Table of Contents

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

For the Fiscal Year Ended December 31, 2021

or

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

Commission File Number: 001-31918

IDERA PHARMACEUTICALS, INC.

(Exact name of Registrant as specified in its charter)

Delaware	**04-3072298**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
505 Eagleview Blvd., Suite 212 **Exton, Pennsylvania** (Address of principal executive offices)	**19341** (Zip Code)

(484) 348-1600

(Registrant's telephone number, including area code)

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

Title of Each Class:	Trading Symbol	Name of Each Exchange on Which Registered
Common Stock, $.001 par value	**IDRA**	**Nasdaq Capital 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 Securities 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, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was $63.8 million based on the last sale price of the registrant's common stock as reported on the Nasdaq Capital Market on June 30, 2021 (the last business day of the registrant's most recently completed second fiscal quarter).

As of March 31, 2022, the registrant had 52,924,870 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2022 annual meeting of stockholders are incorporated by reference into Part III of this Form 10-K where indicated. Such definitive proxy statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the year ended December 31, 2021.

IDERA PHARMACEUTICALS, INC.
FORM 10-K

TABLE OF CONTENTS

Unless the context otherwise indicates, references in this Annual Report on Form 10-K to "Idera", the "Company", "we," "us," and "our" refer to Idera Pharmaceuticals, Inc.

IMO® and Idera® are our trademarks. All other trademarks and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

Website addresses referenced in this Annual Report on Form 10-K are provided for convenience only, and the content on the referenced websites does not constitute a part of this Annual Report on Form 10-K.

All share and per share amounts, including the exercise or conversion price of any of our securities, reflect, as applicable, the occurrence of a 1-for-8 reverse split of our common stock that occurred on July 27, 2018.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K ("Form 10-K") and the documents we incorporate by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements, other than statements of historical fact, included or incorporated in this report regarding our strategy, future operations, clinical trials, collaborations, intellectual property, cash resources, financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. The words "believes," "anticipates," "estimates," "plans," "expects," "intends," "may," "could," "should," "potential," "likely," "projects," "continue," "will," "schedule," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we will achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. These forward-looking statements involve known and unknown risks, uncertainties, and other factors, which may be beyond our control, and which may cause the actual results, performance, or achievements of the Company to be materially different from future results, performance, or achievements expressed or implied by such forward-looking statements.

There are several important factors that could cause our actual results to differ materially from those indicated or implied by forward-looking statements. These important factors include those set forth below under Part I, Item 1A "Risk Factors" and in our other disclosures and filings with the Securities and Exchange Commission ("SEC"). These factors and the other cautionary statements made in this Annual Report on Form 10-K and the documents we incorporate by reference should be read as being applicable to all related forward-looking statements whenever they appear in this Form 10-K and the documents we incorporate by reference.

In addition, any forward-looking statements represent our estimates only as of the date that this Annual Report on Form 10-K is filed with the SEC and should not be relied upon as representing our estimates as of any subsequent date. All forward-looking statements included in this Form 10-K are made as of the date hereof and are expressly qualified in their entirety by this cautionary notice. We disclaim any intention or obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as may be required by law.

PART I.

Item 1. Business.

Overview

We are a biopharmaceutical company with a business strategy focused on the clinical development, and ultimately the commercialization, of drug candidates for rare disease indications characterized by small, well-defined patient populations with serious unmet medical needs. Our current focus is to identify and acquire rights to novel development and commercial stage rare disease programs through new business development opportunities, including additional strategic alternatives. We have in the past and may in the future explore collaborative alliances to support development and commercialization of any of our drug candidates.

Until May 2021, we were developing intratumoral tilsotolimod for the treatment of anti-PD1 refractory metastatic melanoma in combination with ipilimumab, an anti-CTLA4 antibody marketed as Yervoy® by Bristol Myers Squibb Company ("BMS"), in a Phase 3 registration trial (ILLUMINATE-301). During the first quarter of 2021, we announced that ILLUMINATE-301 did not meet its primary endpoint of Objective Response Rate ("ORR"). Based on subsequent evaluation of the full data set, in May 2021 we announced that we would not continue the trial to its Overall Survival ("OS") primary endpoint.

Through December 2021, we were also evaluating intratumoral tilsotolimod in combination with nivolumab, an anti-PD1 antibody marketed as Opdivo® by BMS, and ipilimumab for the treatment of multiple solid tumors in a multicohort Phase 2 trial. In December 2021, we announced that preliminary data from the second 10 patients dosed in the safety cohort of ILLUMINATE-206 showed a safety profile consistent with the first 10 patients in ILLUMINATE-206 and with prior studies. No further enrollment in ILLUMINATE-206 is planned at this time.

While our clinical trials with tilsotolimod have not yet translated into a new treatment alternative for patients, data supporting tilsotolimod's mechanism of action and encouraging safety profile from across the array of pre-clinical and clinical work to date, together with its intellectual property protection, are noteworthy. As a result, in December 2021, we announced that we will consider an out-licensing arrangement so that tilsotolimod's full potential may continue to be explored on behalf of patients who do not respond to traditional immunotherapy.

Recent Events and Updates

Reduction-in-Force

In April 2021, we began to implement a reduction-in-force, which affected approximately 50% of our workforce. The decision was made to align our workforce to our needs considering the topline data results from ILLUMINATE-301's ORR endpoint and the subsequent decision not to continue to the study's OS endpoint. In connection with these actions, we incurred termination costs during the second and third quarters of 2021, which included severance, benefits, and related costs, totaling approximately $1.3 million. No further reduction in force was taken related to the decision to stop enrollment in ILLUMINATE-206.

We are actively evaluating other novel therapeutic assets, including developmental and potentially commercial-stage assets, which may represent an opportunity to expand our pipeline.

Nasdaq Compliance

As previously disclosed, on November 26, 2021, we received a deficiency letter (the "Nasdaq Letter") from the Nasdaq Listing Qualifications Department, notifying us that we are not in compliance with Nasdaq Listing Rule 5550(a)(2), which requires us to maintain a minimum bid price of at least $1 per share for continued listing on The Nasdaq Capital Market (the "Minimum Bid Requirement"). The Company's failure to comply with the Minimum Bid Requirement was based on the Company's common stock per share price being below the $1 threshold for a period of 30 consecutive business days. In accordance with Nasdaq Listing Rule 5810(c)(3)(A) (the "Compliance Period Rule"), the Company has been provided an initial period of 180 calendar days (the "Compliance Date"), to regain compliance with the Minimum Bid Requirement. If, at any time before the Compliance Date, the bid price for the Company's common stock closes at $1.00 or more per share for a minimum of 10 consecutive business

days, as required under Nasdaq requirements, the Staff will provide written notification to the Company that it complies with the Minimum Bid Requirement, unless the Staff exercises its discretion to extend this 10-day period pursuant to Nasdaq Listing Rule 5810(c)(3)(H).

If the Company does not regain compliance with the Minimum Bid Requirement by the Compliance Date, the Company may be eligible for an additional 180 calendar day compliance period (the "Second Compliance Period"). To qualify, the Company would need to meet the continued listing requirement for the market value of publicly held shares and all other initial listing standards of the Nasdaq Capital Market, with the exception of the Minimum Bid Requirement, and provide written notice to the Staff of its intention to cure the deficiency during the Second Compliance Period.

Neither the Nasdaq Letter nor the Company's noncompliance with the Minimum Bid Requirement have an immediate effect on the listing or trading of the Company's common stock, which continues to trade on The Nasdaq Capital Market under the symbol "IDRA."

Clinical Development

Tilsotolimod (IMO-2125)

Tilsotolimod is a synthetic phosphorothioate oligonucleotide that acts as a direct agonist of TLR9 to stimulate the innate and adaptive immune systems. It was developed for administration via intratumoral injection in combination with systemically administered checkpoint inhibitors and costimulation therapies for the treatment of various solid tumors. We referred to our tilsotolimod development program as the ILLUMINATE development program. See additional information under the heading "Collaborative Alliances" for information on the development of tilsotolimod in collaboration with AbbVie Inc. ("AbbVie") for patients with head and neck squamous cell carcinoma ("HNSCC").

ILLUMINATE-206 - Phase 2 Trial of Tilsotolimod (IMO-2125) in Combination with Nivolumab and Ipilimumab for the treatment of Solid Tumors

In September 2019, we initiated a Phase 2, open-label, global, multicohort study to evaluate the safety and effectiveness of tilsotolimod administered intratumorally in combination with nivolumab and ipilimumab for the treatment of solid tumors. We refer to this study as ILLUMINATE-206.

The first solid tumor investigated under ILLUMINATE-206 was relapsed/refractory Microsatellite-Stable Colorectal Cancer ("MSS-CRC") in immunotherapy-naïve patients (the "MSS-CRC Study"). To investigate the safety profile of the combination of tilsotolimod, nivolumab and ipilimumab, ILLUMINATE-206 was designed with a stepwise approach to ipilimumab dosage. An initial group of ten patients in the safety cohort of the MSS-CRC Study, many of whom were heavily pre-treated and rapidly progressing, received 8 mg of intratumoral tilsotolimod and 3 mg/kg of intravenous (IV) nivolumab every two weeks, along with 1 mg/kg of IV ipilumab every eight weeks (the "Low-Dose, Low-Frequency Cohort"). This regimen was generally well tolerated; no patients discontinued treatment due to adverse events ("AEs") and no patients experienced Grade 4 or 5 AEs. As of the response data cutoff date, per Response Evaluation Criteria in Solid Tumors V1.1 ("RECIST V1.1") criteria, one patient experienced stable disease ("SD") and nine patients progressed. Investigators reported that six of the progressing patients had stability or reduction in size of injected lesions and six had stability or reduction in overall size of uninjected lesions.

Based on these results, we enrolled an additional ten patients in the MSS-CRC Study. Changes in the study design intended to improve potential outcomes in the targeted patient population included increasing the frequency of ipilimumab dosing to every three weeks and limiting the number of allowed prior lines of treatment to two. Accordingly, the second group of ten patients enrolled in the MSS-CRC Study received 8 mg of intratumoral tilsotolimod (total of 9 doses over approximately 28 weeks) and 3 mg/kg of intravenous (IV) nivolumab every three

weeks followed by 480 mg of IV nivolumab every four weeks, along with 1 mg/kg of IV ipilimumab every three weeks for four doses (the "Low-Dose, High-Frequency Cohort").

In December 2021, we announced that preliminary data from the second ten patients dosed in the safety cohort of ILLUMINATE-206 showed a safety profile consistent with the first ten patients in ILLUMINATE-206 and with prior studies.

Of the eight patients who had a post-baseline disease assessment evaluated per RECIST v1.1, one experienced SD with disease control for more than six months; the remaining patients experienced Progressive Disease ("PD"). However, one of the RECIST v1.1 PD patients was determined to have experienced pseudo-progression, meaning that the initial increase from baseline in overall tumor burden was followed by a decrease from baseline in overall tumor burden and, based on the total decrease from baseline, was considered an Immune-Related Partial Response ("irPR") by Immune-Related RECIST ("irRECIST"). The patient continued in active treatment, as allowed per protocol, through February 2022, when they withdrew due to travel constraints. As a result, we are in process of concluding all study-related activities for ILLUMINATE-206.

As further discussed in this annual report under the caption "Item 1. Business - Collaborative Alliances", in March 2019 we entered into a clinical trial collaboration and supply agreement with BMS, under which BMS agreed to manufacture and supply ipilimumab and nivolumab, at its cost and for no charge to us, for use in ILLUMINATE-206.

ILLUMINATE-301 - Phase 3 Trial of Tilsotolimod (IMO-2125) in Combination with Ipilimumab in Patients with Anti-PD1 Refractory Melanoma

In the first quarter of 2018, we initiated a Phase 3 trial of intratumoral tilsotolimod in combination with ipilimumab in patients with anti-PD-1 refractory melanoma, which we referred to as ILLUMINATE-301. This trial compared the results of the tilsotolimod–ipilimumab combination to those of ipilimumab alone in a 1:1 randomization. The family of primary endpoints of the trial consisted of ORR by blinded independent central review RECIST v1.1 and median OS.

As discussed above, in March 2021, we reported that ILLUMINATE-301 did not meet its primary endpoint of ORR. In May 2021, following evaluation of the full data set, we announced we would not continue ILLUMINATE-301 to its OS primary endpoint.

Collaborative Alliances

Our current alliances include collaborations with Scriptr Global, Inc. ("Scriptr"), AbbVie, and BMS. We may seek to enter into new collaborative alliances to support development and commercialization of additional drug candidates.

Collaboration with Scriptr

In February 2021, we entered into a collaboration and option agreement with Scriptr, pursuant to which (i) Scriptr and Idera will conduct a research collaboration utilizing Scriptr Platform Technology ("SPT") to identify, research and develop gene therapy candidates (each, a "Collaboration Candidate") for the treatment, palliation, diagnosis or prevention of (a) myotonic dystrophy type 1 ("DM1 Field") and (b) Friedreich's Ataxia ("FA Field") on a Research Program-by-Research Program basis, as applicable, and (ii) we were granted an exclusive option, in our sole discretion, to make effective the Scriptr License Agreement, as defined below, for a given Research Program, as defined below, to make use of Collaboration Candidates and related intellectual property (collectively, the "Scriptr Agreement").

Pursuant to the Scriptr Agreement, Scriptr will use commercially reasonable efforts to carry out research activities set forth in accordance with the applicable DM1 Field and FA Field research plans, including certain pre-clinical proof of concept studies, to identify research Collaboration Candidates utilizing SPT (each, a "Research Program"). Following the completion of activities under a given Research Program, Scriptr will prepare and submit

to us a comprehensive data package (each, a "Data Package") that summarizes, on a Research Program-by-Research Program basis, any Collaboration Candidates researched under the Research Program, including any data and results. Upon receipt of a Data Package, we have, in our sole discretion, up to two-hundred seventy (270) calendar days to make effective the exclusive license agreement entered into by and between Scriptr and us, pursuant to which, among other things, Scriptr grants us exclusive rights and licenses with respect to the development, manufacture and commercialization of licensed candidates and products, subject to certain conditions and limitations (the "Scriptr License Agreement"), for a given Research Program (each licensed Research Program, a "Licensed Program"). The Scriptr License Agreement provides for customary development milestones on candidates developed under a Licensed Program and royalties on licensed products, if any.

In partial consideration of the rights granted by Scriptr to us under the Scriptr Agreement, we made a one-time, non-creditable and non-refundable payment to Scriptr during the first quarter of 2021. In order to fund the Research Programs, we will reimburse Scriptr for costs incurred by or on behalf of Scriptr in connection with the conduct of each Research Program during the research term in accordance with the applicable Research Program budget and payment schedule. We incurred approximately $2.1 million in research and development expenses under the Scriptr Agreement during the year ended December 31, 2021.

Collaboration with AbbVie

Effective August 27, 2019, we entered into a clinical trial collaboration and supply agreement (the "AbbVie Agreement") with AbbVie, a global, research-based biopharmaceutical company, to conduct a clinical study to evaluate the efficacy and safety of combinations of an OX40 agonist (ABBV-368), tilsotolimod, nab-paclitaxel and/or an anti-programmed cell death 1 (PD-1) antagonist (ABBV-181). Under the AbbVie Agreement, we agreed to provide a clinical trial supply of tilsotolimod to AbbVie and AbbVie will sponsor, fund and conduct the study entitled "A Phase 1b, Multicenter, Open-Label Study to Determine the Safety, Tolerability, Pharmacokinetics, and Preliminary Efficacy of ABBV-368 plus Tilsotolimod and Other Therapy Combinations in Subjects with Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma" (the "AbbVie Study").

In December 2021, AbbVie announced the discontinuation of further patient enrollment in the AbbVie Study. The decision to discontinue the AbbVie Study was not related to safety concerns. Current patient treatment and follow-up is ongoing.

Collaboration with Bristol-Meyers Squibb

We entered into two clinical collaboration agreements with BMS, the first in May 2018 and the second in March 2019, to support ILLUMINATE-301 and ILLUMINATE-206, respectively.

Under the May 2018 BMS Agreement, BMS granted us a non-exclusive, non-transferrable, royalty-free license (with a right to sublicense) under its intellectual property to use ipilimumab in ILLUMINATE-301 and agreed to manufacture and supply ipilimumab, at its cost and for no charge to us, for use in ILLUMINATE-301.

Under the March 2019 BMS Agreement, BMS granted us a non-exclusive, non-transferrable, royalty-free license (with a right to sublicense) under its intellectual property to use ipilimumab and nivolumab in ILLUMINATE-206 and agreed to manufacture and supply both ipilimumab and nivolumab, at its cost and for no charge to us, for use in ILLUMINATE-206.

Academic and Research Collaborations

We have entered into research collaborations with scientists at leading academic research institutions. These research collaborations allow us to augment our internal research capabilities and obtain access to specialized knowledge and expertise. In general, our research collaborations may require us to supply compounds and pay various amounts to support the research. Under these research agreements, if a collaborator, solely or jointly with us, creates any invention, we may own exclusively such invention, have an automatic paid-up, royalty-free non-exclusive license or have an option to negotiate an exclusive, worldwide, royalty-bearing license to such invention. Inventions developed solely by our scientists in connection with research collaborations are owned exclusively by us. These collaborative agreements are non-exclusive and may be terminated with limited notice.

Research and Development Expenses

We are committed to redefining the treatment of certain cancers and rare diseases and have historically dedicated a significant portion of our resources to our efforts on the discovery and development of our drug candidates. For the years ended December 31, 2021, 2020, and 2019, we spent approximately $16.4 million, $24.8 million, and $34.9 million, respectively, on research and development activities. We plan to continue to invest in research and development. Accordingly, we anticipate a significant portion of our operating expenses will continue to be related to research and development in 2022 and beyond.

Patents, Proprietary Rights and Trade Secrets

Our success depends in part on our ability to obtain and maintain proprietary protection for our drug candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We use a variety of methods to seek to protect our proprietary position, including filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation, and in-licensing opportunities to develop and maintain our proprietary position.

We have devoted and continue to devote a substantial amount of our resources into establishing intellectual property protection for:

- Novel chemical entities that function as agonists of TLR3, TLR7, TLR8 or TLR9;
- Novel chemical entities that function as antagonists of TLR7, TLR8 or TLR9; and
- Composition and use of our nucleic acid chemistry compounds to treat and prevent a variety of diseases.

On November 5, 2019, the U.S. Patent and Trademark Office ("USPTO") issued to us U.S. Patent No. 10,463,686 entitled "Immune Modulation With TLR9 Agonists For Cancer Treatment," which includes tilsotolimod. The patent includes 24 claims directed to methods of treating melanoma with intratumoral administration of tilsotolimod in combination with certain immune checkpoint inhibitor therapies, including inhibitors of the CTLA-4 and PD-1/PD-L1 pathways. The patent is expected to expire in September 2037.

On September 15, 2020, the USPTO issued U.S. Patent No. 10,772,907 (the "'907 Patent") to us, entitled "Immune Modulation with TLR9 Agonists for Cancer Treatment," which includes our investigational therapy tilsotolimod. The '907 Patent includes 26 claims directed to methods of treating colorectal cancer ("CRC") with intratumoral administration of tilsotolimod in combination with certain immune checkpoint inhibitor therapies, including CTLA-4, PD-1 or PD-L1 inhibitors.

On November 17, 2020, the USPTO issued to us U.S. Patent No. 10,835,550 (the "'550 Patent") entitled "Immune Modulation with TLR9 Agonists for Cancer Treatment," which includes our investigational therapy tilsotolimod. The '550 Patent includes 29 claims directed to methods of treating HNSCC with intratumoral administration of tilsotolimod in combination with certain immune checkpoint inhibitor therapies, including CTLA-4, PD-1 or PD-L1 inhibitors.

On January 18, 2022, the USPTO issued to us U.S. Patent No. 11,224,611 (the "'611 Patent" and, together with '907 Patent and the '550 Patent, the "New Patents") entitled "immune Modulation with TLR9 Agonists for Cancer Treatment," which includes our investigational therapy tilsotolimod. The '611 Patent includes 30 claims directed to methods of treating kidney cancer with intratumoral administration of tilsotolimod in combination with certain immune checkpoint inhibitor therapies, including CTLA-4, PD-1 or PD-L1 inhibitors.

The New Patents expand protection of the first tilsotolimod method-of-use patent, which was directed to methods of treating metastatic melanoma and was issued in November 2019. The New Patents provide exclusivity for certain uses of tilsotolimod through September 2037.

As of March 15, 2022, we owned approximately 56 U.S. patents and patent applications and about 192 patents and patent applications throughout the rest of the world for our TLR-targeted immune modulation technologies. These patents and patent applications include claims covering the chemical compositions of matter and methods of use of our IMO compounds, such as IMO-8400, IMO-9200 and tilsotolimod (IMO-2125), as well as other compounds. These patents and patent applications (if granted) expire at various dates ranging from 2020 to 2042. With respect to IMO-8400, we have ten issued U.S. patents that cover the chemical composition of matter of IMO-8400 and certain methods of its use, the latest of which expires in 2031. With respect to IMO-9200, we have nine issued U.S. patents that cover the chemical composition for IMO-9200 and methods of its use, the latest of which expires in 2034. With respect to tilsotolimod, we have issued U.S. patents that cover the chemical composition of matter of tilsotolimod that will expire between 2023 and 2026, and we have additional U.S. patents

that cover methods of its use, the latest of which will expire in 2037. We have pending applications in the United States and outside of the United States that cover methods of treatment or use of tilsotolimod, which, if granted, will expire between 2035 and 2042.

Because patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in the scientific literature often lag behind actual discoveries, neither we nor our licensors can be certain that we or they were the first to make the inventions claimed in issued patents or pending patent applications, or that we or they were the first to file for protection of the inventions set forth in these patent applications.

Litigation may be necessary to defend against or assert claims of infringement, to enforce patents issued to us, to protect trade secrets or know-how owned by us, or to determine the scope and validity of the proprietary rights of others or to determine the appropriate term for an issued patent. In addition, USPTO may declare interference proceedings to determine the priority of inventions with respect to our patent applications or reexamination or reissue proceedings to determine if the scope of a patent should be narrowed. Litigation or any of these other proceedings could result in substantial costs to and diversion of effort by us, even if the eventual outcome is favorable to us, and could have a material adverse effect on our business, financial condition and results of operations. These efforts by us may not be successful.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent. A patent's term may also be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug, biological product, or medical device approved pursuant to a pre-market approval may also be eligible for patent term extension when U.S. Food and Drug Administration ("FDA") approval is granted, provided statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review and development. The Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act") permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug are extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug.

We may rely, in some circumstances, on trade secrets and confidentiality agreements to protect our technology. Although trade secrets are difficult to protect, wherever possible, we use confidentiality agreements to protect the proprietary nature of our technology. We regularly implement confidentiality agreements with our employees, consultants, scientific advisors, and other contractors and collaborators. However, there can be no assurance that these agreements will not be breached, that we will have adequate remedies for any breach, or that our trade secrets and/or proprietary information will not otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may also arise as to the rights in related or resulting know-how and inventions.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of any of our drug candidates. We currently rely and expect to continue to rely on other companies to manufacture our drug candidates for preclinical and clinical development. We source our bulk drug manufacturing requirements from a limited number of contract manufacturers through the issuance of work orders on an as-needed basis. We currently do not have any long-term supply contracts. We depend and will continue to depend on our contract manufacturers to manufacture our drug candidates in accordance with current Good Manufacturing Practices ("cGMP") regulations for use in clinical trials. We will ultimately depend on contract manufacturers for the manufacture of our products for commercial sale, if and when our drug candidates are approved. Contract manufacturers are subject to extensive governmental regulation.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We recognize that other companies, including large pharmaceutical companies, may be developing or have plans to develop products and technologies that may compete with those we may acquire. Many of our competitors have substantially greater financial, technical, and human resources than we have. In addition, many of our competitors have significantly greater experience than we have in undertaking preclinical studies and human clinical trials of new pharmaceutical products, obtaining FDA and other regulatory approvals of products for use in health care and manufacturing, and marketing and selling approved products. Our competitors may discover, develop or commercialize products or other novel technologies that are more effective, safer, or less costly than any that we may develop. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

We anticipate that the competition with our drug candidates or technologies that we may acquire will be based on a number of factors including product efficacy, safety, availability, and price. The timing of market introduction of products and competitive products will also affect competition among products. We expect the relative speed with which we can develop products, complete the clinical trials and approval processes, and supply commercial quantities of the products to the market to be important competitive factors. Our competitive position will also depend upon our ability to attract and retain qualified personnel, to obtain patent protection or otherwise develop proprietary products or processes, protect our intellectual property, and to secure sufficient capital resources for the period between technological conception and commercial sales.

Risks related to our competitors and our competitive position are discussed in further detail in the section entitled “Risk Factors” of this Annual Report on Form 10-K.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing and sales, pricing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources. Regulatory requirements are also continually evolving. By example, in light of the COVID-19 pandemic, the FDA has issued a number of guidance documents to assist companies navigating product development, and manufacturing concerns raised by COVID-19.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and associated implementing regulations and guidance. The failure to comply with the FDCA and other applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of enforcement letters, product recalls, product seizures, operating restrictions such as the total or partial suspension of production or distribution, import bans, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice ("DOJ") or other governmental entities, including state agencies.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice ("GLP") regulations;
- submission to the FDA of an investigational new drug ("IND") application, which must take effect before human clinical trials may begin in the United States;
- initial and continuing approval by an independent institutional review board ("IRB"), representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("GCP") to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application ("NDA");
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies ("REMS") where applicable, and post-approval studies required by the FDA.

Preclinical Studies and Submission of an IND

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the chemistry, pharmacology, toxicity, purity, and stability, among other attributes, of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as in vitro and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND. Additional preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated, and a statistical analysis plan. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Once an IND is in effect, unapproved product candidates may be shipped in interstate commerce for use in an investigational clinical trial and the investigational product may be administered to humans as part of a clinical trial. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold or partial clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Depending on the conditions under development, multiple INDs may be required for the same drug product.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol, protocol amendments, communications to study subjects and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health (“NIH”) for public dissemination on their ClinicalTrials.gov website. Sponsors or distributors of investigational products for the diagnosis, monitoring, or treatment of one or more serious disease or conditions must also have a publicly available policy on evaluating and responding to requests for expanded access. Investigators must also provide certain information to clinical trial sponsors to allow the sponsors to make certain financial disclosures to the FDA.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data monitoring committee (“DMC”). This group provides recommendations as to whether a trial should move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

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

Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease (e.g. cancer) or condition and tested for safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism, distribution, excretion, and pharmacokinetics and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

Phase 2: The drug is administered to 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 optimal dosage.

Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

The manufacture of investigational drugs for the conduct of human clinical trials is subject to cGMP requirements. Investigational drugs and active ingredients imported into the United States are also subject to regulation by the FDA. Further, the export of investigational products outside the United States is subject to regulatory requirements of the receiving country as well as U.S. export requirements under the FDCA.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and to the IRB and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA, the sponsor or the data monitoring committee for a clinical trial may suspend or terminate the clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, 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. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on clinical studies conducted by or for the product sponsor. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that was not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous approval or a similar product or that the applicant's reliance on published data is scientifically appropriate, such as through bridging studies, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. Companies using this pathway, however, must conduct studies to support any differences from an approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is subject to a substantial application user fee. The sponsor of an approved NDA is also subject to an annual program fee. Exceptions or waivers for these fees exist for a small company (fewer than 500 employees, including employees and affiliates) satisfying certain requirements and products with orphan drug designation for a particular indication are not subject to a fee provided there are no other intended uses in the NDA and provided other exemption requirements are met.

The FDA conducts a preliminary review of an NDA within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission of any filing review issues. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review.

The FDA has agreed to specified performance goals under the Prescription Drug User Fee Act ("PDUFA") guidelines in the review process of NDAs. Under PDUFA, 90% of applications seeking approval of New Molecular Entities ("NMEs"), are meant to be reviewed within ten months from the date on which the FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date that the FDA receives the application. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission. This review period may change as the PDUFA statute must be reauthorized by the U.S. Congress by September 2022.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. 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 will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use ("ETASU"). ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product. The REMS strategy must be approved by the FDA. In addition, the REMS must include a timetable to assess the strategy at 18 months, three years, and seven years after the strategy's approval.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, 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.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are fast track designation, breakthrough therapy designation and priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a

fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

In 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act ("FDASIA"). This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either 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 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 FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner. Like fast track designation, breakthrough designation may be rescinded if the product no longer meets the qualifying criteria.

Third, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality ("IMM"), and 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. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

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. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

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

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including

the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

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

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, are required to list their distributed products, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. The information that must be submitted to FDA regarding manufactured products was expanded through the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") to include the volume of drugs produced during the prior year. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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

- restrictions on the marketing or manufacturing of the product, suspension of the approval, complete withdrawal of the product from the market or product recalls;

- warning letters, untitled letters, cyber letters, or holds or termination of post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or

FDA debarment, injunctions, fines, consent decrees, corporate integrity agreements, suspension and debarment from government contracts, refusal of orders under existing government contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement, or the imposition of civil or criminal penalties, including fines and imprisonment, and adverse publicity.

FDA post-approval requirements are continually evolving. For example, in March 2020, the U.S. Congress passed the CARES Act, which includes various provisions regarding FDA drug shortage and manufacturing volume reporting requirements, as well as provisions regarding supply chain security, such as risk management plan requirements, and the promotion of supply chain redundancy and domestic manufacturing.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the DOJ, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil penalties and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA"), and its implementing regulations, as well as the Drug Supply Chain Security Act ("DSCSA"). The PDMA regulate and limit the distribution and tracing of prescription drug samples at the federal level. The DSCSA imposes requirements to ensure accountability in distribution, that requires certain licensing and licensing standards, and to identify and remove counterfeit and other illegitimate products from the market.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs under abbreviated approval requirements. To obtain approval of a generic drug, an applicant must submit an Abbreviated New Drug Application ("ANDA") to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the Reference Listed Drug ("RLD"). Many states also regulate the distribution of drug product samples and commercial product.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug, among other requirements. Certain differences, however, between the reference listed drug and ANDA

product may be permitted pursuant to a suitability petition. Certain labeling differences may also be permitted if information in the reference listed drug's label is protected by patent or exclusivities. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug."

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD, subject to state law requirements. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in automatic substitution of the generic drug at the pharmacy.

In an effort to increase competition in the drug and biologic product marketplace, Congress, the executive branch, and FDA have taken certain legislative and regulatory steps. For example, measures have been proposed and implemented to facilitate product importation. Moreover, the 2020 Further Consolidated Appropriations Act included provisions requiring that sponsors of approved drug products, including those subject to REMS, provide samples of the approved products to persons developing 505(b)(2) NDA or ANDA drug products within specified timeframes, in sufficient quantities, and on commercially reasonable market-based terms. Failure to do so can subject the approved product sponsor to civil actions, penalties, and responsibility for attorney's fees and costs of the civil action. This same bill also includes provisions with respect to shared and separate REMS programs for reference and generic drug products.

Hatch-Waxman Exclusivities

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA or 505(b)(2) application until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity ("NCE"), is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt, or other noncovalent derivative, responsible for the physiological or pharmacological action of the drug substance. In cases where such exclusivity has been granted, an ANDA or 505(b)(2) application may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period prevents FDA from making a drug approval effective for the same changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication, as the product that holds the exclusivity. The three-year and five-year exclusivities, however, do not prevent the filing or approval of full NDAs.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA or 505(b)(2) applicant files its application with the FDA, the applicant is required to provide a certification to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;

- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or

- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the ANDA applicant is not seeking approval). The applicant may also elect to submit a "Section VIII" statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certifying to a listed method-of-use patent.

If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders within certain specified timeframes. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act ("PREA") of 2003, an NDA or supplement thereto must contain data that are 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. With enactment of the FDASIA in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant 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. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the FFDCA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

In addition, the FDA Reauthorization Act of 2017 introduced a new provision regarding required pediatric studies. Under this statute, for product candidates intended for the treatment of adult cancer which are directed at molecular targets that the FDA determines to be substantially relevant to the growth or progression of pediatric cancer, original application sponsors must submit, with the marketing application, reports from molecularly targeted pediatric cancer investigations designed to yield clinically meaningful pediatric study data, gathered using appropriate formulations for each applicable age group, to inform potential pediatric labeling. The FDA may, on its own initiative or at the request of the applicant, grant deferrals or waivers of some or all of this data, as above. Unlike PREA, orphan products are not exempt from this requirement.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity and on listed patents. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from Prescription Drug User Fee Act fees.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Clinical Trial Approval in the EU

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union ("EU") has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a EU member state in which the clinical

trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents. In April 2014, the EU adopted a new Clinical Trials Regulation, which will be directly applicable to and binding without the need for any national implementing legislation. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU member state or in more than one EU member state. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

Orphan Drug Designation and Exclusivity

Regulation 141/2000 provides that a drug shall be designated as an orphan drug if its sponsor can establish: that the product is intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the [EU] when the application is made, or that the product is intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating, or serious and chronic condition in the [EU] and that without incentives it is unlikely that the marketing of the drug in the [EU] would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the [EU] or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Regulation 847/2000 sets out criteria and procedures governing designation of orphan drugs in the EU. Specifically, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. This 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 drug designation, for example because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of “clinically relevant superiority” by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply). Medicinal products designated as orphan drugs pursuant to Regulation 141/2000 shall be eligible for incentives made available by the [EU] and by the EU member states to support research into, and the development and availability of, orphan drugs.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government healthcare programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Our rebate payments may increase or our prices be adjusted under value-based purchasing arrangements based on evidence-based measures or outcomes-based measures for a patient or beneficiary based on use of our drug. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication, or may impose other market access or utilization management controls.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor’s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, increases in rebates paid, restrictions on reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future. In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies, or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a drug product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other EU member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become 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 competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such restrictions under applicable federal and state healthcare laws and regulations, include the following:

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

- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim, or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government, with potential substantial liability including mandatory treble damages at trial and significant per-claim penalties;

- the Affordable Care Act included a provision requiring certain providers and suppliers of items and services to federal healthcare programs to report and return overpayments within sixty days after they are "identified" (the "Overpayment Statute"), after which the recipient of the overpayment incurs federal civil False Claims Act liability;

- the Affordable Care Act authorized the imposition of civil monetary penalties on manufactures participating in the 340B program for failure to charge the statutory ceiling price, and required HHS to promulgate regulations establishing the standards for implementing this Civil Monetary Penalty, or CMP, authority. CMS' final CMP rule went into effect January 1, 2019;

- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information and sanctions for failing to meet those obligations;

- the federal false statements statute prohibits 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;

- the federal transparency requirements under the Health Care Reform Law, known as the federal Physician Payments Sunshine Act, require manufacturers of covered drugs, devices, biologics and medical supplies to report to the Centers for Medicare & Medicaid Services ("CMS") within the Department of Health and Human Services information related to certain payments and other transfers of value to US-licensed physicians, physician assistants, nurse practitioners, certified registered nurse anesthetists and certified nurse midwifes and US teaching hospitals and to physician ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform in the United States

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last several years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act (the "PPACA") which, among other things, includes changes to the coverage and payment for products under government health care programs. Moreover, in 2017, the U.S. Congress modified and amended certain provisions of the PPACA, which could have an impact on coverage and reimbursement for healthcare items and services covered by the federal and state healthcare programs as well as plans in the private health insurance market. The so-called "individual mandate" was repealed as part of tax reform legislation adopted in December 2017. Legal challenges to the PPACA may continue to arise and there may continue to be future efforts to modify, repeal, or otherwise invalidate all, or certain provisions of the Affordable Care Act. The Biden administration is expected to continue to take measures to further facilitate the implementation of the PPACA. Among the provisions of the PPACA of importance to potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;

- 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;

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price" ("AMP") for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;

- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

- expanded the types of entities eligible for the 340B drug discount program;

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- established the Independent Payment Advisory Board ("IPAB") which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs, subsequently repealed through the Bipartisan Budget Act of 2018; and

- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 , were paused from May 1, 2020 through December 31, 2021, and will continue through 2031 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

More recently, Congress amended the Medicaid statute, effective October 1, 2019, to exclude prices paid by secondary manufacturers for an authorized generic drug (but not a product approved under the BLA process) from the NDA holder's AMP for the brand, thereby increasing the rebate amount and the 340B price for the brand. This was implemented by CMS in a final rule issued December 31, 2020. The rule also expanded the definition of products identified as "line extensions" and, in certain circumstances, required inclusion of patient copay assistance in Medicaid best price (effective January 1, 2023), thereby potentially increasing Medicaid rebates paid by manufacturers for such drugs. 340B program guidance regulations on civil monetary penalties for statutory violations, which had been finalized in early 2017 but deferred, also recently went into effect. On November 27, 2020, CMS issued an interim final rule implementing a Most Favored Nation payment model under which reimbursement for certain Medicare Part B drugs and biologicals will be based on a price that reflects the lowest per capita Gross Domestic Product-adjusted (GDP-adjusted) price of any non-U.S. member country of the Organization for Economic Co-operation and Development (OECD) with a GDP per capita that is at least sixty percent of the U.S. GDP per capita. This rule now has been rescinded, but similar programs have been described in recent legislative proposals.

These healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, payment of increased rebates, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices or the frequency with which products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Since enactment of the PPACA, there have been numerous legal challenges and congressional actions to repeal and replace provisions of the law.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the recent administrations have indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Human Capital Resources

Our vision is to translate scientific breakthroughs into important new medicine. We have a culture where patients are at the center of all we do, with core values that connect us to each other and our stakeholders and define who we are, what we stand for, and how we work.

We are focused on effective attraction, development, and retention of, and compensation and benefits to, human resource talent, including workforce and management development, diversity and inclusion initiatives, succession planning, and corporate culture and leadership quality, which are vital to our success. At December 31, 2021, our total workforce consisted of 13 full-time employees. We consider our relations with our employees to be good.

During 2021, as we worked to manage through the effects of the human capital aspects of the ongoing COVID-19 pandemic, all employees were provided the option of working remotely or at our Exton, Pennsylvania office with appropriate safeguards.

Corporate Information

We were incorporated in Delaware in 1989 and our office headquarters is located at 505 Eagleview Boulevard, Suite 212, Exton, Pennsylvania 19341.

Information Available on the Internet

Our internet address is www.iderapharma.com. We make available free of charge through our web site our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file or furnish such materials to the SEC. The SEC maintains an internet site at www.sec.gov containing reports, proxies and information statements and other information regarding issuers that file electronically with the SEC.

Item 1A. Risk Factors.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks and uncertainties described below in addition to the other information included or incorporated by reference in this Form 10-K before purchasing our common stock. Our business, financial condition and results of operations could be materially and adversely affected by any of these and currently unknown risks or uncertainties. In that case, the market price of our common stock could decline, and you may lose all or part of your investment in our securities.

Risks Relating to Our Financial Position and Need for Additional Capital

Our stock price has been and may continue to be volatile, and the value of an investment in our common stock may decline.

We historically have experienced significant volatility in our stock price. Since December 31, 2021, our common stock has traded as low as $0.41 per share. The realization of any of the risks described in these risk factors or other unforeseen risks could have an adverse effect on the market price of our common stock. The trading price of our common stock is likely to continue to be highly volatile and could be subject to declines in response to numerous factors, including disappointing results in a clinical program, as was the case following the announcement of topline results for ILLUMINATE-301. Other risk factors include results from clinical trials; FDA regulatory actions; announcements by us or our competitors of acquisitions, regulatory approvals, clinical milestones, new products, significant contracts, commercial relationships or capital commitments; additions or departures of key personnel; commencement of, or our involvement in, litigation; and any major change in our Board of Directors or management.

From time to time, we estimate the timing of the potential accomplishment of clinical and other development goals or milestones. These estimated milestones may include the commencement or completion of clinical trials. Also, from time to time, we expect that we will publicly announce the anticipated timing of some of these milestones. All these estimated milestones are based on numerous assumptions. These milestones may change and the actual timing of meeting these milestones may vary dramatically from our estimates, in some cases for reasons beyond our control. If we do not meet these estimated milestones, or the anticipated timing thereof, as publicly announced, our stock price may decline.

We may not be able to comply with Nasdaq's continued listing standards.

Our common stock trades on The Nasdaq Capital Market ("Nasdaq") under the symbol "IDRA." There is also no guarantee that we will be able to perpetually satisfy Nasdaq's continued listing requirements to maintain our listing on Nasdaq for any periods of time. Our failure to continue to meet these requirements may result in our securities being delisted from Nasdaq.

On November 26, 2021, we received a deficiency letter (the "Nasdaq Letter") from the Nasdaq Listing Qualifications Department, notifying us that we are not in compliance with Nasdaq Listing Rule 5550(a)(2), which requires the Company to maintain a minimum bid price of at least $1 per share for continued listing on Nasdaq (the "Minimum Bid Requirement"). The Company's failure to comply with the Minimum Bid Requirement was based on the Company's common stock per share price being below the $1 threshold for a period of 30 consecutive business days. In accordance with Nasdaq Listing Rule 5810(c)(3)(A) (the "Compliance Period Rule"), the Company has been provided an initial period of 180 calendar days (the "Compliance Date"), to regain compliance with the Minimum Bid Requirement. If, at any time before the Compliance Date, the bid price for the Company's common stock closes at $1.00 or more per share for a minimum of 10 consecutive business days, as required under Nasdaq requirements, the Staff will provide written notification to the Company that it complies with the Minimum Bid Requirement, unless the Staff exercises its discretion to extend this 10-day period pursuant to Nasdaq Listing Rule 5810(c)(3)(H).

If the Company does not regain compliance with the Minimum Bid Requirement by the Compliance Date, the Company may be eligible for an additional 180 calendar day compliance period (the "Second Compliance Period"). To qualify, the Company would need to meet the continued listing requirement for the market value of publicly held

shares and all other initial listing standards of the Nasdaq Capital Market, with the exception of the Minimum Bid Requirement, and provide written notice to the Staff of its intention to cure the deficiency during the Second Compliance Period.

Neither the Nasdaq Letter nor the Company's noncompliance with the Minimum Bid Requirement have an immediate effect on the listing or trading of the Company's common stock, which will continue to trade on The Nasdaq Capital Market under the symbol "IDRA."

If we fail to comply with Nasdaq rules and requirements, including, without limitation, the Minimum Bid Requirement, our stock may be delisted. In addition, even if we demonstrate compliance with the Minimum Bid Requirement, we will have to continue to meet other objective and subjective listing requirements to continue to be listed on Nasdaq. Delisting from Nasdaq could make trading our common stock more difficult for investors, potentially leading to declines in our share price and liquidity. Without a Nasdaq listing, stockholders may have a difficult time getting a quote for the sale or purchase of our common stock, the sale or purchase of our common stock would likely be made more difficult, and the trading volume and liquidity of our common stock could decline. Delisting from Nasdaq could also result in negative publicity and could also make it more difficult for us to raise additional capital. The absence of such a listing may adversely affect the acceptance of our common stock as currency or the value accorded by other parties. Further, if we are delisted, we would also incur additional costs under state blue sky laws in connection with any sales of our securities. These requirements could severely limit the market liquidity of our common stock and the ability of our stockholders to sell our common stock in the secondary market. If our common stock is delisted by Nasdaq, our common stock may be eligible to trade on an over-the-counter quotation system, such as the OTCQB Market, where an investor may find it more difficult to sell our stock or obtain accurate quotations as to the market value of our common stock. In the event our common stock is delisted from Nasdaq, we may not be able to list our common stock on another national securities exchange or obtain quotation on an over-the counter quotation system.

We will need additional financing, which may be difficult to obtain on terms attractive to us or at all. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect that we will need to raise additional funds in order to complete the development of, seek regulatory approvals for, and commercialization of our drug candidates for rare disease and to continue to fund our operations. We are seeking and expect to continue to seek additional funding through financings of equity or debt securities, collaborations, or the sale or license of assets. We believe the key factors that will affect our ability to obtain funding are: (i) the results of our clinical development activities in our drug candidates we develop on the timelines anticipated; (ii) the time and expense required to submit an NDA for our drug candidates; (iii) the cost, timing, and outcome of regulatory reviews; (iv) the receptivity of the capital markets to financings by biotechnology companies generally and companies with drug candidates and technologies similar to ours specifically; (v) receptivity of the capital markets to any in-licensing, product acquisition or other transaction we may enter into; and (vi) ability to enter into additional collaborations and the success of such collaborations.

Financing may not be available to us when we need it, or on favorable or acceptable terms, or at all. We could be required to seek funds through collaborative alliances or through other means that may require us to relinquish rights to some of our technologies, drug candidates or drugs that we would otherwise pursue on our own. In addition, if we raise additional funds by issuing equity securities, our existing stockholders may experience dilution, or an equity financing that involves existing stockholders may cause a concentration of ownership. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, and are likely to include rights that are senior to the holders of our common stock. Any additional debt or equity financing may contain terms which are not favorable to us or to our stockholders, such as liquidation and other preferences, or liens or other restrictions on our assets. As discussed in Note 13 to the financial statements appearing elsewhere in this Form 10-K, additional equity financings may also result in cumulative changes in ownership over a three-year period in excess of 50% which would limit the amount of net operating loss and tax credit carryforwards that we may utilize in any one year. If we are unable to obtain adequate funding on a timely basis or at all, we will be required to terminate, modify or delay clinical trials of our drug candidates, or relinquish rights to portions of our technology, drug candidates and/or products.

We expect that we will continue to incur net losses in the foreseeable future.

As of December 31, 2021, we had an accumulated deficit of $735.5 million and a cash and cash equivalents balance of $32.5 million. We expect to incur substantial operating losses in future periods and will require additional capital as we seek to advance any future drug candidates through development to commercialization. We do not expect to generate product revenue, sales-based milestones or royalties until we successfully complete development of and obtain marketing approval for any future drug candidates, either alone or in collaboration with third parties, which may not occur or may take a number of years. To commercialize any future drug candidates, we need to complete clinical development and comply with comprehensive regulatory requirements. We are subject to numerous risks and uncertainties similar to those of other companies of the same size within the biotechnology industry, such as uncertainty of clinical trial outcomes, uncertainty of additional funding and history of operating losses.

Even if we succeed in receiving marketing approval for and commercializing any product candidate, we will continue to incur substantial research and development and other expenditures to develop and market additional potential indications or products. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Risks Relating to Our Business, Strategy, and Industry

Our recent organizational changes undertaken to align to our focus on new business development opportunities may not be successful.

In April 2021, following the announcement that ILLUMINATE-301 did not meet its primary endpoint of ORR, we decided to implement a reduction-in-force affecting approximately 50% of our workforce starting at the second quarter of 2021. The objective of this workforce reduction was to realign our workforce to meet our needs in light of the outcome of ILLUMINATE-301's ORR endpoint. In May 2021, we announced that we would not continue ILLUMINATE-301 toward its OS endpoint. In connection with these actions, we have incurred termination costs, which include severance, benefits, and related costs, totaling $1.3 million in 2021.

We believe these changes were needed to streamline our organization and reallocate our resources to better align with our current strategic goals, including our current focus on new portfolio opportunities. However, these restructuring activities may yield unintended consequences and costs, such as the loss of institutional knowledge and expertise, attrition beyond our intended reduction-in-force, a reduction in morale among our remaining employees, and the risk that we may not achieve the anticipated benefits, all of which may have an adverse effect on our results of operations or financial condition. In addition, while positions have been eliminated certain functions necessary to our reduced operations remain, and we may be unsuccessful in distributing the duties and obligations of departed employees among our remaining employees. We may also discover that the reductions in workforce and cost cutting measures will make it difficult for us to pursue new opportunities and initiatives and require us to hire qualified replacement personnel, which may require us to incur additional and unanticipated costs and expenses. Moreover, there is no assurance we will be successful in our pursuit of any new business development opportunities, including additional strategic alternatives. Our failure to successfully accomplish any of the above activities and goals may have a material adverse impact on our business, financial condition, and results of operations.

As a small biopharmaceutical-focused company with limited resources, we may be unable to attract and retain qualified personnel.

We are a small company with 13 full-time employees as of December 31, 2021. Any future growth will require hiring additional qualified personnel. Also, because of the specialized scientific nature of our business, we face intense competition for qualified employees and consultants from biopharmaceutical companies, research organizations and academic institutions. Failure to attract and retain qualified personnel would materially harm our ability to compete effectively and grow our business.

If we lose any of our officers or key employees, our management and technical expertise could be weakened significantly.

Our success largely depends on the skills, experience, and efforts of our executive officers, especially our President and Chief Executive Officer, Mr. Vincent Milano. We do not maintain key person life insurance policies covering any of our employees. The loss of any of our executive officers could weaken our management and technical expertise significantly and harm our business.

We are depending heavily on the development, regulatory approval, and commercialization of drug candidates. If we are unable to successfully develop and commercialize drug candidates, or experience significant delays in doing so, our business may be materially harmed.

We have made and intend to continue to make a significant investment of our time and financial resources in the development and commercialization of our drug candidates. Our ability to generate product revenues will depend heavily on our ability to successfully develop, obtain regulatory approval for, and commercialize our drug candidates. If we fail to obtain regulatory approval and successfully commercialize our drug candidates, our business would be materially and adversely impacted. Even if our drug candidates receive regulatory approval, we will incur significant expenses to support its commercialization and launch, which investment may never be realized if sales are insufficient.

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

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the U.S.

In addition, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates. Our inability to enroll a sufficient number of patients for our clinical trials could also require us to abandon one or more clinical trials altogether. Enrollment delays may result in increased development costs for our drug candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If our clinical trials are unsuccessful, delayed or terminated, we may not be able to develop and commercialize our drug candidates.

Clinical trials are lengthy, complex, and expensive processes with uncertain results. We may not be able to complete any clinical trial of an investigational product within any specified time period. Moreover, clinical trials may not show our investigational products to have an acceptable safety and efficacy profile. The FDA, IRBs, or other equivalent foreign regulatory agencies may not allow us to complete these trials or commence and complete any other clinical trials.

Numerous unforeseen events may occur during, or as a result of, preclinical testing, nonclinical testing or the clinical trial process that could delay or inhibit the ability to receive regulatory approval or to commercialize drug products. For example, setbacks in clinical trials may result in enhanced scrutiny by regulators or IRBs of clinical trials of our drug candidates, which could result in regulators or IRBs prohibiting the commencement of clinical trials, requiring additional nonclinical studies as a precondition to commencing clinical trials or imposing restrictions on the design or scope of clinical trials that could slow enrollment of trials, increase the costs of trials or limit the significance of the results of trials. Such setbacks could also adversely impact the desire of investigators to enroll patients in, and the desire of patients to enroll in, clinical trials of our drug candidates.

Other events that could delay or inhibit conduct of our clinical trials include: (i) nonclinical or clinical data may not be readily interpreted, which may lead to delays and/or misinterpretation; (ii) our nonclinical tests, including toxicology studies, or clinical trials may produce negative or inconclusive results; (iii) we might have to suspend or terminate our clinical trials if the participating subjects experience serious adverse events or undesirable side effects or are exposed to unacceptable health risks; (iv) regulators or IRBs may hold, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements, issues identified through inspections of manufacturing or clinical trial operations or clinical trial sites; (v) we, along with our collaborators and subcontractors, may not employ, in any capacity, persons who have been debarred under by FDA or similar foreign regulatory authorities; (vi) we or our contract manufacturers may be unable to manufacture sufficient quantities of our drug candidates for use in clinical trials; (vii) the cost of our clinical trials may be greater than we currently anticipate making continuation and/or completion improbable; (viii) our investigators and contract research organizations may not follow the applicable regulatory requirements; and (ix) our drug candidates may not cause the desired effects or may cause undesirable side effects or our drug candidates may have other unexpected characteristics.

In conducting clinical trials, we cannot be certain that any planned clinical trial will begin on time, if at all. Delays in commencing clinical trials of potential products could increase our drug candidate development costs, delay any potential revenues, reduce the potential length of patent exclusivity and reduce the probability that a potential product will receive regulatory approval. Significant clinical trial delays also could allow our competitors to bring products to market before we do and impair our ability to commercialize our drug candidates.

The technologies on which we rely are unproven and may not result in any approved and marketable products.

Our technologies or therapeutic approaches are relatively new and unproven. Further, the chemical and pharmacological properties of our drug candidates may not be fully recognized in preclinical studies and small-scale clinical trials, and such compounds may interact with human biological systems in unforeseen, ineffective or harmful ways that we have not yet identified. Pre-clinical trials and early stage clinical trials may not be indicative of results that may be obtained in later stage trials. As a result of these factors, we may never succeed in obtaining regulatory approval to market any product.

We face substantial competition, which may result in others discovering, developing, or commercializing drugs before or more successfully than us.

There are many other companies, public and private, actively engaged in discovery, development, and commercializing products and technologies that may compete with our drug candidate and program. Some potentially competitive products have been in development or commercialized for years. Many of the marketed products have been accepted by the medical community, patients, and third-party payors. Our ability to compete may be affected by the previous adoption of such products by the medical community, patients, and third-party payors.

We recognize that other companies, including large pharmaceutical companies, may be developing or have plans to develop products and technologies that may compete with ours. Many of our competitors have substantially greater financial, technical, and human resources than we have and/or may have significantly greater experience than we have in undertaking preclinical studies and human clinical trials of new pharmaceutical products, obtaining FDA and other regulatory approvals of products for use in health care and manufacturing, and marketing and selling approved products. We anticipate that the competition with our drug candidates and technologies will be based on a number of factors including product efficacy, safety, availability, and price. The timing of market introduction of our drug candidates and competitive products will also affect competition among products. We expect the relative speed with which we can develop products, complete the clinical trials and approval processes, and supply commercial quantities of the products to the market to be important competitive factors.

Our business could be adversely affected by the effects of health epidemics, such as the ongoing COVID-19 global pandemic, including disruptions to our clinical trials or the delay of regulatory approvals.

Our business may be adversely affected by the effects of health epidemics, including the ongoing worldwide COVID-19 pandemic. The COVID-19 pandemic has caused significant volatility and uncertainty globally. This has resulted in an economic downturn and may disrupt our business and delay our clinical trials and regulatory approvals. This may also result in an interruption or issues with respect to the manufacture and supply of our product candidates. Quarantines and similar government orders have been enacted in each of the geographies in which we are conducting our clinical trials and may impact the ability of patients to participate in our trials. The patient populations that are eligible for our clinical trials may be immune-compromised and at higher risk for becoming infected with COVID-19. As COVID-19 affects the parts of the world where we are conducting our clinical trials, and the patients involved with these clinical trials become infected with COVID-19, we may have more adverse events and deaths in our clinical trials. The COVID-19 pandemic may also require that changes be made to any clinical trials or product manufacturing that may ultimately have an adverse impact. Additionally, if global health concerns continue to prevent the FDA from conducting its regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Such concerns could also affect the ability of our personnel to perform their normal responsibilities and could result in temporary closures of our facilities.

The COVID-19 pandemic continues to evolve. The ultimate impact of the COVID-19 pandemic 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. However, any one or a combination of these events could have an adverse effect on the operation of and results from our clinical trials, which could prevent or delay us from obtaining approval for our drug candidates, or on our employee resources.

Risks Related to Regulatory Approval and Marketing and Other Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming, and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our drug candidates.

We are not permitted to market our drug candidates in the U.S. or in other countries until we, or any future collaborators, receive approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside of the U.S. The approval process is lengthy, often taking a number of years, is uncertain, and is expensive. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the drug candidate's safety and efficacy. Information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities is also required. Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability or that of any collaborators we may have to generate revenue from the particular drug candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

Our failure to obtain marketing approval in foreign jurisdictions would prevent our drug candidates from being marketed abroad which subjects us to additional business risks that could adversely affect our operations.

We, and any future collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements in foreign jurisdictions. The approval procedure varies among countries and can involve additional studies. The time required to obtain approval may differ substantially from that required to obtain FDA approval. In addition, in many countries outside of the U.S., it is required that the drug be approved for reimbursement before the drug can be approved for sale in that country. We, and any future collaborators, may not obtain approvals from regulatory authorities outside of the U.S. on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in foreign jurisdictions, and approval by one regulatory authority outside of the U.S. does not ensure approval by regulatory authorities in other jurisdictions or by the FDA.

Even if we, or any future collaborators, obtain marketing approvals for our drug candidates, the terms of approvals and ongoing regulation of our drugs may limit how we, or they, manufacture and market our drugs, which could materially impair our ability to generate revenue.

We, and any future collaborators, must comply with requirements concerning advertising and promotion for any of our drug candidates for which we or they obtain marketing approval. Such promotional communications are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the drug’s approved labeling. Thus, we, and any future collaborators, will not be able to promote any drugs we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved drugs and those manufacturers’ facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA, and other regulatory authorities to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or our future collaborators, receive marketing approval for one or more of our drug candidates, we, and our future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and our future collaborators, are not able to comply with post-approval regulatory requirements, we, and our future collaborators, could have the marketing approvals for our drugs withdrawn by regulatory authorities and our, or our future collaborators’, ability to market any future drugs could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Moreover, legislative and regulatory proposals have been made to expand post-approval requirements and restrict promotional activities relating to our drugs. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the

marketing approvals of our drug candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any collaborators to more stringent product labeling and post-marketing testing and other requirements.

Any of our drug candidates for which we, or our future collaborators, obtain marketing approval in the future could be subject to post-approval restrictions or withdrawal from the market and we, and our future collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our drugs following approval.

Any of our drug candidates for which we, or our future collaborators, obtain marketing approval in the future, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such drug, among other things, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a drug candidate is granted, the approval may be subject to limitations on the indicated uses for which the drug may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy, which could include requirements for a restricted distribution system.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a drug. The FDA and other agencies, including the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or our future collaborators, do not market any of our drug candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label promotion.

In addition, later discovery of previously unknown adverse events or other problems with our drugs or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements both before and after product approval, may yield various results, including: (i) litigation involving patients taking our drug; (ii) restrictions on such drugs, manufacturers or manufacturing processes; (iii) restrictions on the labeling or marketing of a drug; (iv) restrictions on drug distribution or use; (v) requirements to conduct post-marketing studies or clinical trials; (vi) warning letters or untitled letters, as well as other enforcement and adverse actions; (vii) withdrawal of the drugs from the market; (viii) refusal to approve pending applications or supplements to approved applications that we submit; (ix) recall of drugs; (x) fines, restitution or disgorgement of profits or revenues; (xi) suspension or withdrawal of marketing approvals; (xii) damage to relationships with any potential collaborators; (xiii) unfavorable press coverage and damage to our reputation; (xiv) refusal to permit the import or export of drugs; (xv) drug seizure; or (xvi) injunctions or the imposition of civil or criminal penalties.

We may not be able to obtain or maintain orphan drug exclusivity for applications of our drug candidates.

The FDA may designate a product 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 U.S. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of seven years of marketing exclusivity. Orphan drug exclusivity may be lost if the FDA 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 June 2017, the FDA granted us orphan drug designation for tilsotolimod for the treatment of melanoma Stages IIb to IV. However, there can be no assurance that we will obtain orphan drug designation or exclusivity for any other disease indications for which we develop tilsotolimod, or for any other drug candidates. There is also no guarantee that we will be able to obtain orphan drug exclusivity if any product candidates with orphan designation are approved. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition or the same drug can 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 be safer, more effective or makes a major contribution to patient care.

A breakthrough therapy, fast track, or other expedited designation for our drug candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that those drug candidates will receive marketing approval.

We may seek a breakthrough therapy, fast track, or other designation for appropriate drug candidates. Designations such as these are within the discretion of the FDA. The receipt of a designation for a drug candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our drug candidates qualify under one of FDA's designation programs, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

We have only limited experience in regulatory affairs and our drug candidates are based on new technologies; these factors may affect our ability or the time we require to obtain necessary regulatory approvals.

We have never obtained regulatory approval for, or commercialized, a drug. It is possible that the FDA may refuse to accept any or all of our planned NDAs for substantive review or may conclude, after review of our data, that our applications are insufficient to obtain regulatory approval of any of our drug candidates. The FDA may also require that we conduct additional clinical or manufacturing validation studies, which may be costly and time-consuming, and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA required studies, approval of any NDA that we submit may be significantly delayed, possibly for years, or may require us to expend more resources than we have available or can secure.

We are subject to extensive and costly governmental regulation, the violation of which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Our product candidates are subject and any future commercial products will be subject to costly, extensive and rigorous domestic and foreign government regulation, as discussed under the caption "Government Regulation" within Item 1 of this Form 10-K. These requirements are continually evolving, which will require us to adapt our practices and processes, which we may not be able to do.

In addition, our future arrangements with third party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. These include, but are not limited to, the following: the Anti-Kickback Statute; the Foreign Corrupt Practices Act; the False Claims Act; privacy laws such as HIPAA; transparency requirements; and analogous state and foreign laws. Additionally, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to drug pricing and to certain payments and other transfers of value to physicians, other healthcare providers, and healthcare entities, or marketing expenditures.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, suspension and debarment from procurement and non-procurement transactions, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

We depend on information technology, infrastructure, and data to conduct our business. Any significant disruption, or cyber-attacks, could have a material adverse effect on our business.

We are dependent upon information technology, infrastructure and data. Computer systems, including ours and those of our suppliers, partners and service providers, contain sensitive confidential information or intellectual property, and are vulnerable to service interruption or destruction, cyber-attacks (both malicious and random) and

other natural or man-made incidents or disasters, which may be prolonged or go undetected. Such events are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. A significant interruption of our information technology could adversely affect our ability to manage and keep our operations running efficiently and effectively. An incident that results in a wider or sustained disruption to our business or products could have a material adverse effect on our business, financial condition and results of operations.

Likewise, data privacy or security breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients or other business partners may be exposed to unauthorized persons or to the public. There can be no assurance that our efforts, or the efforts of our partners and vendors, will prevent service interruptions, or identify breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related breaches.

Risks Relating to Collaborators

Our existing collaborations and any collaborations we enter into in the future may not be successful.

Our current collaboration agreements, as more fully described within Item 1 of this Form 10-K, or any collaborations we may enter into in the future, may not be successful. The success of our collaborative alliances, if any, will depend heavily on the efforts and activities of our collaborators. Our existing collaborations and any potential future collaborations have risks, including the following: (i) our collaborators may control the development (and timing thereof) of the drug candidates being developed with our technologies and compounds and/or the companion diagnostic to be developed for use in conjunction with our drug candidates; (ii) our collaborators may control the public release of information regarding the developments; (iii) disputes may arise in the future with respect to the ownership of or right to use technology and intellectual property developed with our collaborators; (iv) disagreements with our collaborators could delay or terminate the development of our products, or result in litigation or arbitration; (v) we may have difficulty enforcing the contracts if any of our collaborators fail to perform; (vi) our collaborators may terminate their collaborations with us, which could make it difficult for us to attract new collaborators or adversely affect the perception of us in the business or financial communities; (vii) our collaboration agreements are likely to be for fixed terms and subject to termination by our collaborators in the event of a material breach or lack of scientific progress by us; (viii) our collaborators may challenge our intellectual property rights or utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability; (ix) our collaborators may not comply with all applicable regulatory requirements; (x) our collaborators may under fund or not commit sufficient resources to the testing or development of our drug candidates; and (xi) our collaborators may develop alternative products either on their own or in collaboration with others, or encounter conflicts of interest or changes in business strategy or other business issues. Additionally, our collaborators will face the same development risks that we do and may not be successful in their efforts. Given these risks, it is possible that any collaborative alliance into which we enter may not be successful.

If we are unable to establish additional collaborative alliances, our business may be materially harmed.

Collaborators provide the necessary resources and drug development experience to advance our compounds in their programs. We have entered into and expect to continue to seek to enter into collaborative alliances with pharmaceutical companies. Upfront payments and milestone payments received from collaborations help to provide us with the financial resources for our internal research and development programs. We believe additional resources will be required to advance compounds. If we do not reach agreements with additional collaborators in the future or if the terms of such a collaborative alliance on are not favorable to us, we may not be able to obtain the expertise and resources necessary to achieve our business objectives, our ability to advance our compounds will be jeopardized and we may fail to meet our business objectives. Moreover, collaborations are complex and time consuming to negotiate, document, and implement. We may not be successful in our efforts to establish and implement collaborations on a timely basis.

Risks Relating to Intellectual Property

If we are unable to obtain and maintain patent protection for our discoveries, the value of our technology and products will be adversely affected.

Our ability to develop and commercialize drugs depends in significant part on our ability to: (i) obtain and maintain valid and enforceable patents; (ii) obtain licenses to the proprietary rights of others on commercially reasonably terms; (iii) operate without infringing upon the proprietary rights of others; (iv) prevent others from infringing on our proprietary rights; and (v) protect our trade secrets.

We do not know whether any of our currently pending patent applications or those patent applications that we license will result in the issuance of any patents. Our issued patents and those that may be issued in the future, or those licensed to us, may be challenged, invalidated, held unenforceable, narrowed in the course of a post-issuance proceeding or circumvented, and the rights granted thereunder may not provide us proprietary protection or competitive advantages against competitors with similar technology. Moreover, intellectual property laws may change and negatively impact our ability to obtain issued patents covering our technologies or to enforce any patents that issue. Because of the extensive time required for development, testing, and regulatory review of a potential product, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thus reducing any advantage provided by the patent.

Because patent applications in the U.S. and many foreign jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in the scientific literature often lag behind actual discoveries, neither we nor our licensors can be certain that we or they were the first to make the inventions claimed in issued patents or pending patent applications, or that we or they were the first to file for protection of the inventions set forth in these patent applications.

Third parties may own or control patents or patent applications and require us to seek licenses, which could increase our development and commercialization costs, or prevent us from developing or marketing products.

Although we have many issued patents and pending patent applications in the U.S. and other countries, we may not have rights under certain third-party patents or patent applications related to our compounds under development. Third parties may own or control these patents and patent applications in the U.S. and abroad. In particular, we are aware of certain third-party U.S. patents that contain claims related to immunostimulatory polynucleotides and their use to stimulate an immune response, as well as to antisense technology. Although we do not believe any of our TLR or antisense compounds under development infringe any valid claim of these patents, we cannot be assured that the holder of such patents would not seek to assert such patents against us or, if the holder did, that the courts would not interpret the claims of such patents more broadly than we believe appropriate and determine that we are in infringement of such patents. In addition, there may be other patents and patent applications related to our current or future drug candidates of which we are not aware. Therefore, in some cases, in order to develop, manufacture, sell or import some of our drug candidates, we or our collaborators may choose to seek, or be required to seek, licenses under third-party patents issued in the U.S. and abroad or under third-party patents that might issue from U.S. and foreign patent applications. In such an event, we would be required to pay license fees or royalties or both to the licensor. If licenses are not available to us on acceptable terms, we or our collaborators may not be able to develop, manufacture, sell or import these products, or may be delayed in doing so. Either of these results could have a material adverse effect on our business.

We may become involved in expensive patent litigation or other proceedings, which could result in our incurring substantial costs and expenses or substantial liability for damages, require us to stop our development and commercialization efforts or result in our patents being invalidated, interpreted narrowly or limited.

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the biotechnology industry. We may become a party to various types of patent litigation or other proceedings regarding intellectual property rights from time to time even under circumstances where we are not practicing and do not intend to practice any of the intellectual property involved in the proceedings. In addition to litigation, we may become involved in patent office proceedings, including oppositions, reexaminations, supplemental examinations and *inter partes* reviews involving our patents or the patents of third parties. We may initiate such proceedings or have such proceedings brought against us. An adverse determination in any such proceeding, or in litigation, could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates. An adverse determination in a proceeding involving a

patent in our portfolio could result in the loss of protection or a narrowing in the scope of protection provided by that patent.

The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the cost of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. If any patent litigation or other proceeding is resolved against us, we or our collaborators may be enjoined from developing, manufacturing, selling or importing our drugs without a license from the other party and we may be held liable for significant damages. We may not be able to obtain any required license on commercially acceptable terms or at all. In a patent office proceeding, such as an opposition, reexamination or *inter partes* review, our patents may be narrowed or invalidated. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time.

Our intellectual property may be infringed by a third party.

Third parties may infringe one or more of our issued patents or trademarks. We cannot predict if, when or where a third party may infringe one or more of our issued patents or trademarks. To counter infringement, we may be required to file infringement claims, which can be expensive and time-consuming. Moreover, there is no assurance that we would be successful in proving that a third party is infringing one or more of our issued patents or trademarks. Any claims we assert against perceived infringers could also provoke these parties to assert counterclaims against us, alleging that we infringe their intellectual property. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly and/or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question, any of which may adversely affect our business. Even if we are successful in proving in a court of law that a third party is infringing one or more of our issued patents or trademarks there can be no assurance that we would be successful in halting their infringing activities.

Risks Relating to Product Manufacturing, Marketing and Sales, and Reliance on Third Parties

Even if the compounds we may develop are successful in clinical trials and receive regulatory approvals, we or our collaboration partners may not be able to successfully commercialize them.

Even if the compounds were successful in clinical development and receive regulatory approvals, it may never reach or remain on the market, be successfully developed into commercial products or gain market acceptance among physicians, patients, healthcare payors or the medical community for a number of reasons including: (i) it may be found ineffective or cause harmful side effects; (ii) it may be difficult to manufacture on a scale necessary for commercialization; (iii) it may experience excessive product loss due to contamination, equipment failure, inadequate transportation or storage, improper installation or operation of equipment, vendor or operator error, natural disasters or other catastrophic events, inconsistency in yields or variability in product characteristics; (iv) it may be uneconomical to produce; (v) the timing of market introduction of the compounds we may develop and competitive products may be inopportune; (vi) political and legislative changes may make the commercialization of any product candidates we may develop in the future, more difficult; (vii) we may fail to obtain reimbursement approvals or pricing that is cost effective for patients as compared to other available forms of treatment or that covers the cost of production and other expenses; (viii) they may not compete effectively with existing or future alternatives; (ix) we may be unable to develop commercial operations and to sell marketing rights; (x) it may fail to achieve market acceptance; or (xi) we may be precluded from commercialization of a product due to proprietary rights of third parties.

Because we have limited manufacturing experience, and no manufacturing facilities or infrastructure, we are dependent on third-party manufacturers to manufacture drug candidates for us.

We have limited manufacturing experience and no manufacturing facilities, infrastructure or clinical or commercial scale manufacturing capabilities. In order to continue to develop our drug candidates, apply for regulatory approvals, and ultimately commercialize products, we need to develop, contract for or otherwise arrange for the necessary manufacturing capabilities. We currently rely upon third parties to produce material for nonclinical and clinical testing purposes and expect to continue to do so in the future. We also expect to rely upon third parties to produce materials that may be required for the commercial production of our drug candidates, if approved. Our current and anticipated future dependence upon others for the manufacture of our drug candidates may adversely affect our future profit

margins and our ability to develop drug candidates and commercialize any drug candidates on a timely and competitive basis. We currently do not have any long-term supply contracts.

There are a limited number of manufacturers who operate under the FDA's cGMP regulations capable of manufacturing our drug candidates. As a result, we may have difficulty finding manufacturers for our drug candidates suitable for our needs. If we are unable to arrange for third-party manufacturing of our drug candidates on a timely basis, or on acceptable terms, we may not be able to complete development of our drug candidates or market them.

Any contract manufacturers with which we enter into manufacturing arrangements will be subject to extensive regulatory requirements and ongoing periodic, unannounced inspections by the FDA, or foreign equivalent, and corresponding state and foreign agencies or their designees to ensure compliance with cGMP requirements and other governmental regulations and corresponding foreign standards. Any failure by our third-party manufacturers to comply with such requirements, regulations or standards could lead to a delay in the conduct of our clinical trials, or a delay in, or failure to obtain, regulatory approval of any of our drug candidates. Such failure could also result in sanctions being imposed, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, product seizures or recalls, imposition of operating restrictions, total or partial suspension of production or distribution, or criminal prosecution.

Additionally, contract manufacturers may not be able to manufacture our drug candidates at a cost or in quantities necessary to make them commercially viable. Furthermore, changes in the manufacturing process or procedure, including a change in the location where the drug substance or drug product is manufactured or a change of a third-party manufacturer, may require prior FDA review and approval in accordance with the FDA's cGMP and NDA regulations. Contract manufacturers may also be subject to comparable foreign requirements. This review may be costly and time-consuming and could delay or prevent the launch of a drug candidate. The FDA or similar foreign regulatory agencies at any time may also implement new standards or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. If we or our contract manufacturers are unable to comply, we or they may be subject to regulatory action, civil actions or penalties.

We have no experience selling, marketing or distributing potential products and no internal capability to do so.

Advancing compounds through Phase 3 development and regulatory approval will require us to begin commercialization preparation activities and incur related expenses. These activities will include, among other things, the development of an in-house marketing organization and sales force, a market access and payor reimbursement strategy and a distribution function, which will require significant capital expenditures, management resources and time. If we are unable to adequately prepare the market for the potential future commercialization of compounds, we may not be able to generate product revenue once marketing authorization is obtained.

If we are unable or decide not to establish internal sales, marketing and distribution capabilities, we will pursue collaborative arrangements regarding the sales and marketing of our products; however, there can be no assurance that we will be able to establish or maintain such collaborative arrangements on commercially reasonable terms, or if we are able to do so, that they will have effective sales forces. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates. Finally, regardless of whether we contract out our sales and marketing functions, we will be responsible for the marketing and promotion of our products and may be held responsible should any products be improperly marketed or promoted.

If third parties on whom we rely for clinical and preclinical trials do not perform as contractually required or as we expect, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business may suffer.

We do not have the ability to independently conduct the clinical or preclinical trials required to obtain regulatory approval for our drug candidates. We depend on independent investigators, contract research organizations (“CROs”), and other third-party service providers in the conduct of the trials of our drug candidates and expect to continue to do so. We expect to contract with CROs for future clinical trials. We rely heavily on these parties for successful execution of our trials, but do not control many aspects of their activities. We are responsible for ensuring that each of our trials is conducted in accordance with the applicable regulations and protocols for the trial. Third parties may not complete activities on schedule, or at all, or may not conduct our trials in accordance with regulatory

requirements or our protocols. If these third parties fail to carry out their obligations, we may need to enter into new arrangements with alternative third parties. This could be difficult, costly or impossible, and our preclinical or clinical trials may need to be extended, delayed, terminated or repeated, and we may not be able to obtain regulatory approval in a timely fashion, or at all, for the applicable drug candidate, or to commercialize such drug candidate being tested in such trials. If we seek to conduct any of these activities ourselves in the future, we will need to recruit appropriately trained personnel and add to our research, clinical, quality and corporate infrastructure. Moreover, if we need to replace any third parties, we may not be able to do so in a timely fashion or on commercially reasonable terms.

The commercial success of any drug candidates that we may develop will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Any products that we ultimately bring to the market, if they receive marketing approval, may not gain market acceptance by physicians, patients, third-party payors or others in the medical community. For example, current cancer treatments, including chemotherapy and radiation therapy are well-established in the medical community, and doctors may continue to rely on these treatments. If our products do not achieve an adequate level of acceptance, we may not generate product revenue and we may not become profitable. The degree of market acceptance of our products, if approved for commercial sale, will depend on a number of factors, including: (i) the prevalence and severity of any side effects; (ii) the efficacy and potential advantages over alternative treatments; (iii) the ability to offer our drug candidates for sale at competitive prices; (iv) relative convenience and ease of administration; (v) the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; (vi) the strength of marketing and distribution support and the timing of market introduction of competitive products; and (vii) publicity concerning our products or competing products and treatments.

Even if a potential product displays a favorable efficacy and safety profile, market acceptance of the product will not be known until after it is launched. Our efforts to educate patients, the medical community, and third-party payors about our drug candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by conventional methods used by our competitors.

If we are unable to obtain adequate reimbursement from third-party payors for any products that we may develop or acceptable prices for those products, our revenues and prospects for profitability will suffer.

Most patients rely on Medicare, Medicaid, private health insurers, and other third-party payors to pay for their medical needs, including any drugs we may market. If third-party payors do not provide adequate coverage or reimbursement for any products that we may develop, our revenues and prospects for profitability will suffer.

Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly-approved products. These third-party payors may base their coverage and reimbursement on the coverage and reimbursement rate paid by carriers for Medicare beneficiaries. Furthermore, many such payors are investigating or implementing methods for reducing health care costs, such as the establishment of capitated or prospective payment systems. Cost containment pressures have led to an increased emphasis on the use of cost-effective products by health care providers, which could limit the price we might establish for products that we or our current or future collaborators may develop or sell, which would result in lower product revenues or royalties payable to us. In particular, third-party payors may limit the indications for which they will reimburse patients who use any products that we may develop or impose other patient access or utilization controls or limitations.

We face a risk of product liability claims and may not be able to obtain insurance.

Our business exposes us to the risk of product liability claims that is inherent in the manufacturing, testing, and marketing of prescription drugs. We face a risk of product liability exposure related to the testing of our drug candidates in clinical trials and will face an even greater risk if we commercially sell any products. Regardless of merit or eventual outcome, liability claims and product recalls may result in: (i) decreased demand for our drug candidates and products; (ii) damage to our reputation; (iii) regulatory investigations that could require costly recalls or product modifications; (iv) withdrawal of clinical trial participants; (v) costs to defend related ligation; (vi) substantial monetary awards to clinical trial participants or patients; (vii) loss of revenue; (viii) the diversion of

management's attention away from managing our business; and (ix) the inability to commercialize any products that we may develop.

Although we have product liability and clinical trial liability insurance that we believe is adequate, this insurance is subject to deductibles and coverage limitations. We may not be able to obtain or maintain adequate protection against potential liabilities. If we are unable to obtain insurance at acceptable cost or otherwise protect against potential product liability claims, we will be exposed to significant liabilities, which may materially and adversely affect our business and financial position. These liabilities could also prevent or interfere with our commercialization efforts.

Risks Relating to Ownership of Our Common Stock

Provisions in our certificate of incorporation and by-laws and Delaware law, may prevent a change in control that stockholders may consider desirable.

Section 203 of the General Corporation Law of the State of Delaware (the "DGCL") and our certificate of incorporation and by-laws contain provisions that might enable our management to resist a takeover of our company or discourage a third party from attempting to take over our company. These provisions include: (i) a classified board of directors; (ii) limitations on the removal of directors; (iii) limitations on stockholder proposals at meetings of stockholders; (iv) the inability of stockholders to act by written consent or to call special meetings; and (v) the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval. These provisions could: (i) have the effect of delay, defer or prevent a change in control of us or a change in our management that stockholders may consider favorable or beneficial or (ii) discourage proxy contests and make it more difficult for stockholders to elect directors and take other corporate actions.

The Company's amended and restated bylaws ("Bylaws") provide, to the fullest extent permitted by law, that the Court of Chancery of the State of Delaware will be the exclusive forum for certain legal actions between the Company and its stockholders, which could increase costs to bring a claim, discourage claims or limit the ability of the Company's stockholders to bring a claim in a judicial forum viewed by the stockholders as more favorable for disputes with the Company or the Company's directors, officers or other employees.

Our Bylaws provide to the fullest extent permitted by law that unless the Company consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any (i) derivative action or proceeding brought on behalf of the Company, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer, other employee or stockholder of the Company to the Company or its stockholders, (iii) any action arising pursuant to any provision of the DGCL, the Company's Certificate of Incorporation or the Bylaws, (iv) any action to interpret, apply, enforce or determine the validity of the Certificate of Incorporation or the Bylaws, or (v) any action asserting a claim governed by the internal affairs doctrine. The choice of forum provision may increase costs to bring a claim, discourage claims or limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with the Company or its directors, officers or other employees, which may discourage such lawsuits against the Company or its directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in the Company's Bylaws to be inapplicable or unenforceable in an action, the Company may incur additional costs associated with resolving such action in other jurisdictions. The exclusive forum provision in our Bylaws would not apply to claims brought under the Exchange Act or the Securities Act, or any other claim for which the federal courts have exclusive jurisdiction. Additionally, such provision will not relieve us of our duty to comply with the federal securities laws and the rules and regulations thereunder, and stockholders will not be deemed to have waived our compliance with these laws, rules and regulations.

Approximately 24% of our outstanding common stock is held (28% beneficially owned) by three stockholders. If these significant stockholders choose to act together, they could exert substantial influence over our business, and the interests of these stockholders may conflict with those of other stockholders.

There is a concentration of ownership of our outstanding common stock because approximately 24% of our outstanding common stock is owned by three stockholders. As of December 31, 2021: (i) Baker Bros. Advisors LP, and certain of its affiliated funds (collectively, "Baker Brothers") beneficially owned 3.9% of our outstanding common stock, which excludes all convertible securities as a result of certain beneficial ownership limitations as discussed in

Note 15 of this Form 10-K; (ii) entities affiliated with Pillar Invest Corporation (the "Pillar Investment Entities") beneficially owned 19.9% of our outstanding common stock; and (iii) Castellina Ventures Ltd. ("Castellina" and, together with Baker Brothers and Pillar Investment Entities, the "Significant Securityholders") beneficially owned 4.2% of our outstanding common stock. If any of our Significant Securityholders acted together, they could be able to exert substantial influence over our business. Additionally, the interests of the Significant Securityholders may be different from or conflict with the interests of our other stockholders. This concentration of voting power with the Significant Securityholders could delay, defer or prevent a change of control, entrench our management and the board of directors or delay or prevent a merger, consolidation, takeover or other business combination involving us on terms that other stockholders may desire. In addition, conflicts of interest could arise in the future between us, on the one hand, and either of our Significant Securityholders on the other hand, concerning potential competitive business activities, business opportunities, the issuance of additional securities and other matters.

The issuance or sale of shares of our common stock could depress the trading price of our common stock.

If (i)we issue additional shares of our common stock or rights to acquire shares of our common stock in other future transactions, (ii) any of our existing stockholders sells a substantial amount of our common stock, or (iii) the market perceives that such issuances or sales may occur, then the trading price of our common stock may significantly decrease. In addition, our issuance of additional shares of common stock will dilute the ownership interests of our existing common stockholders.

Because we do not intend to pay dividends on our common stock, investor returns will be limited to any increase in the value of our stock.

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business and do not anticipate declaring or paying any cash dividends on our common stock for the foreseeable future.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease approximately 11,000 square feet of office space located in Exton, Pennsylvania. The lease expires on May 31, 2025. We may terminate the lease at any point as long as we remain a member of the landlord's group and require a space with more square footage. We have specified rights to sublease this facility.

Item 3. Legal Proceedings.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II.

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

Market Information

Our common stock is listed under the symbol "IDRA" on the Nasdaq.

Holders of Record

As of March 4, 2022, we had approximately 51 common stockholders of record registered on our books, excluding shares held through banks and brokers.

Dividends

We have never declared or paid cash dividends on our common stock, and we do not expect to pay any cash dividends on our common stock in the foreseeable future. The declaration and payment of dividends in the future, of which there can be no assurance, will be determined by our Board of Directors in light of conditions then existing, including earnings, financial condition, capital requirements and other factors.

Recent Sales of Unregistered Securities

We did not issue any unregistered equity securities during the year ended December 31, 2021.

Issuer Purchases of Equity Securities

We did not repurchase any of our equity securities during the year ended December 31, 2021.

Item 6. Reserved.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our audited financial statements and the related notes appearing elsewhere in this Form 10-K.

Overview

We are a biopharmaceutical company with a business strategy focused on the clinical development, and ultimately the commercialization, of drug candidates for rare disease indications characterized by small, well-defined patient populations with serious unmet medical needs. Our current focus is to identify and potentially acquire rights to novel development and commercial stage rare disease programs through new business development opportunities, including additional strategic alternatives. We have in the past and may in the future explore collaborative alliances to support development and commercialization of any of our drug candidates.

Until May 2021, we were developing tilsotolimod, via intratumoral injection, for the treatment of anti-PD1 refractory metastatic melanoma in combination with ipilimumab, an anti-CTLA4 antibody marketed as Yervoy® by Bristol Myers Squibb Company ("BMS") in a Phase 3 registration trial. During the first quarter of 2021, we announced that ILLUMINATE-301, the Company's pivotal registration trial of tilsotolimod in combination with ipilimumab versus ipilimumab alone in patients with anti-PD-1 refractory advanced melanoma, did not meet its primary endpoint of Objective Response Rate ("ORR"). Based on subsequent evaluation of the full data set, in May 2021, we announced that we would not continue the trial to its Overall Survival ("OS") primary endpoint.

Through December 2021, we were also evaluating intratumoral tilsotolimod in combination with nivolumab, an anti-PD1 antibody marketed as Opdivo® by BMS, and ipilimumab for the treatment of multiple solid tumors in a multicohort Phase 2 trial. In December 2021, we announced that preliminary data from the second 10 patients dosed in the safety cohort of ILLUMINATE-206 showed a safety profile consistent with the first 10 patients in ILLUMINATE-206 and with prior studies. No further enrollment in ILLUMINATE-206 is planned at this time.

While our clinical trials with tilsotolimod have not yet translated into a new treatment alternative for patients, data supporting tilsotolimod's mechanism of action and encouraging safety profile from across the array of pre-clinical and clinical work to date, together with its intellectual property protection, are noteworthy. As a result, in December 2021, we announced that we will consider an out-licensing arrangement so that its full potential may continue to be explored on behalf of patients who do not respond to traditional immunotherapy.

Historically, substantially all our revenues have been from collaboration and license agreements, although we did not generate any such revenue in 2021, and we have received no revenues from the sale of commercial products. Going forward, we plan to continue to invest in research and development. Accordingly, we anticipate a significant portion of our operating expenses will continue to be related to research and development in 2022 and beyond. See additional information below under the headings "Results of Operations" regarding research and development expenses to date and "Financial Condition, Liquidity and Capital Resources" regarding our future funding requirements.

Recent Events and Updates

Reduction-in-Force

In April 2021, following the announcement that the ILLUMINATE-301 trial did not meet its primary endpoint of ORR, we implemented a reduction-in-force which affected approximately 50% of our workforce through September 30, 2021, primarily in the area of research and development. The decision was made in order to align our workforce with our needs in light of the outcome of ILLUMINATE-301's ORR endpoint, our ongoing ILLUMINATE development program, and other business development activities focused on identifying new portfolio opportunities.

In connection with these actions, we incurred and paid termination costs for the reduction in workforce, which includes severance, benefits and related costs, of approximately $1.3 million during the year ended December 31, 2021.

Nasdaq Compliance

As previously disclosed, on November 26, 2021, we received a deficiency letter (the "Nasdaq Letter") from the Nasdaq Listing Qualifications Department, notifying us that the Company is not in compliance with Nasdaq Listing Rule 5550(a)(2), which requires the Company to maintain a minimum bid price of at least $1 per share for continued listing on The Nasdaq Capital Market (the "Minimum Bid Requirement"). The Company's failure to comply with the Minimum Bid Requirement was based on the Company's common stock per share price being below the $1 threshold for a period of 30 consecutive business days. In accordance with Nasdaq Listing Rule 5810(c)(3)(A) (the "Compliance Period Rule"), the Company has been provided an initial period of 180 calendar days (the "Compliance Date"), to regain compliance with the Minimum Bid Requirement. If, at any time before the Compliance Date, the bid price for the Company's common stock closes at $1.00 or more per share for a minimum of 10 consecutive business days, as required under Nasdaq requirements, the Staff will provide written notification to the Company that it complies with the Minimum Bid Requirement, unless the Staff exercises its discretion to extend this 10-day period pursuant to Nasdaq Listing Rule 5810(c)(3)(H).

If the Company does not regain compliance with the Minimum Bid Requirement by the Compliance Date, the Company may be eligible for an additional 180 calendar day compliance period (the "Second Compliance Period"). To qualify, the Company would need to meet the continued listing requirement for the market value of publicly held shares and all other initial listing standards of the Nasdaq Capital Market, with the exception of the Minimum Bid Requirement, and provide written notice to the Staff of its intention to cure the deficiency during the Second Compliance Period.

Neither the Nasdaq Letter nor the Company's noncompliance with the Minimum Bid Requirement have an immediate effect on the listing or trading of the Company's common stock, which continues to trade on The Nasdaq Capital Market under the symbol "IDRA."

Results of Operations

The following is a discussion of results of operations for fiscal 2021 compared to fiscal 2020. For a discussion of results of operations for fiscal 2020 compared to fiscal 2019, please refer to Item 7—Management's Discussion and Analysis of Financial Condition and Results of Operations in the Company's Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 1, 2021.

Years ended December 31, 2021 and 2020

Research and Development Expenses

For each of our research and development programs, we incur both direct and indirect expenses. We track direct research and development expenses by program, which include third-party costs such as contract research, consulting and clinical trial and manufacturing costs. We do not allocate indirect research and development expenses, which may include regulatory, laboratory (equipment and supplies), personnel, facility, and other overhead costs (including depreciation and amortization), to specific programs.

During the fiscal year ended December 31, 2021, our overall research and development expenses declined by 34% as compared to 2020, primarily due to decreases in external development costs associated with tilsotolimod (IMO-2125). This decrease is primarily related to: (i) costs incurred with contract research organizations during the year ended December 31, 2021 to support our ILLUMINATE-301 trial, which was discontinued by the Company in the second quarter of 2021; and (ii) lower costs incurred with drug manufacturing activities. The decrease of the research and development expenses is offset by the costs associated with ILLUMINATE-206 and the Scriptr Agreement.

Tilsotolimod (IMO-2125) external development expenses as well as expenses related to the Scriptr Agreement (as more fully described under the heading "Collaborative Alliances" above in Item 1.) will continue to be a significant portion of our total research and development spending in 2022.

In the table below, research and development expenses are set forth in the following categories: Tilsotolimod (IMO-2125) and other drug development expenses.

($ in thousands)	Year Ended December 31, 2021	2020	% Change 2021 vs 2020
Tilsotolimod (IMO-2125) external development expense	$ 9,247	$ 16,707	(45)%
Other drug development expense	7,128	8,065	(12)%
Total research and development expenses	$ 16,375	$ 24,772	(34)%

Tilsotolimod (IMO-2125) External Development Expenses

These expenses include external expenses we have incurred in connection with the development of tilsotolimod as part of our immuno-oncology program. These external expenses include payments to independent contractors and vendors for drug development activities conducted after the initiation of tilsotolimod clinical development in immuno-oncology, but exclude internal costs such as payroll and overhead expenses.

We commenced clinical development of tilsotolimod as part of our immuno-oncology program in July 2015, and from July 2015 through December 31, 2021, we incurred approximately $91.1 million in tilsotolimod external development expenses, including costs associated with the preparation for and conduct of ILLUMINATE-204, ILLUMINATE-101, ILLUMINATE-301, ILLUMINATE-206, and the manufacture of additional drug substance for use in our clinical trials and additional nonclinical studies.

Other Drug Development Expenses

These expenses include internal costs, such as payroll and overhead expenses, associated with all our clinical development programs. In addition, these expenses include external expenses, such as payments to contract vendors, associated with compounds that were previously being developed but are not currently being developed. We incurred $2.1 million of expenses within other drug development expenses related to our research collaboration with Scriptr in 2021

General and Administrative Expenses

General and administrative expenses consist primarily of payroll, stock-based compensation expense, consulting fees and professional legal fees associated with our patent applications and maintenance, our corporate regulatory filing requirements, our corporate legal matters, and our business development initiatives. For the years ended December 31, 2021 and 2020, general and administrative expenses totaled $10.0 million and $11.9 million, respectively.

General and administrative expenses decreased by approximately $1.9 million, or 16.3%, in 2021 as compared to 2020, primarily due to lower salary, bonus, stock compensation expense, employee-related expense related to terminated employees as part of our reduction-in-force, and commercial research support costs, partially offset by increased consulting expenses.

Restructuring Costs

In April 2021, following the announcement that the ILLUMINATE-301 trial did not meet its primary endpoint of ORR, we implemented a reduction-in-force which affected approximately 50% of the workforce through December 31, 2021, primarily in the area of research and development. The decision was made in order to align our workforce with its needs in light of the outcome of ILLUMINATE-301's ORR endpoint, its ongoing ILLUMINATE development program and other business development activities focused on identifying new portfolio opportunities.

Restructuring costs for the year ended December 31, 2021 totaled approximately $1.3 million and is comprised of termination costs including severance, benefits and related costs. No such costs were incurred during the year ended December 31, 2020.

Interest Income

Interest income for the years ended December 31, 2021 and 2020 totaled $0.1 million and $0.2 million, respectively. The decrease in 2021, as compared to 2020, was primarily due to lower interest rates and decrease in average short-term investment and cash balances and yields.

Amounts may fluctuate from period to period due to changes in average investment balances, including commercial paper and money market funds classified as cash equivalents, and composition of investments.

Warrant Revaluation Gain or Loss

During the years ended December 31, 2021 and 2020, we recorded a non-cash warrant revaluation gain (loss) of approximately $7.0 million and $(3.7) million, respectively.

The non-cash gain for the fiscal year ended December 31, 2021 relates to the derecognition of the warrant liability in the first quarter of 2021 due to the termination of such liability-classified warrants that were issued in connection with our December 2019 Private Placement.

The non-cash loss for the fiscal year ended December 31, 2020 relate to the revaluation of our liability-classified warrants issued in connection with the December 2019 Private Placement. Due to the nature of and inputs in the model used to assess the fair value of our outstanding warrants, it is not abnormal to experience significant fluctuations during each remeasurement period. These fluctuations may be due to a variety of factors, including changes in our stock price and changes in estimated stock price volatility over the remaining life of the warrants. Warrant revaluation loss for 2020 was driven primarily by an increase in our stock price during each period. More specifically, the significant warrant revaluation loss for the 2020 period was primarily due to the approximate 102% increase in our stock price during the period January 1, 2020 to December 31, 2020.

The non-cash warrant revaluation gain (loss) mentioned above are fully described in Note 7 of the Notes to Financial Statements appearing elsewhere in this Form 10-K.

Future Tranche Right Revaluation Gain or Loss

During the years ended December 31, 2021 and 2020, we recorded a non-cash future tranche right revaluation gain (loss) of approximately $118.8 million and $(72.4) million, respectively.

The non-cash gain for the fiscal year ended December 31, 2021 relates to the derecognition of the future tranche right liability in the first quarter of 2021 due to the termination of the future tranche rights that were issued in connection with our December 2019 Private Placement.

The non-cash loss for the fiscal year ended December 31, 2020 relates to the revaluation of our liability-classified tranche rights liability issued in connection with the December 2019 Private Placement. Due to the nature of and inputs in the model used to assess the fair value of the future tranche rights, it is not abnormal to experience significant fluctuations during each remeasurement period. These fluctuations may be due to a variety of factors, including changes in our stock price and changes in estimated stock price volatility over the remaining estimated lives of the future tranche rights. Changes in the fair value of the future tranche right liability and resulting future tranche right revaluation loss for 2020 was driven primarily by an increase in our stock price during the periods. More specifically, the significant future tranche right revaluation loss for the 2020 period was primarily due to the approximate 102% increase in our stock price during the period January 1, 2020 to December 31, 2020.

Both non-cash future tranche right revaluation gain (loss) for the respective periods are fully described in Note 7 of the Notes to Financial Statements appearing elsewhere in this Form 10-K.

Net Income or Loss to Common Stockholders

As a result of the factors discussed above, our net income (loss) was $98.1 million and $(112.7) million for the years ended December 31, 2021 and 2020, respectively. See Note 16 of the Notes to Financial Statements appearing elsewhere in this Annual Report on Form 10-K for additional details.

Net Operating Loss Carryforwards

We have completed several financings since the effective date of the Tax Reform Act of 1986, which as of December 31, 2021, have resulted in ownership changes that will significantly limit our ability to utilize our net operating loss carryforwards ("NOLs") and tax credit carryforwards. In December 2017, we completed a study which determined that ownership changes had occurred. The federal and state net operating loss and tax credit carryforwards and related deferred tax assets discussed below and included in Note 13 to the financial statements appearing elsewhere in this Form 10-K have been adjusted to reflect the limitations that resulted from this study. The Company continues to monitor equity activity and potential ownership changes.

As of December 31, 2021, we had cumulative federal and state NOLs of approximately $327.5 million and $322.0-million available to reduce federal and state taxable income, respectively. As a result of the Tax Cuts and Jobs Act of 2017, federal net operating losses incurred for taxable years beginning after January 1, 2018 have an unlimited carryforward period, but can only be utilized to offset 80% of taxable income in future taxable periods. Of the $327.5 million of federal NOLs, $130.1 million have an unlimited carryforward and the remaining NOLs are still subject to expiration through 2037. State NOLs are still subject to expiration according to the laws of each respective jurisdiction. The Company files state tax returns in Massachusetts and Pennsylvania whereby both jurisdictions impose a 20-year carryforward period. All $322.0 million of state NOLs expire through 2041, with the first year of expiration being 2032 for $23.4 million of Massachusetts NOLs. In addition, at December 31, 2021, the Company had cumulative federal and state tax credit carryforwards of $26.7 million and $1.9 million, respectively, available to reduce federal and state income taxes, respectively, which expire through 2041 and 2033, respectively, for federal and state purposes, other than those that have an unlimited carryforward period.

Financial Condition, Liquidity and Capital Resources

Financial Condition

As of December 31, 2021, we had an accumulated deficit of $735.5 million. To date, substantially all our revenues have been from collaboration and license agreements and we have received no revenues from the sale of commercial products. We generated no revenue for the fiscal year ended December 31, 2021.

We have devoted substantially all our efforts to research and development, including clinical trials, and we have not completed development of any commercial products. Our research and development activities, together with our general and administrative expenses, are expected to continue to result in substantial operating losses for the foreseeable future. These losses, among other things, have had and will continue to have an adverse effect on our stockholders' equity, total assets and working capital. Because of the numerous risks and uncertainties associated with developing drug candidates, and if approved, commercial products, we are unable to predict the extent of any future losses, whether or when any of our drug candidates will become commercially available or when we will become profitable, if at all.

Liquidity and Capital Resources

Overview

We require cash to fund our operating expenses and to make capital expenditures. Historically, we have funded our cash requirements primarily through the following:

(i) sale of common stock, preferred stock and future tranche rights and warrants (including pre-funded warrants);

(ii) exercise of warrants;

(iii) debt financing, including capital leases;

(iv) license fees, research funding and milestone payments under collaborative and license agreements; and

(v) interest income.

We filed a shelf registration statement on Form S-3 on August 4, 2020, which was declared effective on September 2, 2020, relating to the sale, from time to time, in one or more transactions, up to $150.0 million of common stock, preferred stock, depository shares and warrants.

LPC Purchase Agreement

On March 4, 2019, we entered into a Purchase Agreement with Lincoln Park Capital Fund, LLC ("Lincoln Park"), pursuant to which, upon the terms and subject to the conditions and limitations set forth therein, Lincoln Park has committed to purchase an aggregate of $35.0 million of shares of Company common stock from time to time at our sole discretion (the "LPC Purchase Agreement").

During the years ended December 31, 2021 and 2020, we sold 800,000 and 750,000 shares of common stock, respectively, pursuant to the LPC Purchase Agreement, resulting in net proceeds of $4.2 million and $1.7 million, respectively. The LPC Purchase Agreement had a 36-month term which expired on March 4, 2022. Accordingly, we no longer have access to capital under the LPC Purchase Agreement.

ATM Agreement

In November 2018, we entered into an Equity Distribution Agreement (the "ATM Agreement") with JMP Securities LLC ("JMP") pursuant to which we may issue and sell shares of its common stock having an aggregate offering price of up to $50.0 million through JMP as its agent.

During the years ended December 31, 2021 and 2020, we sold 5,117,357 and 3,608,713 shares of common stock, respectively, pursuant to the ATM Agreement, resulting in net proceeds, after deduction of commissions and other offering expenses, of $15.3 million and $12.3 million, respectively. As of March 31, 2022, we may sell up to an additional $19.5 million of shares under the ATM Agreement.

The LPC Purchase Agreement and ATM Agreement are more fully described in Note 8 of the notes to our financial statements included elsewhere in this Form 10-K.

Funding Requirements

We had cash and cash equivalents of approximately $32.5 million at December 31, 2021. We believe based on our current operating plan, our existing cash, cash equivalents on hand as of December 31, 2021 will enable us to fund our operations through the one-year period subsequent to the filing date of this Form 10-K. Specifically, we believe our available funds will be sufficient to enable us to perform the following:

(i) fund business development related activities, such as identifying and potentially acquiring rights to novel development and commercial stage rare disease programs, including additional strategic alternatives;

(ii) conclude our current Low-Dose, High-Frequency Cohort of our Phase 2 study of tilsotolimod in combination with nivolumab and ipilimumab for the treatment of MSS-CRC (ILLUMINATE-206);

(iii) conclude our Phase 3 clinical trial of tilsotolimod in combination with ipilimumab for the treatment of anti-PD1 refractory metastatic melanoma (ILLUMINATE-301);

(iv) fund certain research including investigator initiated clinical trials of tilsotolimod and the Scriptr Agreement; and

(v) maintain a level of general and administrative expenses to support the business.

In addition, we are seeking and expect to continue to seek additional funding through collaborations, the sale or license of assets or financings of equity or debt securities. We believe the key factors which will affect our ability to obtain funding are:

(i) the receptivity of the capital markets to any in-licensing, product acquisition or other transaction we may enter into;

(ii) the receptivity of the capital markets to financings by biotechnology companies generally and companies with drug candidates and technologies similar to ours specifically;

(iii) the results of our clinical development activities in our drug candidates we develop on the timelines anticipated;

(iv) competitive and potentially competitive products and technologies and investors' receptivity to our drug candidates we develop and the technology underlying them in light of competitive products and technologies;

(v) the cost, timing, and outcome of regulatory reviews;

(vi) our ability to enter into additional collaborations with biotechnology and pharmaceutical companies and the success of such collaborations; and

(vii) the impact of the COVID-19 pandemic to global economy and capital markets, and to our business and our financial results.

In addition, increases in expenses or delays in clinical development may adversely impact our cash position and require additional funds or cost reductions.

Cash Flows

The following table presents a summary of the primary sources and uses of cash for the years ended December 31, 2021 and 2020:

(in thousands)	Year Ended December 31, 2021	2020
Net cash provided by (used in):		
Operating activities	$ (24,597)	$ (33,772)
Investing activities	4,500	(1,687)
Financing activities	19,413	28,669
Decrease in cash and cash equivalents	**$ (684)**	**$ (6,790)**

Operating Activities. The net cash used in operating activities for all periods presented consists primarily of our net income (losses) adjusted for non-cash charges/gains and changes in components of working capital. The decrease in cash outflow for the year ended December 31, 2021, as compared to 2020, related primarily to lower costs incurred for our tilsotolimod development program during 2021.

Investing Activities. Net cash provided by (used in) investing activities primarily consisted of the following amounts relating to our investments in available-for-sale securities and purchases and disposals of property and equipment:

- For the year ended December 31, 2021, proceeds from the maturity of available-for-sale securities were $4.5 million; and
- For the year ended December 31, 2020, proceeds from the maturity of available-for-sale securities of $10.5 million, substantially offset by the purchase of $12.2 million of available-for-sale securities.

Financing Activities. Net cash provided by financing activities primarily consisted of the following amounts raised in connection with the following transactions:

- For the year ended December 31, 2021, aggregate net proceeds of $19.5 million from financing arrangements consisting of $4.2 million received pursuant to the LPC Purchase Agreement and $15.3 million received under the ATM Agreement, plus $0.3 million received from the exercise of stock options and warrants, partially offset by $0.4 million in payments related to our short-term insurance premium financing arrangement; and
- For the year ended December 31, 2020, aggregate net proceeds of $28.8 million from financing arrangements consisting of $14.8 million received pursuant to the April 2020 and July 2020 Securities Purchase Agreements, $1.7 million received pursuant to the LPC Purchase Agreement and $12.3 million received under the ATM Agreement, plus an additional $0.1 million in proceeds from employee stock purchases under our 2017 Employee Stock Purchase Plan, partially offset by $0.2 million in payments related to our short-term insurance premium financing arrangement.

Material Cash Requirements

As of December 31, 2021, we had a material lease commitment in an aggregate amount of $0.8 million relating to our facility in Exton, Pennsylvania. This lease expires on May 31, 2025. See Note 12 of the Notes to Financial Statements in this Form 10-K for additional information.

Critical Accounting Policies and Estimates

This management's discussion and analysis of financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates and judgments, including those related to warrant and future tranche right liabilities and related revaluation gains (losses), research and development prepayments, accruals and related expenses, and stock-based compensation. Management bases its estimates and judgments on historical experience and on various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We regard an accounting estimate or assumption underlying our financial statements as a "critical accounting estimate" where:

- the nature of the estimate or assumption is material due to the level of subjectivity and judgment necessary to account for highly uncertain matters or the susceptibility of such matters to change; and
- the impact of the estimates and assumptions on financial condition or operating performance is material.

While our significant accounting policies are described in more detail in Note 2 to our financial statements appearing elsewhere in this Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

Research and Development Prepayments, Accruals and Related Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued and prepaid expenses for research and development activities performed by third parties, including Clinical Research Organizations ("CROs") clinical investigators and our research collaboration partners. These estimates are made as of the reporting date of the work completed over the life of the individual study in accordance with agreements established with CROs and clinical trial sites. Some CROs invoice us on a monthly basis, while others invoice upon achievement of milestones and the expense is recorded as services are rendered. We determine the estimates of research and development activities incurred at the end of each reporting period through discussion with internal personnel and outside service providers and research collaboration partners as to the progress or stage of completion of trials or services, as of the end of each reporting period, pursuant to contracts with clinical trial centers and CROs and the agreed upon fee to be paid for such services. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Clinical trial site costs related to patient enrollments are recorded as patients are entered into the trial.

Stock-Based Compensation

We recognize all share-based payments to employees and directors as expense in our statements of operations based on their fair values. We record compensation expense over an award's requisite service period, or vesting period, based on the award's fair value at the date of grant. Our policy is to charge the fair value of stock options as an expense, adjusted for forfeitures, on a straight-line basis over the vesting period, which is generally four years for employees and one year for directors.

We use the Black-Scholes option pricing model to estimate the fair value of stock option grants. The Black-Scholes option pricing model relies on a number of key assumptions to calculate estimated fair values, including assumptions as to average risk-free interest rate, expected dividend yield, expected life and expected volatility. For the assumed risk-free interest rate, we use the U.S. Treasury security rate with a term equal to the expected life of the option. Our assumed dividend yield of zero is based on the fact that we have never paid cash dividends to common stockholders and have no present intention to pay cash dividends. We use an expected option life based on actual experience. Our assumption for expected volatility is based on the actual stock-price volatility over a period equal to the expected life of the option.

If factors change and we employ different assumptions for estimating stock-based compensation expense in future periods, or if we decide to use a different valuation model, the stock-based compensation expense we recognize in future periods may differ significantly from what we have recorded in the current period and could materially affect our loss from operations, net income (loss) and earnings (loss) per share. It may also result in a lack of comparability with other companies that use different models, methods and assumptions. The Black-Scholes option pricing model was developed for use in estimating the fair value of traded options that have no vesting restrictions and are fully transferable. These characteristics are not present in our option grants. Although the Black-Scholes option pricing model is widely used, existing valuation models, including the Black-Scholes option pricing model, may not provide reliable measures of the fair values of our stock-based compensation.

Warrant and Future Tranche Right Liabilities and Related Revaluation Gain (Loss)

We entered into the December 2019 Securities Purchase Agreement, as more fully described in Note 7 of the Notes to Financial Statements appearing elsewhere in this Form 10-K, pursuant to which we issued shares of convertible preferred stock with detachable warrants. Additionally, the December 2019 Securities Purchase Agreement contains call options on redeemable preferred shares with warrants (conditionally exercisable for shares that are puttable), which we refer to as future tranche rights.

We determined that these warrants and future tranche rights represent freestanding financial instruments and account for both the warrants and future tranche rights as liabilities, which requires the measurement of the fair value of the liability at the time of issuance and recording changes as a charge to current earnings at each reporting period, which is included in Warrant Liability Revaluation Expense and/or Future Tranche Right Liability Revaluation Expense in our statements of operations.

Warrant Liability. We use an option pricing model to value our liability-classified warrants. Inherent in the valuation model are assumptions related to volatility, risk-free interest rate, expected term, dividend rate, and other scenarios (i.e. probability of complex features of the warrants being triggered). Due to the nature of and inputs in the model used to assess the fair value of the warrants, it is not abnormal to experience significant fluctuations during each remeasurement period.

Future Tranche Right Liability. We use both a lattice model and a Monte Carlo simulation to value the future tranche rights. We selected these models as we believe they are reflective of all significant assumptions that market participants would likely consider in negotiating the transfer of the future tranche rights. Such assumptions include, among other inputs, stock price volatility, risk-free rates, and expected terms inclusive of early exercise and cancellation assumptions. Due to the nature of and inputs in the model used to assess the fair value of the future tranche rights, it is not abnormal to experience significant fluctuations during each remeasurement period.

All outstanding warrants and future tranche rights previously issued pursuant to the December 2019 Securities Purchase Agreement were terminated during the three months ended March 31, 2021. Accordingly, we are no longer eligible to receive additional proceeds pursuant to the December 2019 Securities Purchase Agreement and the related warrant liability and future tranche right liability were derecognized during the three months ended March 31, 2021.

New Accounting Pronouncements

New accounting pronouncements are discussed in Note 2 of the Notes to Financial Statements in this Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk.

As of December 31, 2021, all material assets and liabilities are in U.S. dollars, which is our functional currency.

We maintain investments in accordance with our investment policy. The primary objectives of our investment activities are to preserve principal, maintain proper liquidity to meet operating needs and maximize yields. Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investment. We regularly review our investment holdings in light of the then current economic environment. At December 31, 2021, all our invested funds were invested in money market funds classified in cash and cash equivalents on the accompanying balance sheet.

Based on a hypothetical ten percent adverse movement in interest rates, the potential losses in future earnings, fair value of risk sensitive financial instruments, and cash flows are immaterial to our earnings, although the actual effects may differ materially from the hypothetical analysis.

Item 8. Financial Statements and Supplementary Data.

All financial statements required to be filed hereunder are filed as listed under Item 15(a) of this Form 10-K and are incorporated herein by this reference.

There have been no retrospective changes to our statements of operations for any of the quarters within the two years in the period ended December 31, 2021.

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

None.

Item 9A. Controls and Procedures.

Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2021. In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our principal executive officer and principal financial officer concluded that as of December 31, 2021, our disclosure controls and procedures were (1) designed to ensure that material information relating to us is made known to our principal executive officer and principal financial officer by others, particularly during the period in which this report was prepared, and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Internal Control over Financial Reporting

a) Management's Annual Report on Internal Control over Financial Reporting

Our management, with the participation of our principal executive officer and principal financial officer, is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the Company's principal executive and principal financial officers and effected by the Company's Board of Directors, management and other personnel, to provide reasonable

assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2021. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control — Integrated Framework* (2013).

Based on its assessment, management believes that, as of December 31, 2021, the Company's internal control over financial reporting is effective based on those criteria.

b) Attestation Report of the Registered Public Accounting Firm

Not Applicable.

c) Changes in Internal Control over Financial Reporting.

No change in our internal control over financial reporting occurred during the fourth quarter of the fiscal year ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III.

Item 10. Directors, Executive Officers, and Corporate Governance.

The information required by this item is incorporated by reference to our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2021.

We have adopted a written code of business conduct and ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted a current copy of the Code of Business Conduct and Ethics in the "Investors — Corporate Governance" section of our website, which is located at www.iderapharma.com. We intend to satisfy the disclosure requirements under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of our code of business conduct and ethics by posting such information on our website at www.iderapharma.com.

Item 11. Executive Compensation.

The information required by this item is incorporated by reference to our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2021.

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

The information required by this item is incorporated by reference to our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2021.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table provides information as of December 31, 2021 regarding total shares subject to outstanding stock options, warrants, and rights and total additional shares available for issuance under our existing equity incentive and employee stock purchase plans. In addition, from time to time, we may grant "inducement grants" pursuant to Nasdaq Listing Rule 5635(c)(4).

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights (a)	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights (b)	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a)) (c)
Equity compensation plans approved by stockholders (1)	5,452,709	$ 6.75	396,098
Equity compensation plans not approved by stockholders (2)	325,000	$ 27.82	—
Total	5,777,709	$ 8.06	396,098

(1) Consists of our: 2008 Stock Incentive Plan, 2013 Stock Incentive Plan, and 2017 Employee Stock Purchase Plan. Amounts in column (a) include stock options and unvested restricted stock units outstanding. Shares are available for future issuance only under our 2013 Stock Incentive Plan and 2017 Employee Stock Purchase Plan.

(2) Consists of stock options issued as inducement grants (issued prior to 2017) as of December 31, 2021. These stock options are generally subject to the same terms and conditions as those awarded pursuant to the plans approved by our stockholders.

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

The information required by this item is incorporated by reference to our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2021.

Item 14. Principal Accountant Fees and Services.

The information required by this item is incorporated by reference to our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2021.

PART IV.

Item 15. Exhibits and Financial Statement Schedules.

(a) (1) *Financial Statements.*

(2) We are not filing any financial statement schedules as part of this Annual Report on Form 10-K because they are not applicable or the required information is included in the financial statements or notes thereto.

(3) The list of Exhibits filed as a part of this Annual Report on Form 10-K is set forth on the Exhibit Index below.

(b) The list of Exhibits filed as a part of this Annual Report on Form 10-K is set forth on the Exhibit Index below.

(c) None.

Exhibit Index

Exhibit Number	Description	Incorporated by Reference to			
		Form	SEC File No.	Exhibit(s)	Filing Date
1.1	Equity Distribution Agreement, dated November 26, 2018, by and between Idera Pharmaceuticals, Inc. and JMP Securities LLC	8-K	001-31918	1.1	November 26, 2018
2.1	Agreement and Plan of Merger, dated as January 21, 2018, by and among Idera Pharmaceuticals, Inc., BioCryst Pharmaceuticals, Inc., Nautilus Holdco, Inc., Island Merger Sub, Inc. and Boat Merger Sub, Inc.	8-K	001-31918	2.1	January 22, 2018
3.1	Restated Certificate of Incorporation of Idera Pharmaceuticals, Inc., as amended.	10-Q	001-31918	3.1	August 2, 2018
3.2	Certificate of Amendment to the Restated Certificate of Incorporation of Idera Pharmaceuticals, Inc.	8-K	001-31918	3.1	May 18, 2020
3.3	Amended and Restated Bylaws of Idera Pharmaceuticals, Inc.	10-K	001-31918	3.2	March 7, 2018
3.4	Certificate of Designations, Preferences and Rights of Series B1 Convertible Preferred Stock, Series B2 Convertible Preferred Stock, Series B3 Convertible Preferred Stock and Series B4 Convertible Preferred Stock of the Company	8-K	001-31918	3.1	December 23, 2019
4.1	Specimen Certificate for shares of Common Stock, $.001 par value, of Idera Pharmaceuticals, Inc.	S-1	33-99024	4.1	December 8, 1995
4.2	Unit Purchase Agreement by and among Idera Pharmaceuticals, Inc. and certain persons and entities listed therein, dated April 1, 1998	10-K	000-27352	10.39	April 1, 2002
4.3	Form of Warrant issued in May 2013 to purchasers in Idera Pharmaceuticals, Inc.'s registered public offering on Idera Pharmaceuticals, Inc.'s registration statement on Form S-1 (File No. 333-187155)	10-Q	001-31918	10.5	May 15, 2013
4.4	Form of Warrant issued in September 2013 to purchasers in Idera Pharmaceuticals, Inc.'s registered public offering on Idera Pharmaceuticals, Inc.'s registration statement on Form S-3 (File No. 333-191073)	8-K	001-31918	4.1	September 26, 2013
4.5	Form of Warrant issued in February 2014 to purchasers in Idera Pharmaceuticals, Inc.'s registered public offering on Idera Pharmaceuticals, Inc.'s registration statement on Form S-3 (File No. 333-191073)	8-K	001-31918	4.1	February 5, 2014
4.6	Form of Warrant issued in December 2019 to purchasers in Idera Pharmaceuticals, Inc. private placement transaction	8-K	001-31918	4.1	December 23, 2019

Exhibit Number	Description	Incorporated by Reference to			
		Form	SEC File No.	Exhibit(s)	Filing Date
4.7	Warrant Amendment Agreement, dated as of December 23, 2019, by and among Idera Pharmaceuticals, Inc. and certain holders of warrants named therein	10-K	001-31918	4.13	March 12, 2020
4.8	Form of Pre-Funded Warrant issuable pursuant to the April 2020 Securities Purchase Agreement	8-K	001-31918	4.1	April 7, 2020
4.9	Form of Warrant issuable pursuant to the April 2020 Securities Purchase Agreement	8-K	001-31918	4.2	April 7, 2020
4.10	Form of Pre-Funded Warrant issuable pursuant to the July 2020 Securities Purchase Agreement	8-K	001-31918	4.1	July 15, 2020
4.11	Form of Warrant issuable pursuant to the July 2020 Securities Purchase Agreement	8-K	001-31918	4.2	July 15, 2020
4.12	Registration Rights Agreement, dated March 24, 2006, by and among Idera Pharmaceuticals, Inc. and the Investors named therein	8-K	001-31918	10.2	March 29, 2006
4.13	Registration Rights Agreement, dated February 9, 2015, among Idera Pharmaceuticals, Inc. and the Selling Stockholders named therein	8-K	001-31918	4.1	February 9, 2015
4.14	Amendment to the Registration Rights Agreement, dated January 21, 2018, by and among Idera Pharmaceuticals, Inc., 667, L.P., Baker Brothers Life Sciences, L.P. and 14159, L.P.	8-K	001-31918	10.1	January 22, 2018
4.15	Registration Rights Agreement, dated as of March 4, 2019, by and between Idera Pharmaceuticals, Inc. and Lincoln Park Capital Fund, LLC	10-K	001-31918	4.5	March 6, 2019
4.16	Registration Rights Agreement, dated December 23, 2019, by and among Idera Pharmaceuticals, Inc. and certain investors named therein	10-K	001-31918	4.11	March 12, 2020
4.17	Voting Agreement, dated as of December 23, 2019, by and among Idera Pharmaceuticals, Inc. and certain investors named therein	10-K	001-31918	4.12	March 12, 2020
4.18	Registration Rights Agreement, dated April 7, 2020, by and among Idera Pharmaceuticals, Inc. and Pillar Partners Foundation, L.P.	8-K	001-31918	4.4	April 7, 2020
4.19	Voting Agreement, dated April 7, 2020, by and among Idera Pharmaceuticals, Inc. and Pillar Partners Foundation, L.P.	8-K	001-31918	4.3	April 7, 2020
4.20	Registration Rights Agreement, dated July 13, 2020, by and among Idera Pharmaceuticals, Inc. and Pillar Partners Foundation, L.P.	8-K	001-31918	4.3	July 15, 2020

Exhibit Number	Description	Incorporated by Reference to			
		Form	SEC File No.	Exhibit(s)	Filing Date
4.21	Description of the Idera Pharmaceuticals, Inc. Securities Registered Under Section 12 of the Securities Exchange Act of 1934	10-K	001-31918	4.21	March 1, 2021
10.1†	2008 Stock Incentive Plan, as amended	8-K	001-31918	99.2	June 17, 2011
10.2†	2013 Stock Incentive Plan, as amended	8-K	001-31918	10.1	June 13, 2014
10.3†	Amendment to 2013 Stock Incentive Plan, as amended	8-K	001-31918	10.1	June 11, 2015
10.4†	Amendment to 2013 Stock Incentive Plan, as amended	8-K	001-31918	10.1	June 9, 2017
10.5†	Amendment to 2013 Stock Incentive Plan, as amended	DEF14A	001-31918	Appendix A	April 25, 2019
10.6†	2017 Employee Stock Purchase Plan	8-K	001-31918	10.2	June 9, 2017
10.7†	Amendment to 2017 Employee Stock Purchase Plan	DEF14A	001-31918	Appendix C	April 25, 2019
10.8	Policy on Treatment of Stock Options in the Event of Retirement, approved April 28, 2014	10-Q	001-31918	10.1	August 12, 2014
10.9†	Form of Incentive Stock Option Agreement Granted Under the 2008 Stock Incentive Plan	8-K	001-31918	10.2	June 10, 2008
10.10†	Form of Nonstatutory Stock Option Agreement Granted Under the 2008 Stock Incentive Plan	8-K	001-31918	10.3	June 10, 2008
10.11†	Form of Nonstatutory Stock Option Agreement (Non-Employee Directors) Granted Under the 2008 Stock Incentive Plan	8-K	001-31918	10.4	June 10, 2008
10.12†	Form of Restricted Stock Agreement Under the 2008 Stock Incentive Plan	8-K	001-31918	10.5	June 10, 2008
10.13†	Form of Incentive Stock Option Agreement granted under the 2013 Stock Incentive Plan	8-K	001-31918	10.2	July 29, 2013
10.14†	Form of Nonstatutory Stock Option Agreement granted under the 2013 Stock Incentive Plan	8-K	001-31918	10.3	July 29, 2013
10.15†	Form of Nonstatutory Stock Option Agreement (Non-Employee Directors) granted under the 2013 Stock Incentive Plan	8-K	001-31918	10.4	July 29, 2013
10.16†	Form of Inducement Stock Option Award – Nonstatutory Stock Option Agreement	10-Q	001-31918	10.1	November 6, 2015
10.17†	Form of Restricted Stock Agreement under the 2013 Stock Incentive Plan	10-Q	001-31918	10.3	August 8, 2019
10.18†	Form of Performance-Based Restricted Stock Agreement under the 2013 Stock Incentive Plan	10-Q	001-31918	10.3	October 29, 2020
10.19†	Employment Letter Agreement, dated December 1, 2014, by and between Idera Pharmaceuticals, Inc. and Vincent Milano	10-K	001-31918	10.24	March 12, 2015
10.20†	Amendment to Employment Agreement, dated January 10, 2020, by and between the Company and Vincent J. Milano	8-K	001-31918	10.1	January 15, 2020

Exhibit Number	Description	Incorporated by Reference to			
		Form	SEC File No.	Exhibit(s)	Filing Date
10.21†	Form of Vincent J. Milano Restricted Stock Unit Agreement	8-K	001-31918	10.2	January 15, 2020
10.22†	Employment Letter, dated January 26, 2015, by and between Idera Pharmaceuticals, Inc. and Clayton Fletcher	10-Q	001-31918	10.1	May 11, 2015
10.23†	Consulting Agreement, dated December 29, 2020, between the Company and R. Clayton Fletcher	8-K	001-31918	10.1	January 5, 2021
10.24†	Employment Offer Letter, dated October 15, 2015, by and between Idera Pharmaceuticals, Inc. and John J. Kirby	10-K	001-31918	10.26	March 6, 2019
10.25†	Employment Offer Letter, dated November 16, 2020, by and between Idera Pharmaceuticals, Inc. and Daniel Soland	10-K	001-31918	10.25	March 1, 2021
10.26†	Severance and Change of Control Agreement, dated February 19, 2021, by and between the Company and Daniel Soland	10-K	001-31918	10.26	March 1, 2021
10.27†	Employment Offer Letter, dated August 20, 2018, by and between Idera Pharmaceuticals, Inc. and Bryant D. Lim	10-Q	001-31918	10.1	November 6, 2018
10.28†	Employment Offer Letter, dated June 26, 2019, by and between Idera Pharmaceuticals, Inc. and Elizabeth Tarka	10-Q	001-31918	10.4	August 8, 2019
10.29†	Form of Director and Officer Indemnification Agreement	10-Q	001-31918	10.1	May 4, 2017
10.30†	Form of Executive Severance and Change of Control Agreement	10-Q	001-31918	10.2	May 4, 2017
10.31††	Development and Commercialization Agreement, dated May 1, 2014, by and between Abbott Molecular Inc. and Idera Pharmaceuticals, Inc.	10-Q	001-31918	10.3	August 12, 2014
10.32††	License Agreement, dated November 28, 2016, by and between Idera Pharmaceuticals, Inc. and Vivelix Pharmaceuticals, Ltd.	10-K	001-31918	10.56	March 15, 2017
10.33††	Clinical Trial Collaboration and Supply Agreement, by and between Idera Pharmaceuticals, Inc. and Bristol-Myers Squibb Company, dated May 18, 2018	10-Q	001-31918	10.1	August 2, 2018
10.34††	Clinical Trial Collaboration and Supply Agreement, by and between Idera Pharmaceuticals, Inc. and Bristol-Myers Squibb Company, dated March 11, 2019	10-Q	001-31918	10.1	May 2, 2019
10.35††	Clinical Trial Collaboration and Supply Agreement, effective August 27, 2019, by and between AbbVie Inc. and Idera Pharmaceuticals, Inc.	10-Q	001-31918	10.1	November 6, 2019
10.36	Lease Agreement dated March 31, 2015, between Idera Pharmaceuticals, Inc. and 505 Eagleview Boulevard Associates, L.P.	10-K	001-31918	10.45	March 7, 2018

Exhibit Number	Description	Incorporated by Reference to			
		Form	SEC File No.	Exhibit(s)	Filing Date
10.37	First Amendment dated September 23, 2015 to Lease Agreement dated March 31, 2015 between Idera Pharmaceuticals, Inc. and 505 Eagleview Boulevard Associates, L.P.	10-K	001-31918	10.46	March 7, 2018
10.38	Second Amendment dated January 13, 2020 to Lease Agreement dated March 31, 2015 between Idera Pharmaceuticals, Inc. and 505 Eagleview Boulevard Associates, L.P.	10-K	001-31918	10.42	March 12, 2020
10.39	Purchase Agreement, dated as of March 4, 2019, by and between Idera Pharmaceuticals, Inc. and Lincoln Park Capital Fund, LLC	10-K	001-31918	10.37	March 6, 2019
10.40	First Amendment to Purchase Agreement, dated as of September 2, 2020, by and between Idera Pharmaceuticals, Inc. and Lincoln Park Capital Fund, LLC	8-K	001-31918	10.1	September 3, 2020
10.41	Securities Purchase Agreement, dated December 23, 2019, by and among the institutional investors named therein	8-K	001-31918	10.1	December 23, 2019
10.42	Securities Purchase Agreement, dated April 7, 2020, by and among Idera Pharmaceuticals, Inc. and Pillar Partners Foundation, L.P.	8-K	001-31918	10.1	April 7, 2020
10.43	Securities Purchase Agreement, dated July 13, 2020, by and among Idera Pharmaceuticals, Inc. and Pillar Partners Foundation, L.P.	8-K	001-31918	10.1	July 15, 2020
10.44	Amendment to the Securities Purchase Agreement and Registration Rights Agreement, dated December 11, 2020, by and among Idera Pharmaceuticals, Inc., Pillar Partners Foundation, L.P. and Pillar Pharmaceuticals 6, L.P.	8-K	001-31918	10.2	December 15, 2020
23.1*	Consent of Independent Registered Public Accounting Firm				
31.1*	Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14 and 15d-14, as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002				
31.2*	Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14 and 15d-14, as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002				
32.1*	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
32.2*	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				

Exhibit Number	Description	Incorporated by Reference to			
		Form	SEC File No.	Exhibit(s)	Filing Date
101.INS	Inline XBRL Instance Document				
101.SCH	Inline XBRL Taxonomy Extension Schema Document				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document				
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101)				

* Filed or furnished, as applicable, herewith.

† Management contract or compensatory plan or arrangement required to be filed as an Exhibit to the Form 10-K.

†† In accordance with Item 601(b)(10) of Regulation S-K, portions of this exhibit have been omitted in order for them to remain confidential.

Item 16. Form 10-K Summary.

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on this 31st day of March 2022.

Idera Pharmaceuticals, Inc.

By: /S/ VINCENT J. MILANO
Vincent J. Milano
President and
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/S/ VINCENT J. MILANO Vincent J. Milano	President, Chief Executive Officer and Director (Principal Executive Officer)	March 31, 2022
/S/ JOHN J. KIRBY John J. Kirby	Chief Financial Officer (Principal Financial and Accounting Officer)	March 31, 2022
/S/ MICHAEL DOUGHERTY Michael Dougherty	Chairman of the Board of Directors	March 31, 2022
/S/ CRISTINA CSIMMA Cristina Csimma, Pharm. D., M.H.P.	Director	March 31, 2022
/S/ JAMES A. GERAGHTY James A. Geraghty	Director	March 31, 2022
/S/ MARK GOLDBERG Mark Goldberg, M.D.	Director	March 31, 2022
/S/ MAXINE GOWEN Maxine Gowen, Ph.D.	Director	March 31, 2022
/S/ CAROL A. SCHAFER Carol A. Schafer	Director	March 31, 2022

IDERA PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS
December 31, 2021

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Idera Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Idera Pharmaceuticals, Inc. (the Company) as of December 31, 2021 and 2020, and the related statements of operations, redeemable preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

Critical Audit Matter

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: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter 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.

Accounting for Research and Development Prepayments, Accruals and Related Expenses

Description of the Matter	As disclosed in Note 2 to the financial statements, the Company is required to estimate prepaid and accrued expenses for research and development costs performed by third parties at each balance sheet date. The Company recorded prepaid research and development costs, which are included in prepaid expenses and other current assets on the December 31, 2021 balance sheet, and accrued expenses for the research and development costs, which are included in accrued expenses on the December 31, 2021

balance sheet. The amounts recorded for prepaid and accrued research and development costs within the aforementioned balance sheet captions represent the Company's estimate of the prepaid and unpaid research and development costs based on the progress of the research and development services compared to the amounts paid for those services through December 31, 2021.

Auditing the Company's prepaid and accrued research and development costs involved a higher degree of subjectivity due to the estimation required by management in determining the progress to completion of services that have been performed by the third parties, including clinical research organizations, clinical investigators and research collaborators.

How We Addressed the Matter in Our Audit

To test the prepaid and accrued research and development costs, our audit procedures included, among others, reviewing a sample of agreements with the service providers to corroborate key financial and contractual terms, and testing the accuracy and completeness of the underlying data used in the accrual and prepaid expense computations. We also evaluated management's estimates of the progress of a sample of research and development activities by making direct inquiries of the Company's operations personnel that oversee the external research and development activities and obtaining information directly from certain service providers about the service providers' estimate of costs that had been incurred through December 31, 2021. Additionally, we assessed the historical accuracy of management's estimates when evaluating the current period estimate. To evaluate the completeness of the accruals, we also examined subsequent invoices from the service providers and cash disbursements to the service providers, to the extent such invoices were received, or payments were made prior to the date that the financial statements were issued.

/s/ ERNST & YOUNG LLP

We have served as the Company's auditor since 2002.

Philadelphia, Pennsylvania
March 31, 2022

IDERA PHARMACEUTICALS, INC.
BALANCE SHEETS

(In thousands)	December 31, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 32,545	$ 33,229
Short-term investments	—	4,499
Prepaid expenses and other current assets	1,493	3,627
Total current assets	34,038	41,355
Property and equipment, net	22	44
Operating lease right-of-use assets	734	930
Other assets	70	70
Total assets	$ 34,864	$ 42,399
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 565	$ 329
Accrued expenses	4,088	6,072
Operating lease liability	209	191
Other current liability	—	435
Total current liabilities	4,862	7,027
Warrant liability, long-term	—	6,983
Future tranche right liability, long-term	—	118,803
Operating lease liability, net of current portion	549	758
Total liabilities	5,411	133,571
Commitments and contingencies (Note 12)		
Preferred stock, $0.01 par value, Authorized — 5,000 shares:		
Series B1 redeemable convertible preferred stock (Note 7); Designated — 278 shares, Issued and outstanding — 0 and 24 shares at December 31, 2021 and December 31, 2020, respectively	—	—
Stockholders' equity (deficit):		
Preferred stock, $0.01 par value, Authorized — 5,000 shares:		
Series A convertible preferred stock; Designated — 1,500 shares, Issued and outstanding — 1 share	—	—
Common stock, $0.001 par value, Authorized — 140,000 shares; Issued and outstanding — 52,818 and 38,291 at December 31, 2021 and December 31, 2020, respectively	53	38
Additional paid-in capital	764,861	742,342
Accumulated deficit	(735,461)	(833,552)
Total stockholders' deficit	29,453	(91,172)
Total liabilities and stockholders' deficit	$ 34,864	$ 42,399

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

IDERA PHARMACEUTICALS, INC.
STATEMENTS OF OPERATIONS

(In thousands, except per share amounts)	Year Ended December 31, 2021	2020	2019
Alliance revenue	$ —	$ —	$ 1,448
Operating expenses:			
Research and development	16,375	24,772	34,853
General and administrative	9,976	11,915	12,481
Restructuring costs	1,322	—	181
Total operating expenses	27,673	36,687	47,515
Loss from operations	(27,673)	(36,687)	(46,067)
Other income (expense):			
Interest income	9	165	1,150
Interest expense	(7)	(3)	—
Warrant revaluation gain (loss)	6,983	(3,742)	(598)
Future tranche right revaluation gain (loss)	118,803	(72,367)	(10,964)
Foreign currency exchange loss	(24)	(28)	(36)
Net income / (loss)	$ 98,091	$ (112,662)	$ (56,515)
Deemed dividend on preferred stock related to December 2019 Private Placement (see Note 7)	—	—	(28,043)
Undistributed earnings to preferred stockholders	(1,150)	—	—
Net income (loss) applicable to common stockholders	$ 96,941	$ (112,662)	$ (84,558)
Net income (loss) applicable to common stockholders (Note 16)			
— Basic	$ 96,941	$ (112,662)	$ (84,558)
— Diluted	$ (28,845)	$ (112,662)	$ (84,558)
Net income (loss) per share applicable to common stockholders (Note 16)			
— Basic	$ 1.97	$ (3.33)	$ (2.96)
— Diluted	$ (0.58)	$ (3.33)	$ (2.96)
Weighted-average number of common shares used in computing net income (loss) per share applicable to common stockholders			
— Basic	49,203	33,821	28,545
— Diluted	50,127	33,821	28,545

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

IDERA PHARMACEUTICALS, INC.
STATEMENTS OF REDEEMABLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

(In thousands)	Series B1 Preferred Number of Shares	Series B1 Preferred $0.01 Par Value	Common Stock Number of Shares	Common Stock $0.001 Par Value	Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance, December 31, 2018	—	$ —	27,188	$ 27	$ 728,342	$ (664,375)	$ 63,994
Sale of common stock, net of issuance costs	—	—	2,068	3	5,295	—	5,298
Sale of redeemable convertible preferred stock	24	—	—	—	—	—	—
Deemed dividend related to December 2019 Private Placement (Note 7)	—	—	—	—	(28,043)	—	(28,043)
Issuance of commitment shares	—	—	270	—	—	—	—
Issuance of common stock under employee stock purchase plan	—	—	61	—	121	—	121
Issuance of common stock upon exercise of common stock options and warrants	—	—	38	—	3	—	3
Issuance of common stock for services rendered	—	—	47	—	129	—	129
Stock-based compensation	—	—	—	—	3,845	—	3,845
Net loss	—	—	—	—	—	(56,515)	(56,515)
Balance, December 31, 2019	24	$ —	29,672	$ 30	$ 709,692	$ (720,890)	$ (11,168)
Sale of common stock, net of issuance costs	—	—	8,218	8	28,638	—	28,646
Issuance of common stock under employee stock purchase plan (vesting of restricted stock units)	—	—	177	—	—	—	—
Issuance of common stock under employee stock purchase plan	—	—	76	—	113	—	113
Issuance of common stock upon exercise of stock options	—	—	5	—	15	—	15
Issuance of common stock for services rendered	—	—	143	—	243	—	243
Stock-based compensation	—	—	—	—	3,641	—	3,641
Net loss	—	—	—	—	—	(112,662)	(112,662)
Balance, December 31, 2020	24	$ —	38,291	$ 38	$ 742,342	$ (833,552)	$ (91,172)
Sale of common stock, net of issuance costs	—	—	5,918	6	19,509	—	19,515
Conversion of Series B1 preferred stock	(24)	—	2,368	2	(2)	—	—
Issuance of common stock under employee stock purchase plan	—	—	49	—	59	—	59
Issuance of common stock under employee stock purchase plan (vesting of restricted stock units)	—	—	237	—		—	—
Issuance of common stock upon exercise of common stock options and warrants	—	—	5,871	7	264	—	271
Issuance of common stock for services rendered	—	—	84	—	152	—	152
Stock-based compensation	—	—	—	—	2,537	—	2,537
Net income	—	—	—	—	—	98,091	98,091
Balance, December 31, 2021	—	$ —	52,818	$ 53	$ 764,861	$ (735,461)	$ 29,453

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

IDERA PHARMACEUTICALS, INC.
STATEMENTS OF CASH FLOWS

(In thousands)	Year Ended December 31, 2021	2020	2019
Cash Flows from Operating Activities:			
Net income (loss)	$ 98,091	$ (112,662)	$ (56,515)
Adjustments to reconcile net income (loss) to net cash used in operating activities:			
Stock-based compensation	2,537	3,641	3,845
Warrant liability revaluation loss (gain)	(6,983)	3,742	598
Future tranche right liability revaluation (gain) loss	(118,803)	72,367	10,964
Issuance of common stock for services rendered	152	243	129
Accretion of discounts on short-term investments	(1)	(46)	(372)
Depreciation and amortization expense	22	61	120
(Gain) loss on disposal of property and equipment	—	—	(10)
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	2,134	500	(2,160)
Accounts payable, accrued expenses, and other liabilities	(1,751)	(1,629)	(1,105)
Other	5	11	8
Net cash used in operating activities	(24,597)	(33,772)	(44,498)
Cash Flows from Investing Activities:			
Purchases of available-for-sale securities	—	(12,178)	(44,502)
Proceeds from maturity of available-for-sale securities	4,500	10,499	42,100
Proceeds from the sale of property and equipment	—	—	11
Purchases of property and equipment	—	(8)	(11)
Net cash (used in) provided by investing activities	4,500	(1,687)	(2,402)
Cash Flows from Financing Activities:			
Proceeds from private placement	—	—	10,072
Proceeds from common stock financings, net	19,518	28,758	5,298
Proceeds from employee stock purchases	59	113	121
Proceeds from exercise of common stock options and warrants	271	15	3
Payments on note payable and seller-financed purchases	(435)	(217)	—
Other	—	—	(6)
Net cash provided by financing activities	19,413	28,669	15,488
Net decrease in cash and cash equivalents	(684)	(6,790)	(31,412)
Cash and cash equivalent, beginning of period	33,229	40,019	71,431
Cash and cash equivalents, end of period	$ 32,545	$ 33,229	$ 40,019
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 5	$ 3	$ —
Increase to operating lease right-of-use asset upon adoption of ASC 842	$ —	$ —	$ 1,236
Increase to operating lease right-of-use assets upon acquisition	$ —	$ 54	$ —
Increase to operating lease liability upon adoption of ASC 842	$ —	$ —	$ 1,236
Increase to operating lease liability upon acquisition	$ —	$ 54	$ —
Supplemental disclosure of non-cash financing and investing activities:			
Offering costs in accounts payable and accrued expenses	$ 3	$ 112	$ 165
Non-cash seller-financed purchases	$ —	$ 652	$ —

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

IDERA PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS
December 31, 2021

Note 1. Business and Organization

Business Overview

Idera Pharmaceuticals, Inc. ("Idera" or the "Company"), a Delaware corporation, is a biopharmaceutical company with a business strategy focused on the clinical development, and ultimately the commercialization, of drug candidates for rare disease indications characterized by small, well-defined patient populations with serious unmet medical needs. The Company's current focus is to identify and potentially acquire rights to novel development or commercial stage rare disease programs, through new business development opportunities, including additional strategic alternatives. The Company has in the past and may in the future explore collaborative alliances to support development and commercialization of any of our drug candidates.

Until May 2021, the Company was developing tilsotolimod, via intratumoral injection, for the treatment of anti-PD1 refractory metastatic melanoma in combination with ipilimumab, an anti-CTLA4 antibody marketed as Yervoy® by Bristol Myers Squibb Company ("BMS") in a Phase 3 registration trial. During the first quarter of 2021, the Company announced that ILLUMINATE-301, its pivotal registration trial of tilsotolimod in combination with ipilimumab versus ipilimumab alone in patients with anti-PD-1 refractory advanced melanoma, did not meet its primary endpoint of Objective Response Rate ("ORR"). Based on subsequent evaluation of the full data set, in May 2021, the Company announced that it would not continue the trial to its Overall Survival ("OS") primary endpoint.

Through December 2021, the Company was also evaluating intratumoral tilsotolimod in combination with nivolumab, an anti-PD1 antibody marketed as Opdivo® by BMS, and ipilimumab for the treatment of multiple solid tumors in a multicohort Phase 2 trial. In December 2021, the Company announced that preliminary data from the second 10 patients dosed in the safety cohort of ILLUMINATE-206 showed a safety profile consistent with the first 10 patients in ILLUMINATE-206 and with prior studies. No further enrollment in ILLUMINATE-206 is planned at this time.

The Company believes that while the clinical trials with tilsotolimod have not yet translated into a new treatment alternative for patients, data supporting tilsotolimod's mechanism of action and encouraging safety profile from across the array of pre-clinical and clinical work to date, together with its intellectual property protection, are noteworthy. As a result, in December 2021, the Company announced that it will consider an out-licensing arrangement so that tilsotolimid's full potential may continue to be explored on behalf of patients who do not respond to traditional immunotherapy.

Reduction-in-Force

In April 2021, following the announcement that the Company's ILLUMINATE-301 trial did not meet its primary endpoint of ORR, the Company implemented a reduction-in-force which affected approximately 50% of its workforce through September 30, 2021. The Company eliminated 17 positions primarily in the area of research and development. The decision was made in order to align the Company's workforce with its needs in light of the outcome of ILLUMINATE-301's ORR endpoint, its ongoing ILLUMINATE development program and other business development activities focused on identifying new portfolio opportunities.

In connection with these actions, the Company incurred and paid termination costs for the reduction in workforce, which includes severance, benefits and related costs, of approximately $1.3 million during the year ended December 31, 2021.

Note 1. Business and Organization (Continued)

Nasdaq Compliance

As previously disclosed, on November 26, 2021, we received a deficiency letter (the "Nasdaq Letter") from the Nasdaq Listing Qualifications Department, notifying us that the Company is not in compliance with Nasdaq Listing Rule 5550(a)(2), which requires the Company to maintain a minimum bid price of at least $1 per share for continued listing on The Nasdaq Capital Market (the "Minimum Bid Requirement"). The Company's failure to comply with the Minimum Bid Requirement was based on the Company's common stock per share price being below the $1 threshold for a period of 30 consecutive business days. In accordance with Nasdaq Listing Rule 5810(c)(3)(A) (the "Compliance Period Rule"), the Company has been provided an initial period of 180 calendar days (the "Compliance Date"), to regain compliance with the Minimum Bid Requirement. If, at any time before the Compliance Date, the bid price for the Company's common stock closes at $1.00 or more per share for a minimum of 10 consecutive business days, as required under Nasdaq requirements, the Staff will provide written notification to the Company that it complies with the Minimum Bid Requirement, unless the Staff exercises its discretion to extend this 10-day period pursuant to Nasdaq Listing Rule 5810(c)(3)(H).

If the Company does not regain compliance with the Minimum Bid Requirement by the Compliance Date, the Company may be eligible for an additional 180 calendar day compliance period (the "Second Compliance Period"). To qualify, the Company would need to meet the continued listing requirement for the market value of publicly held shares and all other initial listing standards of the Nasdaq Capital Market, with the exception of the Minimum Bid Requirement, and provide written notice to the Staff of its intention to cure the deficiency during the Second Compliance Period.

Neither the Nasdaq Letter nor the Company's noncompliance with the Minimum Bid Requirement have an immediate effect on the listing or trading of the Company's common stock, which continue to trade on The Nasdaq Capital Market under the symbol "IDRA."

Liquidity and Financial Condition

As of December 31, 2021, the Company had an accumulated deficit of $735.5 million and a cash and cash equivalents balance of $32.5 million. The Company expects to incur substantial operating losses in future periods and will require additional capital as it seeks to advance any future drug candidates through development to commercialization. The Company does not expect to generate product revenue, sales-based milestones, or royalties until the Company successfully completes development of and obtains marketing approval for any future drug candidates, either alone or in collaboration with third parties, which the Company expects will take a number of years, if at all. To commercialize any future drug candidates, the Company needs to complete clinical development and comply with comprehensive regulatory requirements. The Company is subject to a number of risks and uncertainties similar to those of other companies of the same size within the biotechnology industry, such as uncertainty of clinical trial outcomes, uncertainty of additional funding, and history of operating losses.

The Company follows the provisions of Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 205-40, *Presentation of Financial Statements—Going Concern*, which requires management to assess the Company's ability to continue as a going concern within one year after the date the financial statements are issued. Management currently anticipates that the Company's balance of cash and cash equivalents on hand as of December 31, 2021 is sufficient to enable the Company to continue as a going concern through the one-year period subsequent to the filing date of this Form 10-K. The Company has and will continue to evaluate available alternatives to extend its operations beyond this date, which include the ATM Agreement (Note 8) or additional financing or strategic transactions. Additionally, management's plans may include the possible deferral of certain operating expenses unless additional capital is received. Management's operating plan, which underlies the analysis of the Company's ability to continue as a going concern, involves the estimation of the amount and timing of future cash inflows and outflows. Actual results could vary from the operating plan.

Note 2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP").

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates, judgements, and assumptions that affect the reported amounts of assets, liabilities, equity, revenues and expenses, and related disclosure of contingencies in the accompanying financial statements and these notes. In addition, management's assessment of the Company's ability to continue as a going concern involves the estimation of the amount and timing of future cash inflows and outflows. On an ongoing basis, the Company evaluates its estimates, judgments and methodologies. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable. Actual results could differ materially from those estimates.

Segment Information

Operating segments are defined as components of an enterprise in which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and assessing performance. The Company views its operations and manages its business as one operating segment, which is the business of developing novel therapeutics for rare diseases and oncology.

Financial Instruments

The fair value of the Company's financial instruments is determined and disclosed in accordance with the three-tier fair value hierarchy specified in Note 3. The Company is required to disclose the estimated fair values of its financial instruments. As of December 31, 2021, the Company's financial instruments consisted of cash and cash equivalents. As of December 31, 2020, the Company's financial instruments consisted of cash, cash equivalents, short-term investments, and warrant and future tranche right liabilities. The estimated fair values of these financial instruments approximate their carrying values as of December 31, 2021 and 2020. As of December 31, 2021, the Company did not have any other derivatives, hedging instruments or other similar financial instruments.

Concentration of Credit Risk

Financial instruments that subject the Company to credit risk primarily consist of cash, cash equivalents and short-term investments. The Company's credit risk is managed by investing in highly rated money market instruments, U.S. treasury bills, corporate bonds, commercial paper and/or other debt securities. Due to these factors, no significant additional credit risk is believed by management to be inherent in the Company's assets. As of December 31, 2021, all of the Company's cash and cash equivalents were held at two financial institutions.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of 90 days or less when purchased to be "cash equivalents." Cash and cash equivalents at December 31, 2021 consisted of cash and money market funds. Cash and cash equivalents at December 31, 2020 consisted of cash and cash equivalents and short-term investments.

Note 2. Summary of Significant Accounting Policies (Continued)

Property and Equipment

Property and equipment are carried at acquisition cost less accumulated depreciation, subject to review for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable as described further under the heading "Impairment of Long-Lived Assets" below. The cost of normal, recurring, or periodic repairs and maintenance activities related to property and equipment are expensed as incurred. The cost for planned major maintenance activities, including the related acquisition or construction of assets, is capitalized if the repair will result in future economic benefits.

Depreciation and amortization are computed using the straight-line method based on the estimated useful lives of the related assets. Leasehold improvements are amortized over the remaining lease term or the related useful life, if shorter. Equipment and other long-lived assets are depreciated over three to five years.

When an asset is disposed of, the associated cost and accumulated depreciation is removed from the related accounts on the Company's balance sheet with any resulting gain or loss included in the Company's statement of operations.

Operating Lease Right-of-use Asset and Lease Liability

The Company accounts for leases under ASC 842, *Leases*. Operating leases are included in “Operating lease right-of-use assets” within the Company’s balance sheets and represent the Company’s right to use an underlying asset for the lease term. The Company’s related obligation to make lease payments are included in “Operating lease liability” and “Operating lease liability, net of current portion” within the Company’s balance sheets. Operating lease right-of-use (“ROU”) assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. As most of the Company’s leases do not provide an implicit rate, the Company uses its incremental borrowing rates, which are the rates incurred to borrow on a collateralized basis over a similar term, an amount equal to the lease payments in a similar economic environment. Lease expense for lease payments is recognized on a straight-line basis over the lease term. The ROU assets are tested for impairment according to ASC 360, *Property, Plant, and Equipment* (“ASC 360”). Leases with an initial term of 12 months or less are not recorded on the balance sheet and are recognized as lease expense on a straight-line basis over the lease term.

As of December 31, 2021 and 2020, the Company’s operating lease ROU assets and corresponding short-term and long-term lease liabilities primarily relate to its existing Exton, Pennsylvania facility operating lease, which expires on May 31, 2025.

Impairment of Long-Lived Assets

In accordance with ASC 360-10-35, *Impairment or Disposal of Long-Lived Assets*, the Company reviews its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable (i.e. impaired). Once an impairment is determined, the actual impairment recognized is the difference between the carrying amount and the fair value (less costs to sell for assets to be disposed of) as estimated using one of the following approaches: income, cost and/or market. Fair value using the income approach is determined primarily using a discounted cash flow model that uses the estimated cash flows associated with the asset or asset group under review, discounted at a rate commensurate with the risk involved. Fair value utilizing the cost approach is determined based on the replacement cost of the asset reduced for, among other things, depreciation and obsolescence. Fair value, utilizing the market approach, benchmarks the fair value against the carrying amount.

Note 2. Summary of Significant Accounting Policies (Continued)

Other Current Liability

In October 2020, the Company entered into a short-term financing arrangement with a third-party vendor to finance insurance premiums. The aggregate amount financed under this agreement was $0.6 million. As of December 31, 2020, the balance of $0.4 million, which was included in "Other current liability' in the Company's balance sheets, was paid in monthly installments through June 2021. Accordingly, as of December 31, 2021, no amounts were outstanding under this agreement.

Warrant Liability

The Company accounts for stock warrants as either equity instruments, liabilities or derivative liabilities in accordance with ASC 480, *Distinguishing Liabilities from Equity* ("ASC 480") and/or ASC 815, *Derivatives and Hedging* ("ASC 815"), depending on the specific terms of the warrant agreement. Freestanding warrants for shares that are potentially redeemable, whereby the Company may be required to transfer assets (e.g. cash or other assets) outside of its control, are classified as liabilities. Liability-classified warrants are recorded at their estimated fair values at each reporting period until they are exercised, terminated, reclassified or otherwise settled. Changes in the estimated fair value of liability-classified warrants are recorded in Warrant Revaluation (Loss) Gain in the Company's statements of operations. Equity classified warrants are recorded within additional paid-in capital at the time of issuance and not subject to remeasurement. During the three months ended March 31, 2021, all the Company's liability-classified warrants terminated and, accordingly, the liability balance was derecognized. For additional discussion on warrants and warrant liabilities, see Note 7 and 8.

Future Tranche Right Liability

On December 23, 2019, the Company entered into a Securities Purchase Agreement (the "December 2019 Securities Purchase Agreement") with institutional investors affiliated with Baker Brothers (the "Purchasers"), an existing stockholder and related party (see Note 15). As more fully described in Note 7, the December 2019 Securities Purchase Agreement contained call options on redeemable preferred shares with warrants (conditionally exercisable for shares that are puttable). The Company determined that these call options represent freestanding financial instruments and accounts for the options as liabilities ("Future Tranche Right Liability") under ASC 480, which requires the measurement and recognition of the fair value of the liability at the time of issuance and at each reporting period. Any change in fair value is recognized in Future Tranche Right Liability Revaluation (Loss) Gain in the Company's statements of operations.

As of December 31, 2020, the Future Tranche Right Liability was classified as a long-term liability in the Company's balance sheet as settlement is in the form of the applicable Series B convertible preferred stock and warrants exercisable for shares of either Series B1 Preferred Stock or the Company's common stock. During the three months ended March 31, 2021, the liability-classified call options provided for under the December 2019 Securities Purchase Agreement terminated and, accordingly, the liability balance was derecognized. For additional discussion on the Future Tranche Right Liability, see Note 7.

Preferred Stock

The Company applies ASC 480 when determining the classification and measurement of its preferred stock. Preferred shares subject to mandatory redemption are classified as liability instruments and are measured at fair value. Conditionally redeemable preferred shares (including preferred shares that feature redemption rights that are either within the control of the holder or subject to redemption upon the occurrence of uncertain events not solely within the Company's control) are classified as temporary equity. At all other times, preferred shares are classified as stockholders' equity.

Accretion of redeemable convertible preferred stock includes the accretion of the Company's Series B redeemable convertible preferred stock to its stated value. The carrying value of the Series B redeemable convertible preferred stock is being accreted to redemption value using the effective interest method, from the date of issuance to the earliest date the holders can demand redemption or until the redeemable convertible preferred stock ceases to be outstanding.

Note 2. Summary of Significant Accounting Policies (Continued)

Redeemable Preferred Stock Issued with Other Freestanding Instruments

The Company considers guidance within ASC 470-20, *Debt* (ASC 470), ASC 480, and ASC 815 when accounting for a redeemable equity instrument issued with other freestanding instruments (e.g. detachable warrants and future tranche right liabilities), such as in the December 2019 Private Placement (Note 7). In circumstances in which redeemable convertible preferred stock is issued with freestanding liability-classified instruments, the proceeds from the issuance of the convertible preferred stock are first allocated to those instruments at their full estimated fair value. The remaining proceeds, as further reduced by discounts created by the bifurcation of embedded derivatives and/or beneficial conversion features, if any, are allocated to the redeemable equity instrument.

Revenue Recognition

The Company recognizes revenue in accordance with ASC 606, *Revenue from Contracts with Customers* ("ASC 606"), which applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. In accordance with 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 entity 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, it performs the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligations in the contract; and

(v) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company only applies the five-step model to contracts when it determines that it is probable it will collect the consideration to which it is entitled in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in the Company's balance sheet. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Alliance Revenues

The Company's revenues have primarily been generated through collaborative research, development and/or commercialization agreements. The terms of these agreements may include payment to the Company of one or more of the following: nonrefundable, up-front license fees; research, development and commercial milestone payments; and other contingent payments due based on the activities of the counterparty or the reimbursement by licensees of costs associated with patent maintenance. Each of these types of revenue are recorded as Alliance revenues in the Company's statements of operations.

See Note 10, "Collaboration and License Agreements" for additional details regarding the Company's collaboration and out-licensing arrangements.

Note 2. Summary of Significant Accounting Policies (Continued)

Research and Development Prepayments, Accruals and Related Expenses

All research and development expenses are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities, including drug development trials and studies, research collaborations, drug manufacturing, laboratory supplies, external research, payroll including stock-based compensation and overhead. The Company is required to estimate our accrued and prepared expenses for research and development activities performed by third parties, including Clinical Research Organizations ("CRO's") and clinical investigators. These estimates are made as of the reporting date of the work completed over the life of the individual study in accordance with agreements established with CRO's and other clinical sites. Some CRO's invoice the Company on a monthly basis, while others invoice upon the achievement of milestones. The Company determines the estimates of research and development activities incurred at the end of each reporting period through discussion with internal personnel, outside service providers, and research collaboration partners as to the progress or stage of completion of trials or services, as of the end of the reporting period, pursuant to contracts with clinical trial centers or CRO's and the agreed upon fee to be paid for such services. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are accepted by the Company or the services are performed. As of December 31, 2021 and 2020, the Company recorded approximately $0.9 million and $2.5 million as prepaid research and development, respectively, which is included within prepaid expenses and other current assets in the accompanying balance sheets.

Stock-Based Compensation

The Company accounts for stock-based compensation using ASC 718, *Compensation – Stock Compensation*, or ASC 505-50, *Equity – Equity Based Payments to Non-Employees*, as applicable. The Company accounts for stock-based awards to employees and non-employee directors using the fair value based method to determine compensation expense for all arrangements where shares of stock or equity instruments are issued for compensation.

The Company recognizes all share-based payments to employees and directors as expense in the statements of operations based on their fair values. The Company records compensation expense on a straight-line basis over an award's requisite service period, or vesting period, based on the award's fair value at the date of grant. Vesting for time-based options and restricted stock units is generally four years for employees and one year for directors. The Company uses a Black-Scholes option-pricing model to determine the fair value of each option grant as of the date of grant for expense incurred. The Black-Scholes option pricing model requires inputs for risk-free interest rate, dividend yield, expected stock price volatility and expected term of the options. Forfeitures are accounted for as they occur. See Note 11, "Stock-based Compensation" for additional details.

Income Taxes

An asset and liability approach is used for financial accounting and reporting for income taxes. Deferred income taxes arise from temporary differences between income tax and financial reporting and principally relate to recognition of revenue and expenses in different periods for financial and tax accounting purposes and are measured using currently enacted tax rates and laws. In addition, a deferred tax asset can be generated by a net operating loss carryover. If it is more likely than not that some portion or all of a deferred tax asset will not be realized, a valuation allowance is recognized.

In the event the Company is charged interest or penalties related to income tax matters, the Company would record such interest as interest expense and would record such penalties as other expense in the Statements of Operations. No such charges have been incurred by the Company. For each of the years ended December 31, 2021, 2020 and 2019, the Company had no uncertain tax positions. See Note 13, "Income Taxes" for additional details.

Note 2. Summary of Significant Accounting Policies (Continued)

Net Income (Loss) per Common Share applicable to Common Stockholders

The Company uses the two-class method to compute net income per common share during periods the Company realizes net income and has securities outstanding (e.g. redeemable convertible preferred stock) that entitle the holder to participate in dividends and earnings of the Company. In addition, the Company analyzes the potential dilutive effect of outstanding redeemable convertible preferred stock under the "if-converted" method when calculating diluted earnings per share and reports the more dilutive of the approaches (two class or "if-converted"). The two-class method is not applicable during periods with a net loss, as the holders of the redeemable convertible preferred stock have no obligation to fund losses. The Company also analyzes the potential dilutive effect of outstanding stock options, unvested restricted stock units, warrants and shares underlying future tranche rights under the treasury stock method (as applicable), during periods of income, or during periods in which income is recognized related to changes in fair value of its liability-classified securities.

New Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB and rules are issued by the SEC that the Company has or will adopt as of a specified date. Unless otherwise noted, management does not believe that any other recently issued accounting pronouncements issued by the FASB or guidance issued by the SEC had, or is expected to have, a material impact on the Company’s present or future financial statements.

Recently Adopted Accounting Pronouncements

In June 2016, the FASB issued Accounting Standard Update (“ASU”) No. 2016-13, *Financial Instruments— Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* (“ASU 2016-13”). This standard requires that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, this standard now requires allowances to be recorded instead of reducing the amortized cost of the investment. The Company adopted ASU 2016-13 in the first quarter of 2020. The adoption of this ASU did not have a material effect on the Company’s financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement* (“ASU 2018-13”), which amends ASC 820, *Fair Value Measurement*. ASU 2018-13 modifies the disclosure requirements for fair value measurements by removing, modifying, or adding certain disclosures. The Company adopted ASU 2018-13 in the first quarter of 2020. The adoption of this ASU did not have a material effect on the Company’s financial statements.

In August 2020, the FASB issued ASU No. 2020-06, Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity’s Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity (“ASU 2020-06”), which simplifies the guidance on an issuer’s accounting for convertible instruments and contracts in its own equity. The Company adopted ASU 2020-06 in the first quarter of 2021. The adoption of this ASU did not have a material effect on the Company’s financial statements.

COVID-19

While the Company is not aware of a material impact from the continuation of the coronavirus ("COVID-19") pandemic through December 31, 2021, the full extent to which the COVID-19 pandemic will directly or indirectly impact the Company’s business, results of operations, and financial condition, depends on future developments.

Note 3. Fair Value Measurements

Assets and Liabilities Measured at Fair Value on a Recurring Basis

The Company applies the guidance in ASC 820, *Fair Value Measurement*, to account for financial assets and liabilities measured on a recurring basis. Fair value is measured at the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that is determined based on assumptions that market participants would use in pricing an asset or liability.

The Company uses a fair value hierarchy, which distinguishes between assumptions based on market data (observable inputs) and an entity's own assumptions (unobservable inputs). The guidance requires that fair value measurements be classified and disclosed in one of the following three categories:

- Level 1: Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities;
- Level 2: Quoted prices in markets that are not active or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liability; and
- Level 3: Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

Determining which category an asset or liability falls within the hierarchy requires significant judgment. The Company evaluates its hierarchy disclosures each reporting period. There were no transfers between Level 1, 2, and 3 during the year ended December 31, 2021.

The table below presents the assets and liabilities measured and recorded in the financial statements at fair value on a recurring basis at December 31, 2021 and 2020 categorized by the level of inputs used in the valuation of each asset and liability.

	December 31, 2021			
(In thousands)	Total	Level 1	Level 2	Level 3
Assets				
Cash	$ 250	$ 250	$ —	$ —
Cash equivalents – money market funds	32,295	32,295	—	—
Total assets	$ 32,545	$ 32,545	$ —	$ —

	December 31, 2020			
(In thousands)	Total	Level 1	Level 2	Level 3
Assets				
Cash	$ 250	$ 250	$ —	$ —
Cash equivalents – money market funds	32,979	32,979	—	—
Short-term investments – commercial paper	3,499	—	3,499	—
Short-term investments – US treasury bills	1,000	—	1,000	—
Total assets	$ 37,728	$ 33,229	$ 4,499	$ —
Liabilities				
Warrant liability	$ 6,983	$ —	$ —	$ 6,983
Future tranche right liability	118,803	—	—	118,803
Total liabilities	$ 125,786	$ —	$ —	$ 125,786

The Level 1 assets consist of money market funds, which are actively traded daily. The Level 2 assets consist of commercial paper and US treasury bills whose fair value may not represent actual transactions of identical securities. The fair value of commercial paper is generally determined based on the relationship between the investment’s discount rate and the discount rates of the same issuer’s commercial paper available in the market which may not be actively traded daily. Since these fair values may not be based upon actual transactions of identical securities, they are classified as Level 2.

Note 3. Fair Value Measurements (Continued)

Changes in Level 3 Liabilities Measured at Fair Value on a Recurring Basis

Warrant Liability and Future Tranche Right Liability

The reconciliation of the Company's warrant and future tranche right liability measured at fair value on a recurring basis using unobservable inputs (Level 3) is as follows:

(In thousands)	Warrant Liability	Future Tranche Right Liability
Balance, December 31, 2019	$ 3,241	$ 46,436
Change in the fair value of liability	3,742	72,367
Balance, December 31, 2020	$ 6,983	$ 118,803
Change in the fair value of liability (1)	(6,983)	(118,803)
Balance, December 31, 2021	$ —	$ —

(1) During the year ended December 31, 2021, the Company's liability-classified warrants and future tranche rights terminated, and accordingly, the liabilities were derecognized. See Notes 7 and 8.

Assumptions Used in Determining Fair Value of Liability-Classified Warrants

The Company utilizes an option pricing model to value its liability-classified warrants. Inherent in the valuation model are assumptions related to volatility, risk-free interest rate, expected term, dividend rate, and other scenarios (i.e. probability of complex features of the warrants being triggered).

The fair value of the warrants has been estimated with the following weighted-average assumptions:

	December 31, 2020	December 31, 2019
Risk-free interest rate	0.50%	1.79%
Expected dividend yield	—	—
Expected term (years)	5.98	6.98
Expected volatility	80%	80%
Exercise price (per share)	$ 1.52	$ 1.52

Assumptions Used in Determining Fair Value of Future Tranche Rights

The Company utilizes a lattice model to value the Series B2 and B3 future tranche rights and a Monte Carlo simulation to value the Series B4 future tranche rights. The Company selected these models as it believes they are reflective of all significant assumptions that market participants would likely consider in negotiating the transfer of the Future Tranche Rights (as defined in Note 7). Such assumptions include, among other inputs, stock price volatility, risk-free rates, and expected terms inclusive of early exercise and cancellation assumptions.

The estimated fair value of the Future Tranche Rights is determined using Level 2 and Level 3 inputs. Significant inputs and assumptions used in the valuation models are as follows:

	December 31, 2020	December 31, 2019
Risk-free interest rate	0.64% - 0.73%	1.84% - 1.88%
Expected dividend yield	—	—
Expected term (years) of call options on preferred stock	0.25 - 1.12	1.16 - 2.16
Expected term (years) of warrants	7.25 - 8.12	8.16 - 9.16
Expected volatility	80%	80%
Exercise price (per share) for common stock equivalent for preferred stock and warrant	$ 1.52 - 1.82	$ 1.52 - 1.82

Note 4. Investments

The Company had no available-for-sale investments at December 31, 2021. The Company's available-for-sale investments at fair value consisted of the following at December 31, 2020:

	December 31, 2020			
(In thousands)	Cost	Gross Unrealized (Losses)	Gross Unrealized Gains	Estimated Fair Value
Short-term investments – commercial paper	$ 3,499	$ —	$ —	$ 3,499
Short-term investments – US treasury bills	1,000	—	—	1,000
Total short-term investments	$ 4,499	$ —	$ —	$ 4,499

The Company had no realized gains or losses from the sale of investments in available-for-sale securities during each of the years ended December 31, 2021 and 2020. In accordance with ASU 2016-13, if the fair value of the Company's investments in available-for-sale debt securities is less than the amortized cost, the Company records (i) an allowance for credit losses with a corresponding charge to net income (loss) for any credit-related impairment, with subsequent improvements in expected credit losses recognized as a reversal of the allowance, and/or (ii) any non-credit impairment loss to other comprehensive income (loss).

As of December 31, 2020, the Company had no allowance for credit losses pertaining to the Company's investments in available-for-sale debt securities. Additionally, there were no impairment charges or recoveries recorded during each of the years ended December 31, 2021 and 2020.

Note 5. Property and Equipment

At December 31, 2021 and 2020, net property and equipment at cost consisted of the following:

(In thousands)	December 31, 2021	December 31, 2020
Leasehold improvements	$ 107	$ 107
Equipment and other	712	770
Total property and equipment, at cost	$ 819	$ 877
Less: Accumulated depreciation and amortization	797	833
Property and equipment, net	$ 22	$ 44

Depreciation and amortization expense on property and equipment was approximately $0.1 million for each of the years ended December 31, 2021, 2020, and 2019.

Note 6. Accrued Expenses

At December 31, 2021 and 2020, accrued expenses consisted of the following:

(In thousands)	December 31, 2021	December 31, 2020
Payroll and related costs	$ 477	$ 2,133
Clinical and nonclinical trial expenses	2,909	3,229
Professional and consulting fees	591	584
Other	111	126
Total accrued expenses	$ 4,088	$ 6,072

Note 7. Redeemable Convertible Preferred Stock

December 2019 Private Placement

On December 23, 2019, the Company entered into the December 2019 Securities Purchase Agreement, under which the Company sold 23,684 shares of Series B1 convertible preferred stock ("Series B1 Preferred Stock") and warrants to purchase 2,368,400 shares of the Company's common stock at an exercise price of $1.52 per share (or, if the holder elected to exercise the warrants for shares of Series B1 Preferred Stock, 23,684 shares of Series B1 Preferred Stock at an exercise price of $152 per share) for aggregate gross proceeds of $3.9 million (the "Initial Closing").

In addition, the Company agreed to sell to the purchasers, at their option and subject to certain conditions, (i) 98,685 shares of Series B2 convertible preferred stock ("Series B2 Preferred Stock") and 9,868,500 warrants to purchase common stock at an exercise price of $1.52 per share (or, at the election of the holder, 98,685 shares of Series B2 Preferred Stock at an price of $152 per share), for aggregate gross proceeds of $15 million (the "Series B2 Tranche"), (ii) 82,418 shares of Series B3 convertible preferred stock ("Series B3 Preferred Stock") and 6,593,440 warrants to purchase common stock at an exercise price of $1.82 per share (or, at the election of the holder, 65,934 shares of Series B3 Preferred Stock at a price of $182 per share), for aggregate gross proceeds of $15 million (the "Series B3 Tranche"), and (iii) 82,418 shares of Series B4 convertible preferred stock ("Series B4 Preferred Stock") and 6,593,440 warrants to purchase common stock at an exercise price of $1.82 per share (or, at the election of the holder, 65,934 shares of Series B3 Preferred Stock at a price of $182 per share), for aggregate gross proceeds of $15 million (the "Series B4 Tranche") over a period of up to 21 months following the Company's 2020 Annual Meeting of Stockholders held on May 12, 2020, where stockholders of the Company voted to approve an amendment to the Company's Restated Certificate of Incorporation to increase the authorized number of shares of the Company's common stock to 140,000,000. As consideration for the future tranche rights, the Company received aggregate gross proceeds of $6.2 million in December 2019.

The purchase and sale of the securities issuable under the Series B2, B3, and B4 tranches described above were subject to three separate closings, each to be conducted at the purchasers' discretion. The right of the purchasers to purchase Series B2, Series B3 and Series B4 Preferred Stock was set to expire on the 10th business day following the Company's ORR Data Announcement as defined in the December 2019 Securities Purchase Agreement for its ILLUMINATE-301 study. As a result of the purchasers not exercising the Series B2 Tranche prior to expiration, all future tranche rights and outstanding warrants previously issued pursuant to the December 2019 Securities Purchase Agreement were terminated during the three months ended March 31, 2021. Accordingly, the Company is no longer eligible to receive additional proceeds pursuant to the December 2019 Securities Purchase Agreement and the related warrant liability and future tranche right liability were derecognized during the three months ended March 31, 2021.

Accounting Considerations

The Company determined that the Series B1 Preferred Stock, the accompanying Series B1 warrants, and each of the future tranche rights represent freestanding financial instruments. The Series B1 warrants and the future tranche rights were classified as liabilities until their termination in March 2021 as the underlying shares were potentially redeemable and such redemption was deemed to be outside of the Company's control. The $10.1 million in gross proceeds received in December 2019 was allocated to the Series B1 warrants and the Future Tranche Rights based on their estimated fair values of $2.6 million and $35.5 million, respectively. The excess fair value of $28.0 million over the gross proceeds received of $10.1 million was recorded as a deemed dividend to Baker Brothers, an existing significant shareholder. Costs incurred in connection with the December 2019 Securities Purchase Agreement were expensed as incurred.

Due to the redeemable nature of the Series B1 Preferred Stock, the Series B1 Preferred Stock was classified as temporary equity and the carrying value was being accreted to its redemption value as of December 31, 2020 and while the Series B1 Preferred Stock was outstanding during 2021. During 2021, all the Company's 23,684 shares of Series B1 Preferred Stock outstanding were converted into shares of the Company's common stock. See Note 15 for details. For the years ended December 31, 2021 and 2020, accretion was de minimis.

Note 8. Stockholders' Equity (Deficit)

Preferred Stock

The Restated Certificate of Incorporation, as amended, of the Company permits its Board of Directors to issue up to 5,000,000 shares of preferred stock, par value $0.01 per share, in one or more series, to designate the number of shares constituting such series, and fix by resolution, the powers, privileges, preferences and relative, optional or special rights thereof, including liquidation preferences and dividends, and conversion and redemption rights of each such series.

As of December 31, 2020, the Company has designated the following class of preferred stock:

- Series A: 1,500,000 authorized shares of Series A Convertible Preferred Stock
- Series B1: 277,921 authorized shares of Series B1 Redeemable Convertible Preferred Stock
- Series B2: 98,685 authorized shares of Series B2 Redeemable Convertible Preferred Stock
- Series B3: 82,814 authorized shares of Series B3 Redeemable Convertible Preferred Stock
- Series B4: 82,814 authorized shares of Series B4 Redeemable Convertible Preferred Stock

Series A Convertible Preferred Stock. The dividends on the Series A convertible preferred stock ("Series A Preferred Stock") are payable semi-annually in arrears at the rate of 1% per annum, at the election of the Company, either in cash or additional duly designated, fully paid and nonassessable shares of Series A Preferred Stock. In the event of liquidation, dissolution or winding up of the Company, after payment of debts and other liabilities of the Company, the holders of the Series A Preferred Stock then outstanding will be entitled to a distribution of $1 per share out of any assets available to shareholders. The Series A Preferred Stock is non-voting. All remaining shares of Series A Preferred Stock rank, as to payment upon the occurrence of any liquidation event, senior to the Company's common stock. Shares of Series A Preferred Stock are convertible, in whole or in part, at the option of the holder into fully paid and nonassessable shares of common stock at $272.00 per share, subject to adjustment. As of December 31, 2021 and 2020, there were 655 shares of Series A Preferred Stock outstanding.

Series B Convertible Preferred Stock. As of December 31, 2020, there were 23,684 shares of Series B Preferred Stock outstanding. There were no shares outstanding at December 31, 2021.

Common Stock

Common Stock Authorized

As of December 31, 2021, the Company had 140,000,000 shares of common stock authorized of which 23,918,172 shares of common stock were reserved for issuance upon the exercise of outstanding warrants and options to purchase common stock, outstanding restricted stock units, the conversion of Series A convertible preferred stock, shares required to be reserved under the LPC Purchase Agreement (defined below), and shares available for grant under the Company's 2013 Stock Incentive Plan and shares available for purchase under the Company's 2017 Employee Stock Purchase Plan.

The expiration of the LPC Purchase Agreement on March 4, 2022 decreased the reserved shares of the common stock to 14,906,278 shares.

Note 8. Stockholders' Equity (Deficit) (Continued)

Put Shares

Pursuant to the terms of a unit purchase agreement dated as of May 5, 1998, the Company issued and sold a total of 149,960 shares of common stock (the "Put Shares") at a price of $128.00 per share. Under the terms of the unit purchase agreement, the initial purchasers (the "Put Holders") of the Put Shares have the right (the "Put Right") to require the Company to repurchase the Put Shares. The Put Right may not be exercised by any Put Holder unless: (1) the Company liquidates, dissolves or winds up its affairs pursuant to applicable bankruptcy law, whether voluntarily or involuntarily; (2) all of the Company's indebtedness and obligations, including without limitation the indebtedness under the Company's then outstanding notes, has been paid in full; and (3) all rights of the holders of any series or class of capital stock ranking prior and senior to the common stock with respect to liquidation, including without limitation the Series A convertible preferred stock, have been satisfied in full. The Company may terminate the Put Right upon written notice to the Put Holders if the closing sales price of its common stock exceeds $256.00 per share for the twenty consecutive trading days prior to the date of notice of termination. Because the Put Right is not transferable, in the event that a Put Holder has transferred Put Shares since May 5, 1998, the Put Right with respect to those shares has terminated. As a consequence of the Put Right, in the event the Company is liquidated, holders of shares of common stock that do not have Put Rights with respect to such shares may receive smaller distributions per share upon the liquidation than if there were no Put Rights outstanding.

As of December 31, 2021, the Company has repurchased or received documentation of the transfer of 49,993 Put Shares and 4,472 of the Put Shares continued to be held in the name of Put Holders. The Company cannot determine at this time what portion of the Put Rights of the remaining 95,494 Put Shares have terminated.

Equity Financings

April 2020 Private Placement

On April 7, 2020, the Company entered into a Securities Purchase Agreement with Pillar Partners Foundation, L.P. ("Pillar Partners"), a related party as more fully described in Note 15, which was amended on December 11, 2020 (as amended to date, the "April 2020 Securities Purchase Agreement"), under which the Company sold 3,039,514 shares of common stock and accompanying warrants to purchase 3,039,514 shares of the Company's common stock with an exercise price of $2.28 per share, for aggregate gross proceeds of $5.0 million. Each share and the accompanying common warrant had a combined purchase price of $1.645, which included $0.125 for each share of common stock underlying each warrant. The April 2020 Securities Purchase Agreement also provided for the option for Pillar Partners to purchase 2,747,252 shares of the Company's common stock (or pre-funded warrants to purchase shares of the Company's common stock at an exercise price of $0.01 in lieu of certain shares to the extent that purchasing such shares will cause Pillar Investment Entities (as defined below) to beneficially own in excess of 19.99% of the total number of shares of common stock outstanding post transaction) and warrants to purchase up to 1,373,626 shares of the Company's common stock (with an exercise price of $2.71), for aggregate gross proceeds of $5.0 million (the "April 2020 Private Placement Second Closing"). Subsequently, in December 2020, the April 2020 Private Placement Second Closing was consummated. Total net proceeds received pursuant to the April 2020 Securities Purchase Agreement, after deduction of offering expenses, was $9.8 million.

Note 8. Stockholders' Equity (Deficit) (Continued)

July 2020 Private Placement

On July 13, 2020, the Company entered into a Securities Purchase Agreement (the "July 2020 Securities Purchase Agreement") with Pillar Partners, Pillar Pharmaceuticals 6 L.P. ("Pillar 6"), and Pillar Pharmaceuticals 7 L.P. ("Pillar 7" and, together with Pillar Partners and Pillar 6, the "July 2020 Purchasers"), each a related party as more fully described in Note 15, pursuant to which, among other things, provided the July 2020 Purchasers the option to purchase, at their sole discretion, pre-funded warrants to purchase up to 784,615 shares of the Company's common stock, at an exercise price of $0.01 per share, and warrants to purchase up to 274,615 shares of the Company's common stock, at an exercise price of $9.75, for aggregate gross proceeds of $5.1 million (the "July 2020 Private Placement Second Closing"). During the three months ended March 31, 2021, the option to purchase securities in the July 2020 Private Placement Second Closing terminated. As a result, the Company is no longer eligible to receive additional proceeds from the sale of additional securities pursuant to the July 2020 Securities Purchase Agreement. However, the July 2020 Purchasers still hold outstanding warrants previously issued under the July 2020 Securities Purchase Agreement, as detailed below under the heading "Common Stock Warrants".

Common Stock Purchase Agreement

On March 4, 2019, the Company entered into a Purchase Agreement with Lincoln Park Capital Fund, LLC ("Lincoln Park"), which was amended on September 2, 2020 (as amended to date, the "LPC Purchase Agreement"), pursuant to which, upon the terms and subject to the conditions and limitations set forth therein, Lincoln Park has committed to purchase an aggregate of $35.0 million of shares of Company common stock from time to time at the Company's sole discretion over a 36-month period. As consideration for entering into the LPC Purchase Agreement, the Company issued 269,749 shares of Company common stock to Lincoln Park as a commitment fee (the "Commitment Shares"). The closing price of the Company's common stock on March 4, 2019 was $2.84 and the Company did not receive any cash proceeds from the issuance of the Commitment Shares.

During the years ended December 31, 2021 and 2020, the Company sold 800,000 and 750,000 shares, respectively, pursuant to the LPC Purchase Agreement, resulting in net proceeds of $4.2 million and $1.7 million, respectively. The 36-month period noted above for the LPC Purchase Agreement expired on March 4, 2022; accordingly, the Company no longer has access to additional capital under the LPC Purchase Agreement subsequent to this date.

"At-The-Market" Equity Program

In November 2018, the Company entered into an Equity Distribution Agreement (the "ATM Agreement") with JMP Securities LLC ("JMP") pursuant to which the Company may issue and sell shares of its common stock having an aggregate offering price of up to $50.0 million (the "Shares") through JMP as its agent. Subject to the terms and conditions of the ATM Agreement, JMP will use its commercially reasonable efforts to sell the Shares from time to time, based upon the Company's instructions, by methods deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or if specified by the Company, by any other method permitted by law, including but not limited to in negotiated transactions. The Company has no obligation to sell any of the Shares, and the Company or JMP may at any time suspend sales under the ATM Agreement or terminate the ATM Agreement. JMP is entitled to a fixed commission of 3.0% of the gross proceeds from Shares sold.

During the years ended December 31, 2021 and 2020, the Company sold 5,117,357 and 3,608,713 Shares, respectively, pursuant to the ATM Agreement resulting in net proceeds, after deduction of commissions and other offering expenses, of $15.3 million and $12.3 million, respectively. As of March 31, 2022, the Company may sell up to an additional $19.5 million of shares under the ATM Agreement.

Note 8. Stockholders' Equity (Deficit) (Continued)

Common Stock Warrants

In connection with various financing transactions, the Company has issued warrants to purchase shares of the Company's common stock and preferred stock. The Company accounts for common stock and preferred stock warrants as equity instruments or liabilities, depending on the specific terms of the warrant agreement. See Note 2 for further details on accounting policies related to the Company's warrants.

The following table summarizes outstanding warrants to purchase shares of the Company's common stock and/or preferred stock as of December 31, 2021 and 2020:

	Number of Shares			
Description	December 31, 2021	December 31, 2020	Weighted-Average Exercise Price	Expiration Date
Liability-classified Warrants				
December 2019 Series B1 warrants (1)	—	2,368,400	$ 1.52	Dec 2026
	—	2,368,400		
Equity-classified Warrants				
May 2013 warrants	15,437	1,949,754	$ 0.08	None
September 2013 warrants	4,096	514,756	$ 0.08	None
February 2014 warrants	2,171	266,006	$ 0.08	None
April 2020 Private Placement first closing warrants	3,039,514	3,039,514	$ 2.28	Apr 2023
April 2020 Private Placement second closing warrants	1,373,626	1,373,626	$ 2.71	Dec 2023
April 2020 Private Placement second closing warrants	1,143,428	2,677,311	$ 0.01	None
July 2020 Private Placement first closing warrants	389,731	2,014,234	$ 0.01	None
July 2020 Private Placement first closing warrants	2,764,227	2,764,227	$ 2.58	Jul 2023
	8,732,230	14,599,428		
Total outstanding	8,732,230	16,967,828		

(1) The Series B1 warrants were exercisable for either common stock (exercise price of $1.52) or Series B1 Convertible Preferred Stock (exercise price of $152) at the discretion of the warrant holder. However, as more fully disclosed in Note 7, the December 2019 Series B1 warrants were terminated during the three months ended March 31, 2021 contemporaneously with the termination of the future tranche rights.

The table below is a summary of the Company's warrant activity for the year ended December 31, 2021.

	Number of Warrants	Weighted-Average Exercise Price
Outstanding at December 31, 2020	16,967,828	$ 1.28
Issued	—	—
Exercised (1)	(5,867,198)	0.04
Expired	(2,368,400)	1.52
Outstanding at December 31, 2021	8,732,230	$ 2.04

(1) During the year ended December 31, 2021, certain related parties were issued warrants as more fully described in Note 15.

Note 9. Alliance Revenue

There were no Alliance revenues for the years ended December 31, 2021 and 2020. Alliance revenue for the years ended December 31, 2019 represents revenue from contracts with customers accounted for in accordance with ASC 606.

For the year ended December 31, 2019, the Company recognized Alliance revenues totaling $1.4 million which consistent primarily of revenues recognized under the Licensee Agreement, primarily related to the transfer of the IMO-8400 License and IMO-8400 drug product.

See Note 10 for additional details regarding the Company's collaboration arrangements.

Note 10. Collaboration and License Agreements

Option and License Agreement with Licensee

In April 2019, the Company entered into an amended and restated option and license agreement with a privately-held biopharmaceutical company ("Licensee"), pursuant to which the Company granted Licensee (i) exclusive worldwide rights to develop and market IMO-8400 for the treatment, palliation and diagnosis of all diseases, conditions or indications in humans (the "IMO-8400 License"), (ii) an exclusive right and license to develop IMO-9200 in accordance with certain IMO-9200 pre-option exercise protocols (the "IMO-9200 Option Period License"), and (iii) an exclusive one-year option, exercisable at Licensee's discretion, to obtain the exclusive worldwide rights to develop and market IMO-9200 for the treatment, palliation and diagnosis of all diseases, conditions or indications in humans (the "IMO-9200 Option") (collectively, the "Licensee Agreement"). In connection with the Licensee Agreement, the Company transferred certain drug material to Licensee for Licensee's use in development activities. Licensee is solely responsible for the development and commercialization of IMO-8400 and, if Licensee exercises the IMO-9200 Option, Licensee would be solely responsible for the development and commercialization of IMO-9200.

Under the terms of the Licensee Agreement, the Company received upfront, non-refundable fees totaling approximately $1.4 million and ownership of 10% of Licensee's outstanding common stock, subject to future adjustment, for granting Licensee the IMO-8400 License, the IMO-9200 Option Period License and transfer of related drug materials. In addition, following expiry of the IMO-9200 Option in 2020, the Company is now only eligible to receive certain development and sales-based milestone payments and royalties on global net sales related to the IMO-8400 Compound and potential future IMO-8400 Products, each as defined in the Licensee Agreement. The Company does not anticipate the receipt of any of the future milestones or royalties in the short term, if ever.

The Company accounts for the Licensee Agreement in accordance with ASC 606. As of December 31, 2021, the total transaction price of the contract was $1.4 million, which excluded the Option Fee and all development and sales milestones as all such payments were fully constrained. Additionally, as of December 31, 2021, there were no remaining performance obligations under the Licensee Agreement. The Company re-evaluates its performance obligations and transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

As disclosed above, in connection with the Licensee Agreement, the Company owns 10% of Licensee's outstanding common stock, subject to future adjustment. The Company evaluated the guidance in ASC 321, *Investments-Equity Securities*, and elected to account for the investment using the measurement alternative as the equity securities are without a readily determinable fair value, and the arrangement does not result in Idera having control or significant influence over Licensee. Accordingly, the securities are measured at cost, less any impairment, plus or minus changes resulting from observable price changes and are recorded in Other assets at a value of less than $0.1 million in the accompanying balance sheets. As of December 31, 2021, the Company considered the cost of the investment to not exceed the fair value of the investment and did not identify any observable price changes.

Note 10. Collaboration and License Agreement (Continued)

Collaboration Agreement with Scriptr

In February 2021, the Company entered into a collaboration and option agreement with Scriptr, pursuant to which (i) Scriptr and Idera will conduct a research collaboration utilizing Scriptr Platform Technology ("SPT") to identify, research and develop gene therapy candidates (each, a "Collaboration Candidate") for the treatment, palliation, diagnosis or prevention of (a) myotonic dystrophy type 1 ("DM1 Field") and (b) Friedreich's Ataxia ("FA Field") on a Research Program-by-Research Program basis, as applicable, and (ii) the Company was granted an exclusive option, in its sole discretion, to make effective the Scriptr License Agreement, as defined below, for a given Research Program, as defined below, to make use of Collaboration Candidates and related intellectual property (collectively, the "Scriptr Agreement").

Pursuant to the Scriptr Agreement, Scriptr will use commercially reasonable efforts to carry out research activities set forth in accordance with the applicable DM1 Field and FA Field research plans, including certain pre-clinical proof of concept studies, to identify research Collaboration Candidates utilizing SPT (each, a "Research Program"). Following the completion of activities under a given Research Program, Scriptr will prepare and submit to us a comprehensive data package (each, a "Data Package") that summarizes, on a Research Program-by-Research Program basis, any Collaboration Candidates researched under the Research Program, including any data and results. Upon receipt of a Data Package, Idera has, in its sole discretion, up to two-hundred seventy (270) calendar days to make effective the exclusive license agreement entered into by and between Scriptr and the Company, pursuant to which, among other things, Scriptr grants us exclusive rights and licenses with respect to the development, manufacture and commercialization of licensed candidates and products, subject to certain conditions and limitations (the "Scriptr License Agreement"), for a given Research Program (each licensed Research Program, a "Licensed Program"). The Scriptr License Agreement provides for customary development milestones on candidates developed under a Licensed Program and royalties on licensed products, if any.

In partial consideration of the rights granted by Scriptr to Idera under the Scriptr Agreement, the Company made a one-time, non-creditable and non-refundable payment to Scriptr during the first quarter of 2021. In order to fund the Research Programs, Idera will reimburse Scriptr for costs incurred by or on behalf of Scriptr in connection with the conduct of each Research Program during the research term in accordance with the applicable Research Program budget and payment schedule. The Company incurred approximately $2.1 million in research and development expenses under the Scriptr Agreement during the year ended December 31, 2021.

Note 11. Stock-based Compensation

As of December 31, 2021, the only equity compensation plans from which the Company may currently issue new awards are the Company's 2013 Stock Incentive Plan (as amended to date, the "2013 Plan") and 2017 Employee Stock Purchase Plan (the "2017 ESPP"), each as more fully described below.

Equity Incentive and Employee Stock Purchase Plans

2013 Stock Incentive Plan

The Company's board of directors adopted the 2013 Plan, which was approved by the Company's stockholders effective July 26, 2013. Amendments to the 2013 Plan were approved by the Company's stockholders in June 2014, June 2015, June 2017 and June 2019. The 2013 Plan is intended to further align the interests of the Company and its stockholders with its employees, including its officers, non-employee directors, consultants and advisers by providing equity-based incentives. The 2013 Plan allows for the issuance of incentive stock options intended to qualify under Section 422 of the Internal Revenue Code, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units ("RSUs"), other stock-based awards and performance awards. The total number of shares of common stock authorized for issuance under the 2013 Plan is 5,653,057 shares of the Company's common stock, plus such additional number of shares of common stock (up to 868,372 shares) as is equal to the number of shares of common stock subject to awards granted under the Company's 2005 Stock Incentive Plan or 2008 Stock Incentive Plan (the "2008 Plan"), to the extent such awards expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right.

As of December 31, 2021, options to purchase a total of 4,721,038 shares of common stock and 575,703 RSUs were outstanding and up to 199,873 shares of common stock remained available for grant under the 2013 Plan.

Other Awards and Inducement Grants

The Company has not made any awards pursuant to other equity incentive plans, including the 2008 Plan, since the Company's stockholders approved the 2013 Plan. As of December 31, 2021, options to purchase a total of 155,968 shares of common stock were outstanding under the 2008 Plan. In addition, as of December 31, 2021, non-statutory stock options to purchase an aggregate of 325,000 shares of common stock were outstanding that were issued outside of the 2013 Plan to certain employees in 2017, 2015 and 2014 pursuant to the Nasdaq inducement grant exception as a material component of new hires' employment compensation.

2017 *Employee Stock Purchase Plan*

The Company's board of directors adopted the 2017 ESPP which was approved by the Company's stockholders and became effective June 7, 2017. An amendment to the 2017 ESPP was approved by the Company's stockholders in June 2019. The 2017 ESPP is intended to qualify as an "employee stock purchase plan" as defined in Section 423 of the Internal Revenue Code, and is intended to encourage our employees to become stockholders of ours, to stimulate increased interest in our affairs and success, to afford employees the opportunity to share in our earnings and growth and to promote systematic savings by them. The total number of shares of common stock authorized for issuance under the 2017 ESPP is 412,500 shares of common stock, subject to adjustment as described in the 2017 ESPP. Participation is limited to employees that would not own 5% or more of the total combined voting power or value of the stock of the Company after the grant. As of December 31, 2021, 196,225 shares remained available for issuance under the 2017 ESPP.

Note 11. Stock-based Compensation (Continued)

Stock Purchase Plan Administration

The 2017 ESPP provides for offerings to employees to purchase common stock with offerings beginning on dates determined by the compensation committee of the board of directors or on the first business day thereafter. Each offering begins a "plan period" during which payroll deductions are to be made and held for the purchase of common stock at the end of the plan period. The compensation committee may, at its discretion, choose a plan period of 12 months or less for subsequent offerings and/or choose a different commencement date for offerings. During each plan period participating employees may elect to have a portion of their compensation, ranging from 1% to 10% of compensation as defined by the plan, withheld and used for the purchase of common stock at the end of each plan period. The purchase price is equal to 85% of the lower of the fair market value of a share of common stock on the first trading date of each plan period or the fair market value of a share of common stock on the last trading day of the plan period, and is limited by participant to $25,000 in fair value of common stock per year as well as other quarterly plan limitations as defined by each plan.

For the years ended December 31, 2021, 2020 and 2019, the Company issued 49,117, 75,999, and 60,953, shares of common stock, in each year respectively, under the 2017 ESPP and received proceeds of $0.1 million for each year, as a result of stock purchases.

Accounting for Stock-based Compensation

The Company recognizes non-cash compensation expense for stock-based awards under the Company's equity incentive plans and employee stock purchases under the Company's 2017 ESPP as follows:

- Stock Options: Compensation cost is recognized over an award's requisite service period, or vesting period, using the straight-line attribution method, based on the grant date fair value determined using the Black-Scholes option-pricing model.
- RSUs: Compensation cost for time-based RSUs, which vest over time based only on continued service, is recognized on a straight-line basis over the requisite service period based on the fair value of the Company's common stock on the date of grant. Compensation cost for awards that are subject to market considerations is recognized on a straight-line basis over the implied requisite service period, based on the grant date fair value estimated using a Monte Carlo simulation. Compensation cost for awards that are subject to performance conditions is recognized over the period of time commencing when the performance condition is deemed probable of achievement based on the fair value of the Company's common stock on the date of grant.
- Employee Stock Purchases: Compensation cost is recognized over each plan period based on the fair value of the look-back provision, calculated using the Black-Scholes option-pricing model, considering the 15% discount on shares purchased.

Total stock-based compensation expense attributable to stock-based payments made to employees and directors and employee stock purchases included in operating expenses in the Company's statements of operations for the years ended December 31, 2021, 2020 and 2019 was as follows:

(in thousands)	2021	2020	2019
Stock-based compensation:			
Research and development			
Employee Stock Purchase Plan	$ 28	$ 88	$ 36
Equity Incentive Plan	546	673	1,312
	$ 574	$ 761	$ 1,348
General and administrative			
Employee Stock Purchase Plan	$ 3	$ 9	$ 20
Equity Incentive Plan	1,960	2,871	2,477
	$ 1,963	$ 2,880	$ 2,497
Total stock-based compensation expense	$ 2,537	$ 3,641	$ 3,845

Note 11. Stock-based Compensation (Continued)

During the years ended December 31, 2021, 2020 and 2019, the weighted average fair market value of stock options granted was $1.54, $1.25, and $1.64, respectively.

Assumptions Used in Determining Fair Value of Stock Options

Inherent in the Black-Scholes option-pricing model are the following assumptions:

Volatility. The Company estimates stock price volatility based on the Company's historical stock price performance over a period of time that matches the expected term of the stock options.

Risk-free interest rate. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected term assumption.

Expected term. The expected term of stock options granted is based on an estimate of when options will be exercised or cancelled in the future.

Dividend rate. The dividend rate is based on the historical rate, which the Company anticipates will remain at zero.

Forfeitures. The Company accounts for forfeitures when they occur. Ultimately, the actual expense recognized over the vesting period will be for only those shares that vest. See Note 2.

The fair value of each option award at the date of grant was estimated using the Black-Scholes option pricing model. All options granted during the three years in the period ended December 31, 2021 were granted at exercise prices equal to the fair market value of the common stock on the dates of grant**.**

The following weighted average assumptions apply to the options to purchase 1,356,700, 1,215,382, and 1,279,016 shares of common stock granted to employees and directors during the years ended December 31, 2021, 2020 and 2019, respectively:

	2021	2020	2019
Average risk-free interest rate	0.4%	1.0%	2.1%
Expected dividend yield	—	—	—
Expected lives (years)	3.6	3.9	3.7
Expected volatility	94%	84%	84%
Weighted average exercise price (per share)	$ 2.68	$ 2.08	$ 2.75

All options granted during the years ended December 31, 2021, 2020 and 2019 were granted at exercise prices equal to the fair market value of the common stock on the dates of grant**.**

Stock Option Activity

The following table summarizes stock option activity for the year ended December 31, 2021.

($ in thousands, except per share data)	Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2020	4,614,323	$ 9.78	6.8	$ 2,949
Granted	1,356,700	2.68		
Exercised	(22,500)	2.11		
Forfeited	(261,426)	4.44		
Expired	(485,091)	11.52		
Outstanding at December 31, 2021 (1)	5,202,006	$ 8.06	5.9	$ —
Exercisable at December 31, 2021	4,096,875	$ 9.62	5.1	$ —

(1) *Includes both vested stock options as well as unvested stock options for which the requisite service period has not been rendered but that are expected to vest based on achievement of a service condition.*

Note 11. Stock-based Compensation (Continued)

In March 2021, the Company accelerated the vesting of 1,535,578 options, which were previously granted from 2019 to 2021. The modification results in an incremental stock based compensation charge that was not significant. As of December 31, 2021, there was $1.2 million of unrecognized compensation cost related to unvested options, which the Company expects to recognize over a weighted average period of 2.1 years.

Restricted Stock Activity

The following table summarizes restricted stock activity for the year ended December 31, 2021:

	Time-based Awards		Market/Performance-based Awards	
($ in thousands, except per share data)	Number of Shares	Weighted-Average Grant Date Fair Value	Number of Shares	Weighted-Average Grant Date Fair Value
Nonvested shares at December 31, 2020	354,003	$ 2.27	549,318	$ 1.54
Granted				
Cancelled	(48,563)	2.31	(42,290)	1.54
Vested	(236,765)	2.25	—	—
Nonvested shares at December 31, 2021	68,675	$ 2.30	507,028	$ 1.54

Time-based Restricted Stock Units

In December 2020, the Company's Chief Executive Officer was granted an award of 128,170 RSUs, pursuant to the 2013 Plan, in lieu of salary pursuant to a January 10, 2020 amendment to the officers' employment agreement. The RSUs were fully vested on the grant date.

In March 2021, the Company accelerated the vesting of 137,872 unvested time-based restricted stock units which were previously granted in 2019 and 2020. The modification results in an incremental stock based compensation charge that was not significant. During the year ended December 31, 2021, the Company recognized $0.3 million of compensation expense related to these awards. As of December 31, 2021, there was $0.1 million of unrecognized compensation cost related to the Company's time-based RSUs, which is expected to be recognized over a weighted average period of 1.6 years.

Market/Performance-based Restricted Stock Units

In July 2020, the Company granted RSUs to certain employees, including executive officers, under the 2013 Plan, with vesting that may occur upon a combination of specific performance and/or market conditions. Accordingly, the Company views these RSUs as two separate awards: (i) an award that vests if the market condition is achieved, and (ii) an award that vests whether or not the market condition is achieved, so long as the performance condition is achieved.

The Company is currently recognizing compensation expense for these awards over the estimated requisite service period of 2.36 years based on the estimated fair value when considering the market condition of the award, which was determined using a Monte Carlo simulation. During the year ended December 31, 2021, the Company recognized $0.3 million of compensation expense related to these awards. As of December 31, 2021, the remaining unrecognized compensation cost for the market-based component of these awards, which is expected to be recognized over a weighted-average period of 0.9 years, is $0.3 million. In addition, should the performance condition be achieved, the Company would recognize an additional $0.3 million of compensation expense.

Note 12. Commitments and Contingencies

Lease Commitments

As of December 31, 2021, the Company's leased assets primarily consisted of its office headquarters in Exton, Pennsylvania. During 2021, 2020 and 2019, rent expense, including real estate taxes, was $0.3 million, $0.4 million, and $0.3 million, respectively. The leases are classified as operating leases.

Future minimum commitments as of December 31, 2021 under the Company's lease agreements are approximately:

December 31,	Operating Leases *(in thousands)*
2022	249
2023	250
2024	240
2025	101
	$ 840

The Company entered into the Exton, Pennsylvania facility lease on April 1, 2015, which was subsequently amended on September 23, 2015 to include additional space. The Company currently leases approximately 11,000 square feet of office space at our Exton facility. The lease expires on May 31, 2025.

Vendor Financing Arrangement

In October 2020, the Company entered into a short-term financing arrangement with a third-party vendor to finance insurance premiums. As of December 31, 2020, the balance of $0.4 million, was paid in monthly installments through June 2021. Accordingly, as of December 31, 2021, no amounts were outstanding under this agreement.

Note 13. Income Taxes

As of December 31, 2021, the Company had cumulative federal and state net operating loss carryforwards ("NOLs") of approximately $327.5 million and $322.0 million available to reduce federal and state taxable income, respectively. As a result of the Tax Cuts and Jobs Act of 2017, federal net operating losses incurred for taxable years beginning after January 1, 2018 have an unlimited carryforward period, but can only be utilized to offset 80% of taxable income in future taxable periods. Of the $327.5 million of federal NOLs, $130.1 million have an unlimited carryforward and the remaining NOLs are still subject to expiration through 2037. State NOLs are still subject to expiration according to the laws of each respective jurisdiction. The Company files state tax returns in Massachusetts and Pennsylvania whereby both jurisdictions impose a 20-year carryforward period. All $322.0 million of state NOLs expire through 2041, with the first year of expiration being 2032 for $23.4 million of Massachusetts NOLs. In addition, at December 31, 2021, the Company had cumulative federal and state tax credit carryforwards of $26.7 million and $1.9 million, respectively, available to reduce federal and state income taxes, respectively, which expire through 2041 and 2033, respectively, for federal and state purposes, other than those that have an unlimited carryforward period.

Sections 382 and 383 of the Internal Revenue Code prescribe limitations on the amount of NOLs and tax credit carryforwards that may be utilized in any one year. The Company has completed several financings since the effective date of the Tax Reform Act of 1986, which as of December 31, 2021, have resulted in ownership changes that will significantly limit the Company's ability to utilize its net operating loss and tax credit carryforwards. In December 2017, the Company completed a study which determined that ownership changes had occurred. The federal and state net operating loss and tax credit carryforwards and related deferred tax assets shown in the table below have been adjusted to reflect the limitations that resulted from this study. As no study has been completed subsequent to 2017, additional ownership change limitations may result from ownership changes that have occurred, or may occur in the future. The Company continues to monitor equity activity and potential ownership changes.

Note 13. Income Taxes (Continued)

As of December 31, 2021 and 2020, the components of the deferred tax assets are approximately as follows:

(in thousands)	2021	2020
Operating loss carryforwards	$ 90,550	$ 90,895
Tax credit carryforwards	28,226	26,550
Stock-based compensation	6,902	6,820
Capitalized research and development	7,818	—
Lease liabilities	220	276
Other	70	162
Total deferred tax assets	133,786	124,703
Right-of-use asset	(213)	(270)
Valuation allowance	(133,573)	(124,433)
Net deferred tax assets	$ —	$ —

The Company has provided a full valuation allowance for its deferred tax asset due to the uncertainty surrounding the ability to realize these assets.

The difference between the U.S. federal corporate tax rate and the Company's effective tax rate for the years ended December 31, 2021, 2020 and 2019 is as follows:

	2021	2020	2019
Expected federal income tax rate	(21.0)%	(21.0)%	(21.0)%
Expiring credits and NOLs	—	—	—
Change in valuation allowance	(9.3)	10.6	26.2
Federal and state credits	1.7	(3.1)	(8.1)
State income taxes, net of federal benefit	2.1	(1.9)	(4.7)
Warrant and future tranche right revaluation loss	26.9	14.2	4.3
Stock-based compensation	—	0.2	0.5
Other	(0.4)	1.0	2.8
Effective tax rate	0.0 %	0.0 %	0.0 %

The Company applies ASC 740-10, *Accounting for Uncertainty in Income Taxes, an interpretation of ASC 740*. ASC 740-10 clarifies the accounting for uncertainty in income taxes recognized in financial statements and requires the impact of a tax position to be recognized in the financial statements if that position is more likely than not of being sustained by the taxing authority. The Company had no unrecognized tax benefits resulting from uncertain tax positions on December 31, 2021 and 2020.

The Company has not conducted a study of its research and development tax credit carryforwards. Such a study might result in an adjustment to the Company's research and development credit carryforwards, however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position under ASC 740-10. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact on the statements of operations if an adjustment was required.

The Company files income tax returns in the U.S. federal, Massachusetts and Pennsylvania jurisdictions. The Company is no longer subject to tax examinations for years before 2018, except to the extent that it utilizes tax attributes that originated before 2018. The Company does not believe there will be any material changes in its unrecognized tax positions over the next 12 months. The Company has not incurred any interest or penalties. In the event that the Company is assessed interest or penalties at some point in the future, they will be classified in the statements of operations as general and administrative expense.

Note 14. Employee Benefit Plan

The Company has an employee benefit plan under Section 401(k) of the Internal Revenue Code. The plan allows employees to make contributions up to a specified percentage of their compensation. Under the plan, the Company matches up to 5% of employee base salary, by matching 100% of the first 5% of annual base salary contributed by each employee. Approximately $0.3 million of 401(k) benefits was charged to operating expenses for each of the years ended December 31, 2021, 2020 and 2019.

Note 15. Related Party Transactions

Baker Brothers

Julian C. Baker, a member of the Company's Board of Directors until his resignation in September 2018, is a principal of Baker Bros. Advisors, LP. Additionally, Kelvin M. Neu, a member of Company's Board until his resignation in June 2019, is an employee of Baker Bros. Advisors, LP. As of December 31, 2021, Baker Bros. Advisors, LP and certain of its affiliated funds (collectively, "Baker Brothers") held sole voting power with respect to an aggregate of 2,047,180 shares of the Company's common stock, representing approximately 4% of the Company's outstanding common stock.

During 2019, Baker Brothers purchased shares of the Company's Series B1 Preferred Stock and accompanying warrants to purchase common stock in connection with the December 2019 Private Placement, as more fully described in Note 7. Concurrent with the December 2019 Private Placement, the Company amended the warrants initially issued to Baker Brothers and other holders on May 7, 2013, September 30, 2013 and February 10, 2014 to remove expiration date. Under the terms of the warrants issued to Baker Brothers and the December 2019 Securities Purchase Agreement related to the securities issued in connection with the 2019 Private Placement, Baker Brothers is not permitted to convert or exercise any common stock equivalents to the extent that such conversion or exercise would result in Baker Brothers (and its affiliates) beneficially owning more than 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon conversion or exercise of such securities. Baker Brothers has the right to increase this beneficial ownership limitation in its discretion on 61 days' prior written notice to us, provided that in no event is Baker Brothers permitted to convert or exercise such securities to the extent that such exercise would result in Baker Brothers (and its affiliates) beneficially owning more than 19.99% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon conversion or exercise of such securities.

During March 2021, Baker Brothers exercised warrants to purchase 2,708,812 shares of the Company's common stock at an exercise price of $0.08 per share for a total exercise price of approximately $0.2 million. Additionally, Baker Brothers converted 14,150 shares Series B1 Preferred Stock into 1,415,000 shares of the Company's common stock. In April 2021, Baker Brothers converted 9,534 shares Series B1 Preferred Stock into 953,400 shares of the Company's common stock.

Pillar Investment Entities

Youssef El Zein, a member of the Company's Board of Directors until his resignation in October 2017, is a director and controlling stockholder of Pillar Invest Corporation ("Pillar Invest"), which is the general partner of Pillar Pharmaceuticals I, L.P., Pillar Pharmaceuticals II, L.P., Pillar Pharmaceuticals III, L.P., Pillar Pharmaceuticals IV, L.P., Pillar Pharmaceuticals V, L.P., Pillar 6 and Pillar Partners (collectively, the "Pillar Investment Entities"). As of December 31, 2021, the Pillar Investment Entities beneficially owned approximately 19.99% of the Company's common stock.

Note 15. Related Party Transactions (Continued)

During 2020, the Company sold shares of its common stock, prefunded warrants and common stock warrants to entities affiliated with Pillar Invest Corporation in connection with private placement transactions, as more fully descried in Note 8.

During the year ended December 31, 2021, certain of the Pillar Investment Entities exercised warrants to purchase 3,158,386 shares of the Company's common stock at an exercise price of $0.01 per share for a total exercise price of less than $0.1 million. 19,052 shares were used as cashless shares for the exercise costs.

As of December 31, 2021, the Pillar Investment Entities held (i) prefunded warrants to purchase up to 1,533,159 shares of the Company's common stock at an exercise price of $0.01 per share, (ii) warrants to purchase up to 3,039,514 shares of the Company's common stock at an exercise price of $2.28 per share, (iii) warrants to purchase up to 2,764,227 shares of the Company's common stock at an exercise price of $2.58 per share, and (iv) warrants to purchase up to 1,373,626 shares of the Company's common stock at an exercise price of $2.71 per share.

Board Fees Paid in Stock

Pursuant to the Company's director compensation program, in lieu of director board and committee fees of $0.1 million, $0.3 million, and $0.1 million, respectively, incurred during each of the years ended December 31, 2021, 2020 and 2019, respectively, the Company issued 105,691, 145,392, and 53,985, shares of common stock, respectively, to certain of its directors. Director board and committee fees are paid in arrears and the number of shares issued was calculated based on the market closing price of the Company's common stock on the issuance date.

Officer Salary Paid in Stock

In December 2020, the Company's Chief Executive Officer was granted an award of 128,170 RSUs, pursuant to the 2013 Plan, in lieu of salary of $0.6 million pursuant to a January 10, 2020 amendment to the officers' employment agreement. The RSUs were fully vested on the grant date.

No such RSU awards were granted to any executive officers as compensation in 2021.

Note 16. Net Income (Loss) per Common Share Applicable to Common Stockholders

Details in the computation of basic and diluted net income (loss) per common share were as follows:

($ in thousands except per share data)	Year Ended December 31, 2021	2020	2019
Net income (loss) applicable to common stockholders — Basic:			
Net income (loss)	$ 98,091	$ (112,662)	$ (56,515)
Less: Deemed dividend on preferred stock	—	—	(28,043)
Less: Undistributed earnings to preferred stockholders	(1,150)	—	—
Net income (loss) applicable to common stockholders - basic	$ 96,941	$ (112,662)	$ (84,558)
Numerator for basic net income (loss) applicable to common stockholders	$ 96,941	$ (112,662)	$ (84,558)
Denominator for basic net income (loss) applicable to common stockholders	49,203	33,821	28,545
Net income (loss) applicable to common stockholders - basic	$ 1.97	$ (3.33)	$ (2.96)
Net loss applicable to common stockholders — Diluted:			
Net income (loss)	$ 96,941	$ (112,662)	$ (84,558)
Less: Warrant revaluation gain applicable to dilutive liability-classified warrants	(6,983)	—	—
Less: Future tranche right revaluation gain applicable to dilutive liability-classified future tranche rights	(118,803)	—	—
Numerator for diluted net income (loss) applicable to common stockholders	$ (28,845)	$ (112,662)	$ (84,558)
Denominator for basic net income (loss) applicable to common stockholders	49,203	33,821	28,545
Plus: Incremental shares underlying “in the money” liability-classified warrants outstanding	93	—	—
Plus: Incremental shares underlying “in the money” liability-classified future tranche rights outstanding	831	—	—
Denominator for diluted net income (loss) applicable to common stockholders	50,127	33,821	28,545
Net income (loss) applicable to common stockholders - diluted	$ (0.58)	$ (3.33)	$ (2.96)

Total antidilutive securities excluded from the calculation of diluted net loss per share for the years ended December 31, 2021, 2020 and 2019, were as follows:

(in thousands)	2021	2020	2019
Stock options	5,202	4,614	4,220
Restricted stock units	576	903	194
Common stock warrants	8,732	16,968	5,099
Convertible preferred stock	—	2,369	2,369
Future tranche rights	—	50,467	49,407
Total	14,510	75,321	61,289

Note 17. Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-152669) pertaining to the 2008 Stock Incentive Plan of Idera Pharmaceuticals, Inc.

(2) Registration Statement (Form S-8 No. 333-176067) pertaining to the 2008 Stock Incentive Plan and 1995 Employee Stock Purchase Plan of Idera Pharmaceuticals, Inc.

(3) Registration Statement (Form S-8 No. 333-191076) pertaining to the 2013 Stock Incentive Plan of Idera Pharmaceuticals, Inc.

(4) Registration Statement (Form S-8 No. 333-197062) pertaining to the 2013 Stock Incentive Plan of Idera Pharmaceuticals, Inc.

(5) Registration Statement (Form S-8 No. 333-202691) pertaining to Inducement Stock Option Awards of Idera Pharmaceuticals, Inc.

(6) Registration Statement (Form S-8 No. 333-206129) pertaining to the 2013 Stock Incentive Plan, as amended, of Idera Pharmaceuticals, Inc.

(7) Registration Statement (Form S-8 No. 333-210090) pertaining to an Inducement Stock Option Award of Idera Pharmaceuticals, Inc.

(8) Registration Statement (Form S-1 as amended by Form S-3/A No. 333-136610) of Idera Pharmaceuticals, Inc.

(9) Registration Statement (Form S-1 as amended by Form S-3/A No. 333-187155) of Idera Pharmaceuticals, Inc.

(10) Registration Statement (Form S-2 as amended by Form S-3/A No. 333-109630) of Idera Pharmaceuticals, Inc.

(11) Registration Statement (Form S-3 No. 333-119943) of Idera Pharmaceuticals, Inc.

(12) Registration Statement (Form S-3 No. 333-126634) of Idera Pharmaceuticals, Inc.

(13) Registration Statement (Form S-3 No. 333-131804) of Idera Pharmaceuticals, Inc.

(14) Registration Statement (Form S-3 No. 333-133455) of Idera Pharmaceuticals, Inc.

(15) Registration Statement (Form S-3 No. 333-133456) of Idera Pharmaceuticals, Inc.

(16) Registration Statement (Form S-3 No. 333-139830) of Idera Pharmaceuticals, Inc.

(17) Registration Statement (Form S-3 as amended by Form S-3/A No. 333-185392) of Idera Pharmaceuticals, Inc.

(18) Registration Statement (Form S-3 No. 333-186312) of Idera Pharmaceuticals, Inc.

(19) Registration Statement (Form S-3 No. 333-189700) of Idera Pharmaceuticals, Inc.

(20) Registration Statement (Form S-3 No. 333-210140) of Idera Pharmaceuticals, Inc.

(21) Registration Statement (Form S-8 No. 333-217665) pertaining to an Inducement Stock Option Award of Idera Pharmaceuticals, Inc.

(22) Registration Statement (Form S-8 No. 333-219740) pertaining to the 2017 Employee Stock Purchase Plan of Idera Pharmaceuticals, Inc.

(23) Registration Statement (Form S-8 No. 333-219741) pertaining to the 2013 Stock Incentive Plan, as amended, of Idera Pharmaceuticals, Inc.

(24) Registration Statement (Form S-8 No. 333-232609) pertaining to the 2017 Employee Stock Purchase Plan of Idera Pharmaceuticals, Inc.

(25) Registration Statement (Form S-8 No. 333-232610) pertaining to the 2013 Stock Incentive Plan, as amended, of Idera Pharmaceuticals, Inc.

(26) Registration Statement (Form S-3 No. 333-238868) of Idera Pharmaceuticals, Inc.

(27) Registration Statement (Form S-3 No. 333-240361) of Idera Pharmaceuticals, Inc.

(28) Registration Statement (Form S-3 No. 333-240366) of Idera Pharmaceuticals, Inc.

(29) Registration Statement (Form S-3 No. 333-248560) of Idera Pharmaceuticals, Inc.

(30) Registration Statement (Form S-3 and S-3/A No. 333-253804) of Idera Pharmaceuticals, Inc.

of our report dated March 31, 2022, with respect to the financial statements of Idera Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Idera Pharmaceuticals, Inc. for the year ended December 31, 2021.

/s/ ERNST & YOUNG LLP

Philadelphia, Pennsylvania
March 31, 2022

Exhibit 31.1

Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14 and 15d-14, as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002

I, Vincent J. Milano, certify that:

1. I have reviewed this Annual Report on Form 10-K of Idera Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;
    c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d) Disclosed in this report any changes in the registrant's internal control over financial reporting that occurred during the registrant's fourth fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):
    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control and financial reporting.

/s/ Vincent J. Milano
Vincent J. Milano
Chief Executive Officer

Dated: March 31, 2022

Exhibit 31.2

Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14 and 15d-14, as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002

I, John J. Kirby, certify that:

1. I have reviewed this Annual Report on Form 10-K of Idera Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;
    c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d) Disclosed in this report any changes in the registrant's internal control over financial reporting that occurred during the registrant's fourth fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):
    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control and financial reporting.

/s/ John J. Kirby
John J. Kirby
Chief Financial Officer

Dated: March 31, 2022

Exhibit 32.1

Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the Annual Report on Form 10-K of Idera Pharmaceuticals, Inc. (the "Company") for the period ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Vincent J. Milano, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

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

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

A signed original of this written statement has been provided to Idera Pharmaceuticals, Inc. and will be retained by Idera Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

/s/ Vincent J. Milano
Vincent J. Milano
Chief Executive Officer

Dated: March 31, 2022

Exhibit 32.2

Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the Annual Report on Form 10-K of Idera Pharmaceuticals, Inc. (the "Company") for the period ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, John J. Kirby, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

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

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

A signed original of this written statement has been provided to Idera Pharmaceuticals, Inc. and will be retained by Idera Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

/s/ John J. Kirby
John J. Kirby
Chief Financial Officer

Dated: March 31, 2022