP deletion bladder cancer, in an IDEAYA-sponsored clinical trial pursuant to the Gilead CSCSA. Under the mutually non-exclusive Gilead CSCSA, we will receive Trodelvy drug supply from Gilead and will sponsor the Phase 1 clinical combination trial evaluating ID397 and Trodelvy. Gilead will bear internal or external costs incurred in connection with its supply of Trodelvy. We will bear all internal and external costs and expenses associated with the conduct of the combination study. We and Gilead will jointly oversee clinical development of the combination therapy through a Joint Steering Committee responsible for coordinating all regulatory and other activities under the Gilead CSCSA. We and Gilead each retain commercial rights to our respective compounds, including with respect to use as a monotherapy agent or combination agent.

Cancer Research UK and University of Manchester Exclusive Option and License Agreement

In January 2022, the Company exercised its option for an exclusive worldwide license covering a broad class of PARG inhibitors from Cancer Research Technology Ltd. (CRT) and the University of Manchester, and in connection therewith, paid a one-time option exercise fee of £250,000. The Company will be obligated to make payments to CRT aggregating up to a total of £19.5 million upon the achievement of specific development and regulatory approval events for development of a PARG inhibitor in oncologic diseases. The Company will also pay low single-digit tiered royalties, and potentially also sales-based milestones, to CRT based on net sales of licensed products. In addition, in the event the Company sublicenses the intellectual property, it will also be obligated to pay CRT a specified percentage of any sublicense revenue.

In April 2023, we incurred an obligation to pay milestone payments in an aggregate amount of £750,000 to CRT based upon the achievement of certain milestones relating to first and second tumor histologies in connection with the Phase 1 portion of the Phase 1/2 clinical trial in oncologic diseases.

The Company will be obligated to make additional payments to CRT aggregating up to £18.75 million upon the achievement of specific development and regulatory approval events for development of a PARG inhibitor in oncologic diseases, including an aggregate of up to £1.5 million and up to £2.25 for the achievement of certain Phase 2 and Phase 3 development milestones, respectively, in each case as relating to first and second tumor histologies.

11. Revenue Recognition

The Company recognizes revenue in accordance with ASC 606 for the GSK Collaboration Agreement (see No. 10, Significant Agreements).

Disaggregation of Revenue

The following table presents revenue disaggregated by research program (in thousands):

	Year Ended December 31,	
	2023	**2022**
MAT2A	$ 3,722	$ 29,756
Pol Theta	3,002	13,894
WRN	16,661	7,281
Total collaboration revenue	$ 23,385	$ 50,931

Contract balances

As of December 31, 2023 and December 31, 2022, the Company had accounts receivable of zero and $0.2 million, respectively, and contract liabilities of zero and $13.8 million, respectively, related to the GSK Collaboration Agreement.

As of December 31, 2023, we have fully recognized the contract liabilities related to the upfront payment and reimbursements for the research and development performance obligations under the GSK Collaboration Agreement. There are no remaining contract liabilities as of December 31, 2023 as we concluded all the research and development performance obligations under the GSK Collaboration Agreement. The future revenue recognition will be contingent on additional milestones earned, profit sharing and royalties on any net product sales under our collaborations. We expect that any revenue we recognize or generate under the GSK Collaboration Agreement will fluctuate from period to period due to period to period variability in milestone payments and other payments.

Performance obligations

The Company has identified the following six performance obligations associated with the GSK Collaboration Agreement:

(i) Preclinical and Phase 1 Monotherapy clinical research and development services under the MAT2A program (“MAT2A R&D Services”)

(ii) Preclinical research services and the related license to IDEAYA-owned technology under the Pol Theta program (“Pol Theta R&D Services”)

(iii) Preclinical research services and the related license to IDEAYA-owned technology under the WRN program ("WRN R&D Services")

(iv) Material right associated with the option to license IDEAYA-owned technology under the MAT2A program ("Option")

(v) Material right associated with the option to license to IDEAYA-owned technology under the MAT2A program to the extent necessary for preclinical activities in preparation for the MAT2A Combination Trial ("Preclinical MAT2A License")

(vi) Material right associated with the supply of MAT2A product for the MAT2A Combination Trial ("MAT2A Supply")

The Company recognizes revenue related to amounts allocated to the MAT2A R&D services as the underlying services are performed over the period through the delivery of the Option data package, which is generated from its conduct of the dose escalation portion of the MAT2A Phase 1 monotherapy clinical trial. The Company uses its internal research and development capability and also engages third-party clinical research organizations, or CROs, for which the Company acts as a principal. The Company has delivered the Option data package to GSK. Accordingly, the performance obligation related to the MAT2A R&D services has been fulfilled.

With respect to the Pol Theta and WRN programs, the Company identified two promises: (1) granting of the license to develop and commercialize Pol Theta and WRN products, respectively, and (2) the preclinical research services. The Company has determined that these two promises are not distinct within the context of the contract.

After the Company and GSK identify a development candidate, a series of IND-enabling studies will be conducted before an Investigational New Drug application is submitted to the FDA. Due to the early stage of development, the Company's preclinical research services are expected to transform the underlying technology and significantly modify or customize the license. Therefore, the two promises are not distinct from each other and are accounted for as a single performance obligation for each of the Pol Theta and WRN programs, respectively. An IND for GSK101 was submitted and has been cleared by the FDA and GSK has dosed a first patient in the Phase 1 clinical trial. GSK plans to evaluate GSK101 in combination with niraparib, the GSK small molecule inhibitor of PARP for the treatment of patients having tumors with BRCA or other HRD.

For the Pol Theta product, we achieved and earned a $7.0 million payment for a milestone in August 2023 based on acceptance of the IND by the FDA, payment. An earlier preclinical development $3.0 million milestone payment from GSK was achieved in August 2022 in connection with ongoing IND-enabling studies to support evaluation of GSK101. We have the potential to receive an additional $10.0 million milestone payment upon initiation of Phase 1 clinical dose expansion.

For the WRN product, we achieved and earned a $3.0 million payment for a milestone in October 2023 in connection with IND-enabling studies for the Werner Helicase Inhibitor DC. We are, in collaboration with GSK, targeting an IND submission in 2024 to enable first-in-human clinical evaluation of our Werner Helicase Inhibitor DC in high MSI tumors.

The Company recognized revenue related to amounts allocated to the Pol Theta R&D Services and WRN R&D Services as the underlying services are performed over the period through the completion of the Pol Theta and WRN preclinical research programs, respectively. Within 90 days from the end of each calendar quarter, GSK reimbursed the Pol Theta program costs incurred by the Company. Within 75 days from the end of each calendar quarter, the Company and GSK determined the amounts of WRN program costs incurred by both parties and the net amount owed by GSK to the Company or by the Company to GSK, which was paid within 75 days from such determination by a reimbursing party. The Company used its internal research capability and may also engage third-party clinical research organizations, or CROs, in transferring the Pol Theta R&D services and WRN R&D services, for which the Company acts as a principal. The Company completed Pol Theta R&D services during December 2022. Accordingly, the performance obligation related to the Pol Theta R&D services has been fulfilled.

Subject to exercise of the Option, at Option closing following HSR clearance, GSK would have obtained an exclusive license to develop and commercialize MAT2A products. The Company has concluded that this Option results in a material right as the option exercise fee contains a discount that GSK would not have otherwise received. The Company has determined the nature of the license to develop and commercialize MAT2A products to be functional.

The Company delivered an Option data package to GSK pursuant to the GSK Collaboration Agreement comprising preclinical and clinical data resulting from the Company's conduct of a dose-escalation portion of the MAT2A Phase 1 monotherapy clinical trial, following which, the Option was exercisable by GSK within a specified period of time. In August 2022, the Company received notice from GSK waiving its rights to exercise its Option to obtain an exclusive license to further develop and commercialize IDE397, as well as other IDEAYA compounds, if any, directly targeting MAT2A, or the

GSK MAT2A Option Waiver, pursuant to the GSK Collaboration Agreement. As such, the Company retains and fully owns all right, title and interest in and to IDE397 and the MAT2A program, including all worldwide commercial rights thereto. The Company will be responsible for the costs of further research and clinical development activities that the Company conducts for the MAT2A program following the GSK MAT2A Option Waiver. Accordingly, the Company recognized revenue of $17.4 million related to GSK's waiver of its rights to exercise its Option during the year ended December 31, 2022.

If GSK had elected to conduct the MAT2A Combination Trial, the Company would have an obligation to supply MAT2A product to be used for the MAT2A Combination Trial at its own cost. The Company has concluded that this supply option results in a material right as it involves a discount that GSK would not have otherwise received. The Company would have recognized revenue, as it transferred the control of the MAT2A product to GSK. In January 2022, GSK waived its rights under the GSK Collaboration Agreement to initiate, or request that the Company initiate, prior to GSK's exercise of the Option, a Phase 1 combination clinical trial for a MAT2A product and GSK's Type I PRMT inhibitor (GSK3368715) product, or the MAT2A Combination Trial. Accordingly, the Company has no further obligation under the GSK Collaboration Agreement to supply MAT2A product for the MAT2A Combination Trial at its own cost. The Company recognized revenue of $2.4 million during the year ended 2022 related to the material right to supply MAT2A compound as the material right no longer exists and the Company has no further obligation related to the MAT2A Combination Trial.

As of December 31, 2023, there are no remaining performance obligations related to the WRN, Pol Theta and MAT2A program.

Significant judgments

In applying ASC 606 to the GSK Collaboration Agreement, the Company made the following judgments that significantly affect the timing and amount of revenue recognition:

(i) Determination of the transaction price, including whether any variable consideration is included at inception of the contract

The transaction price is the amount of consideration that the Company expects to be entitled to in exchange for transferring promised goods or services to the customer. The transaction price must be determined at inception of a contract and may include amounts of variable consideration. However, there is a constraint on inclusion of variable consideration in the transaction price, if there is uncertainty at inception of the contract as to whether such consideration will be recognized in the future.

The decision as to whether or not it is probable that a significant reversal of revenue will occur in the future, depends on the likelihood and magnitude of the reversal and is highly susceptible to factors outside the Company's influence (for example, the Company cannot determine the outcome of clinical trials; the Company cannot determine if or when the counterparty will initiate or complete clinical trials; and the Company cannot determine if or when an regulatory agency provides any approval). In addition, the uncertainty is not expected to be resolved for a long period and finally, the Company has limited experience in the field. Therefore, at inception of the GSK Collaboration Agreement, development and regulatory milestones were fully constrained and were not included in the transaction price based on the factors noted above.

The Company constrains estimates of other variable consideration, such as reimbursable program costs, to amounts that are not expected to result in a significant revenue reversal in the future. The Company re-evaluates the transaction price, including the estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

(ii) Determination of the timing of satisfaction of performance obligations

The Company recognizes revenue from the MAT2A R&D Services, Pol Theta R&D Services and WRN R&D Services over time, as GSK simultaneously receives and consumes the benefits provided by the Company's performance as the Company performs. The Company measures its progress toward complete satisfaction of the MAT2A R&D Services, Pol Theta R&D Services and WRN R&D Services based on the costs incurred as a percentage of the estimated total costs to be incurred to complete the performance obligations. As the Company performs, it shares the results of research and development studies with GSK through the joint development committee. Accordingly, the cost incurred method faithfully depicts the Company's performance of the MAT2A R&D Services, Pol Theta R&D Services and WRN R&D Services.

12. Net Loss Per Share Attributable to Common Stockholders

The following table sets forth the computation of basic and diluted net loss per share attributable to common stockholders (in thousands, except share and per share data):

	Year Ended December 31,		
	2023	2022	2021
Numerator:			
Net loss attributable to common stockholders	$ (112,961)	$ (58,655)	$ (49,762)
Denominator:			
Weighted-average shares outstanding, basic [1]	57,519,929	41,444,696	35,262,987
Less: weighted-average shares of restricted stock that are subject to repurchase	—	—	(10,544)
Weighted-average shares used in computing net loss per share attributable to common stock, basic and diluted [1]	57,519,929	41,444,696	35,252,443
Net loss per share attributable to common stockholders, basic and diluted	$ (1.96)	$ (1.42)	$ (1.41)

(1) The shares underlying the pre-funded warrants to purchase shares of the Company's common stock have been included in the calculation of the weighted-average number of shares outstanding, basic and diluted, for the twelve months ended December 31, 2023.

The following outstanding shares of potentially dilutive securities were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods presented because including them would have been antidilutive:

	As of December 31,		
	2023	2022	2021
Options to purchase common stock	6,269,975	5,097,263	3,620,666

13. Subsequent Events

Subsequent to December 31, 2023, from January 1, 2024 through January 17, 2024, we sold an aggregate of 6,115,516 shares of our common stock for aggregate net proceeds of $215.9 million at a weighted average sales price of approximately $36.39 per share under the at-the-market offering pursuant to the June 2023 Sales Agreement with Jefferies as sales agent.

On January 19, 2024, we entered into a new Open Market Sales Agreement, or January 2024 Sales Agreement, with Jefferies relating to an at-the-market offering program under which we may offer and sell, from time to time at our sole discretion, shares of our common stock, par value $0.0001 per share, having aggregate gross proceeds of up to $350.0 million through Jefferies as sales agent.

On January 24, 2024, pursuant to the January Open Market Sales Agreement, we sold an aggregate of 3,119,866 shares of our common stock for aggregate net proceeds of $126.4 million at a weighted average sales price of approximately $41.50 per share under the at-the-market offering pursuant to the January 2024 Sales Agreement with Jefferies as sales agent. As of January 24, 2024, approximately $220.5 million of common stock remained available to be sold under the ATM facility.

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, in South San Francisco, California on February 20, 2024.

IDEAYA Biosciences, Inc.

By: /s/ Yujiro Hata
Yujiro Hata
President and Chief Executive Officer

Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Yujiro Hata and Andres Briseno, and each of them acting individually, as his or her true and lawful attorneys-in-fact and agents, each with full power of substitution, for him in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K (including post-effective amendments), and to file the same, with all exhibits thereto and other documents in connection therewith, with the SEC, granting unto said attorneys-in-fact and agents, with full power of each to act alone, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Yujiro Hata Yujiro Hata	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 20, 2024
/s/ Andres Ruiz Briseno Andres Ruiz Briseno	Senior Vice President and Head of Finance and Investor Relations *(Principal Financial and Accounting Officer)*	February 20, 2024
/s/ Terry Rosen, Ph.D. Terry Rosen, Ph.D.	Chairman of the Board of Directors	February 20, 2024
/s/ Garret Hampton, Ph.D. Garret Hampton, Ph.D.	Director	February 20, 2024
/s/ Susan L. Kelley, M.D. Susan L. Kelley, M.D.	Director	February 20, 2024
/s/ Catherine Mackey, Ph.D. Catherine Mackey, Ph.D.	Director	February 20, 2024
/s/ Scott Morrison Scott Morrison	Director	February 20, 2024
/s/ Jeffrey Stein, Ph.D. Jeffrey Stein, Ph.D.	Director	February 20, 2024
/s/ Wendy Yarno Wendy Yarno	Director	February 20, 2024

Stock Performance Graph

The following performance graph compares the performance of our common stock to the Nasdaq Composite Index and to the Nasdaq Biotechnology Index from May 23, 2019, the date of our initial pubic offering, through December 31, 2023. The graph assumes an investment of $100 on May 23, 2019 in our common shares, the Nasdaq Composite Index and the Nasdaq Biotechnology Index and assumes that any dividends are reinvested. The comparisons shown in the graph below are based upon historical data. The stock price performance included in this graph is not necessarily indicative of, nor is it intended to forecast, future stock price performance.

The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the Securities and Exchange Commission, or SEC, for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, nor shall such information be incorporated by reference into any future filing under the Exchange Act or Securities Act of 1933, as amended, or the Securities Act, except to the extent that we specifically incorporate it by reference into such filing.