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, 2020
OR

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

For the transition period from to
Commission file number 001-38150

KALA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**27-0604595**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
490 Arsenal Way, Suite 120 **Watertown, MA**	**02472**
(Address of principal executive offices)	(Zip Code)

(781) 996-5252
(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, $0.001 par value per share	**KALA**	**Nasdaq Global Select Market**

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 ☒

As of June 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the Common Stock held by non-affiliates of the registrant was approximately $411.8 million, based on the closing price of the registrant's common stock on June 30, 2020.

There were 61,552,352 shares of Common Stock ($0.001 par value) outstanding as of February 24, 2021.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2021 Annual Meeting of Stockholders, which is expected to be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2020.

Table of Contents

References to Kala

Throughout this Annual Report on Form 10-K, the "Company," "Kala", "Kala Pharmaceuticals," "we," "us," and "our," except where the context requires otherwise, refer to Kala Pharmaceuticals, Inc. and its consolidated subsidiary, and "our board of directors" refers to the board of directors of Kala Pharmaceuticals, Inc.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "target," "should," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- our commercialization efforts for EYSUVIS™ (loteprednol etabonate ophthalmic suspension) 0.25% and INVELTYS® (loteprednol etabonate ophthalmic suspension) 1%;
- our development efforts for our product candidates and our ability to discover and develop new programs and product candidates;
- our estimates regarding potential future revenue from sales of EYSUVIS and INVELTYS;
- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms and processes on a timely basis, or at all, with third-party payors for EYSUVIS and INVELTYS;
- our ability to maintain regulatory approvals for EYSUVIS and INVELTYS;
- our expectations regarding our ability to fund our operating expenses, lease and debt service obligations, and capital expenditure requirements with our cash on hand and anticipated revenue from product sales;
- the potential advantages of EYSUVIS, INVELTYS and our product candidates;
- the rate and degree of market acceptance and clinical utility of our products;
- our estimates regarding the potential market opportunity for EYSUVIS, INVELTYS and our product candidates;
- the timing of and our ability to submit applications for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- our estimates regarding expenses, future revenue, timing of any future revenue, capital requirements and needs for additional financing;

- the impact of government laws and regulations;
- our competitive position;
- developments relating to our competitors and our industry;
- our ability to maintain and establish collaborations or obtain additional funding;
- the impact of COVID-19 on our business and operations; and
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart our Business Startups Act of 2012.

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

You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K and have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements except as required by applicable law.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by us and third parties as well as our estimates of potential market opportunities. Industry publications, third-party and our own research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for EYSUVIS, INVELTYS and our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

Risks Factor Summary

Our business is subject to a number of risks that if realized could materially affect our business, financial condition, results of operations, cash flows and access to liquidity. These risks are discussed more fully in the "Risk Factors" section of this Annual Report on Form 10-K. Our principal risks include the following:

- We have incurred significant losses from operations and negative cash flows from operations since our inception. We expect to incur additional losses and may never achieve or maintain profitability. As of December 31, 2020, we had an accumulated deficit of $399.8 million.
- We may need substantial additional funding. 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.
- Our substantial indebtedness may limit cash flow available to invest in the ongoing needs of our business.

- The ongoing novel coronavirus pandemic and the efforts to prevent its spread have adversely impacted our operations and the market for INVELTYS, could impact the launch and commercialization of EYSUVIS and may continue to adversely affect our business, results of operations and financial condition.

- EYSUVIS, INVELTYS or any of our product candidates that receive marketing approval may fail to achieve market acceptance by clinicians and patients, or adequate formulary coverage, pricing or reimbursement by third-party payors and others in the medical community, and the market opportunity for these products may be smaller than we estimate.

- Even if we are able to successfully commercialize EYSUVIS, INVELTYS or any product candidate that we may develop, the products may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

- If we are unable to maintain our sales, marketing and distribution capabilities, establish additional capabilities if and when necessary, or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing EYSUVIS, INVELTYS or any of our product candidates that we may develop if and when they are approved.

- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do. Our product candidates will, if approved, also compete with existing branded, generic and off-label products.

- We are dependent on the success of EYSUVIS, INVELTYS, and any product candidate for which we receive marketing approval. If we are unable to successfully commercialize our products and product candidates, our business will be materially harmed.

- We contract with third parties for the manufacture of EYSUVIS and INVELTYS and plan to contract with third parties for clinical and commercial supply of any future product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our products and product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

- We may be unable to obtain and maintain patent protection for our technology, products and product candidates, or the scope of the patent protection obtained may not be sufficiently broad or enforceable, such that our competitors could develop and commercialize technology, products and product candidates similar or identical to ours, and our ability to successfully commercialize our technology, products and product candidates may be impaired.

- EYSUVIS, INVELTYS and certain aspects of our AMPPLIFY technology are protected by patents exclusively licensed from other companies or institutions. If these third parties terminate their agreements with us or fail to maintain or enforce the underlying patents, or we otherwise lose our rights to these patents, our competitive position and our market share in the markets for any of our approved products will be harmed. If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

- The terms of approvals, ongoing regulations and post-marketing restrictions for our products may limit how we manufacture and market our products, which could materially impair our ability to generate revenue.

- Recently enacted and future legislation may affect our ability to commercialize and the prices we obtain for any products that are approved in the United States or foreign jurisdictions.

Part I

Item 1. BUSINESS

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of innovative therapies for diseases of the eye. We have worldwide rights to a portfolio of innovative products and product candidates that include two marketed therapies utilizing our proprietary mucus penetrating particle, or MPP, drug delivery technology, which we refer to as our AMPPLIFY® technology, to address medical needs for the front of the eye, and a pipeline of proprietary new chemical entities, or NCEs, targeted to address front and back of the eye diseases.

Our two marketed products are EYSUVIS™ (loteprednol etabonate ophthalmic suspension) 0.25%, for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease, and INVELTYS® (loteprednol etabonate ophthalmic suspension) 1%, a topical twice-a-day ocular steroid for the treatment of post-operative inflammation and pain following ocular surgery. Both products apply our AMPPLIFY technology to loteprednol etabonate, or LE, a corticosteroid designed for ocular applications. The AMPPLIFY technology uses selectively-sized nanoparticles that each have a proprietary coating. We believe that these two key attributes enable even distribution of drug particles on mucosal surfaces and significantly increase drug delivery to target tissues by enhancing mobility of drug particles through mucus and preventing drug particles from becoming trapped and eliminated by mucus.

EYSUVIS is the first and only FDA-approved prescription product with an indication for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease. The U.S. Food and Drug Administration, or FDA, approved EYSUVIS in October 2020 based on results from four clinical trials, including three Phase 3 clinical trials and one Phase 2 clinical trial, which demonstrated significant improvements in both the signs and symptoms of dry eye disease. Specifically, statistical significance was achieved after two weeks of dosing for the sign endpoint of conjunctival hyperemia in all three Phase 3 clinical trials. Statistical significance was observed in two of the three Phase 3 clinical trials for the symptom endpoints of ocular discomfort severity in both the overall intent-to-treat, or ITT, population and in a predefined subgroup of ITT patients with more severe ocular discomfort at baseline. EYSUVIS was well-tolerated across the four trials, with adverse events and intraocular pressure, or IOP, increases comparable to that observed with vehicle. We believe that EYSUVIS' broad mechanism of action, rapid onset of relief of both signs and symptoms, favorable tolerability profile and potential to be complementary to existing therapies, will result in a favorable profile for the management of dry eye flares and other dry eye associated conditions that would benefit from short-term treatment of dry eye signs and symptoms. We further believe that these features of EYSUVIS may be attractive to prescribing clinicians and EYSUVIS could become the preferred first-line prescription therapy for the short-term treatment of the signs and symptoms of dry eye disease, including the treatment of dry eye flares that affect the vast majority of dry eye patients. We commenced full promotional launch of EYSUVIS in January 2021.

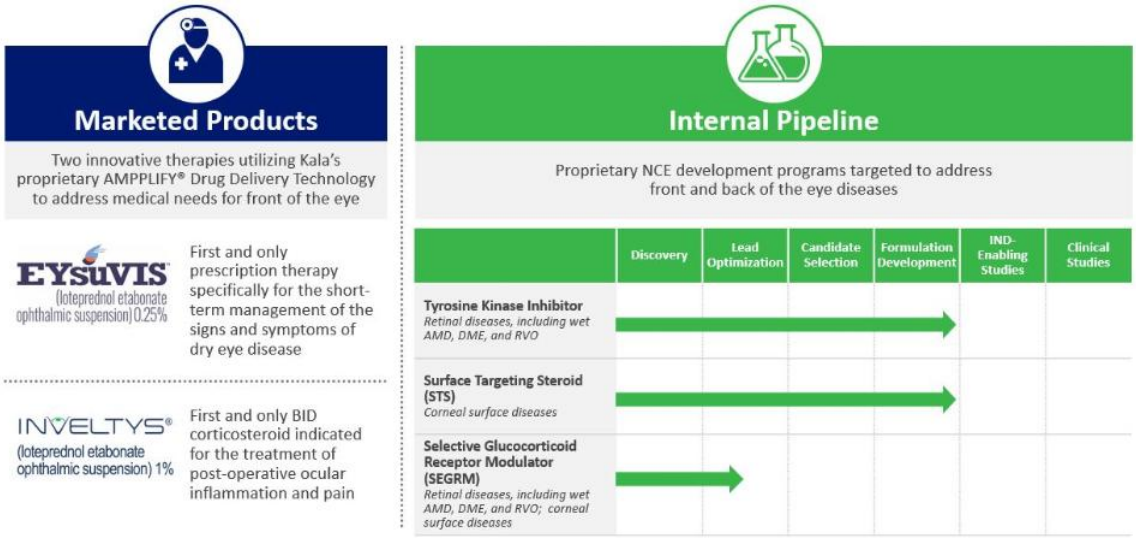
INVELTYS is the first and only FDA-approved ocular corticosteroid product with a twice-a-day dosing regimen for the treatment of post-operative inflammation and pain following ocular surgery. In clinical trials, INVELTYS showed statistical significance in the primary efficacy endpoints of complete resolution of inflammation at day eight maintained through day 15 with no need for rescue medication compared to placebo and complete resolution of pain at day eight maintained through day 15 with no need for rescue medications compared to placebo. The FDA approved INVELTYS in August 2018, and we commercially launched the product in January 2019.

We are also progressing our pipeline of proprietary preclinical development programs targeted to address front and back of the eye diseases. These preclinical development programs, all of which are NCEs, include our receptor Tyrosine Kinase Inhibitor program, or rTKI, that is designed to inhibit the vascular endothelial growth factor pathway, for the treatment of retinal diseases, including wet age-related macular degeneration, or Wet AMD; our selective glucocorticoid receptor modulators, or SEGRMs, which are a novel class of therapies designed to modify the downstream activity of the receptors to exhibit the anti-inflammatory and immunomodulatory properties of the corticosteroid class of therapies without their associated side effects; and our novel surface targeting steroid, or STS, designed to target the ocular surface and thus have the potential to have fewer side effects compared to traditional topical steroids. We own all intellectual property and worldwide rights to these pipeline preclinical development programs.

We have retained worldwide commercial rights for EYSUVIS, INVELTYS and our preclinical development programs. Starting with FDA approval of INVELTYS, we have built a commercial infrastructure with our own focused, specialty sales force which now includes 91 territory sales managers, or TSMs, 14 regional sales leaders, or RSLs, two area sales leaders, or ASLs, and three directors of national accounts, or DNAs. In 2021, we plan to increase our sales force from 91 TSMs to approximately 125 TSMs, pending the status of the COVID-19 pandemic. Our sales representatives promote both EYSUVIS and INVELTYS. We expect to commercialize in the United States any of our product candidates that receive marketing approval as well. We also expect to explore commercialization of EYSUVIS for the treatment of dry eye disease in certain markets outside the United States, including the European Union, or EU, utilizing a variety of collaboration, distribution and other marketing arrangements with one or more third parties.

We own and/or exclusively license patents relating to EYSUVIS, INVELTYS, our preclinical development programs and our AMPPLIFY technology, including U.S. and foreign issued patents and pending patent applications. The expiration dates of issued U.S. and ex-U.S. patents covering EYSUVIS and INVELTYS are in 2033. The expiration dates of issued U.S. and ex-U.S. patents relating to our AMPPLIFY technology are in 2025 through 2036.

The following table describes our marketed products and the stage of each of our current preclinical development programs:



Our Products

EYSUVIS for Dry Eye Disease

Dry eye disease is a chronic, episodic, multifactorial disease affecting the tears and ocular surface that can result in tear film instability, inflammation, discomfort, visual disturbance and ocular surface damage. Dry eye disease can have a significant impact on quality of life and can potentially cause long-term damage to the ocular surface. Due to the impact of dry eye disease on tear film dynamics, the condition can affect performance of common vision-related activities such as reading, using a computer and driving, and can lead to complications associated with visual impairment. In addition, the vast majority of dry eye patients experience acute exacerbations of their symptoms, which are commonly referred to as flares, at various times throughout the year. These flares can be triggered by numerous factors, including exposure to allergens, pollution, wind and low humidity, intense visual concentration such as watching television and working at a computer, hormonal changes, contact lens wear, smoking and sleep deprivation, which cause ocular surface inflammation and impact tear production and/or tear film stability.

We estimate dry eye disease affects approximately 38 million people in the United States based on an estimated dry eye disease prevalence of 14.5% described below and applied to the population of the United States over 20 years old. Based on third-party academic research, we believe dry eye disease results in approximately $55 billion in direct and indirect costs in the United States each year, of which approximately $3.8 billion are direct medical costs. The exact prevalence of dry eye disease is unknown due to the difficulty in defining the disease and the lack of a single diagnostic test to confirm its presence. The Beaver Dam Offspring Study, a major epidemiological study published in 2014 in the *American Journal of Ophthalmology*, reported that in a cohort of over 3,000 patients, dry eye disease was self-reported by 14.5% of the patients. The prevalence of dry eye disease increases with age, and we expect that the number of dry eye disease cases will increase as the U.S. population continues to age. Epidemiology and market research commissioned by us indicate that there are an estimated 17.2 million patients with a diagnosis of dry eye disease in the United States. We also commissioned three surveys of 503, 297 and 500 dry eye disease patients, which we refer to as our patient surveys, in 2017, 2018 and 2020, respectively. The patient surveys included a representative set of dry eye patients based on demographics and disease characteristics, such as age, sex and therapeutic history. The patients represented a broad range of dry eye disease severity. Based upon our review of the patient surveys as well as a 2020 independent study of 774 dry eye sufferers, we believe dry eye disease is a burdensome disease that has a significant impact on the quality of life of patients with dry eye disease.

The most commonly used treatments for dry eye disease in the United States are over-the-counter eye drops, often referred to as "artificial tears," and three prescription pharmaceutical products, Restasis®, Cequa™ and Xiidra®. Artificial tears are intended to be palliative in nature to supplement insufficient tear production or improve tear film instability, but do not treat the underlying inflammation in dry eye disease. Restasis and Cequa increase tear production and Xiidra treats the signs and symptoms of dry eye disease, however, Restasis, Cequa and Xiidra are typically used chronically for dry eye patients who have continuous symptoms. As each of Restasis, Cequa and Xiidra have a relatively long onset of action, they are not generally used for the short-term treatment of episodic dry eye flares. We believe there is a larger proportion of dry eye patients whose symptoms are primarily episodic as opposed to chronic, and for whom a chronic therapy is not necessary. For these patients, we believe an FDA-approved, acute, short-term therapy can address a significant unmet need. For example, our patient surveys and the independent study of 774 dry eye suffers indicate that approximately 75% to 90% of surveyed patients experience dry eye flares, with flares lasting on average approximately four days and occurring approximately six times per year. These results are also consistent with a multi-sponsored Gallup Poll survey indicating that dry eye patients suffer on average five to six flares per year lasting on average four days. In addition, according to our patient surveys, the most common reason given by patients for discontinuing the two leading branded dry eye treatments were insufficient efficacy, side effects and product price.

We developed EYSUVIS for the short-term treatment of the signs and symptoms of dry eye disease, utilizing a two-week course of therapy administered four times a day. We believe that EYSUVIS' broad mechanism of action, rapid onset of relief of both signs and symptoms, favorable tolerability profile and potential to be complementary to existing therapies, offers a favorable profile for the management of dry eye flares and other dry eye associated conditions that would benefit from temporary relief of dry eye signs and symptoms. We further believe that these features of EYSUVIS may be attractive to prescribing clinicians and that EYSUVIS could become the preferred first-line prescription therapy for the short-term treatment of the signs and symptoms of dry eye disease, including the treatment of dry eye flares that affect the vast majority of dry eye patients. In our 2020 survey of 201 eye care professionals, or ECPs, nearly all, 99%, reported that their dry eye disease patients experience flares, but many underestimated the actual number of patients with flares. This survey also revealed that interest in prescribing a product with the EYSUVIS profile was high among the surveyed ECPs.

The FDA approved EYSUVIS based on results from four clinical trials, including three Phase 3 clinical trials and one Phase 2 clinical trial, which demonstrated significant improvements in both the signs and symptoms of dry eye disease. Specifically, statistical significance was achieved after two weeks of dosing for the sign endpoint of conjunctival hyperemia in all three Phase 3 clinical trials. Statistical significance was observed in two of the three Phase 3 clinical trials for the symptom endpoints of ocular discomfort severity in both the ITT population and in a predefined subgroup of ITT patients with more severe ocular discomfort at baseline. EYSUVIS was well-tolerated across the four trials, with adverse events and interocular pressure, or IOP, increases comparable to that observed with vehicle.

INVELTYS for Post-Operative Inflammation and Pain

Ocular inflammation and pain are common complications following ocular surgery. According to Marketscope, a third-party provider of market data, in 2019 there were approximately 8.6 million ocular surgeries in the United States. Tissue damage caused by ocular surgery leads to the production of prostaglandins, lipids that aid in recovery at the site of an injury, and an increase in blood flow to the affected area, which contribute to inflammation. The standard of care for post-operative inflammation and pain includes anti-inflammatory drugs such as corticosteroids, which improve patient comfort and accelerate recovery through disruption of the inflammatory cascade.

INVELTYS received FDA approval in August 2018 for the treatment of post-surgical inflammation and pain following all ocular surgery, and was commercially launched in the United States in January 2019. INVELTYS is the first and only post-operative ocular steroid shown effective and FDA approved for twice-a-day, or BID, dosing, has the highest concentration (1%) of LE on the market in the United States and is formulated with our AMPPLIFY technology, which enables INVELTYS to deliver 3.75x more drug to the target ocular tissue compared to an active comparator. We believe INVELTYS offers advantages over existing post-surgical treatment options due to its AMPPLIFY technology and being the first and only topical twice daily dosing, two-week course of treatment and safety data, including low incidence of reported IOP spikes, and efficacy data from our clinical trials.

In each of the two Phase 3 clinical trials of INVELTYS in patients who had undergone cataract surgery, administration of INVELTYS two times a day for 14 days achieved statistical significance for both primary efficacy endpoints of complete resolution of inflammation at day eight maintained through day 15 with no need for rescue medication and complete resolution of pain at day eight maintained through day 15 with no need for rescue medication. In each of these trials, INVELTYS was well tolerated with similar increases in IOP, a common side effect of steroids, compared to placebo and with no treatment-related significant adverse events observed during the course of either trial.

Our Preclinical Development Programs

We are progressing a pipeline of proprietary NCE development programs targeted to address front and back of the eye diseases, including our rTKI program, SEGRM program and STS program.

rTKI Program for Retinal Diseases (KPI-285/KPI-286)

The vascular endothelial growth factor, or VEGF, pathway plays a critical role in the formation of new blood vessels and increased permeability, two pathological processes that contribute to the vision loss associated with certain retinal diseases. These retinal diseases include Wet AMD, which involves either the leakage of existing blood vessels or the proliferation of poorly formed and leaky blood vessels at the back of the eye. These eye diseases can significantly reduce vision and eventually lead to blindness.

We have developed several novel, potent, selective rTKIs, including K0066, which can inhibit the VEGF pathway. We are assessing K0066 in two formulations, topical (KPI-285) and injectable depot (KPI-286) for the treatment of various retinal diseases. In preclinical rabbit studies, topical administration of KPI-285 achieved concentrations in tissues in the back of the eye well above the concentrations required for in vitro inhibition of 50% of the VEGF receptor kinase activity. We are exploring a depot formulation (KPI-286) that could provide extended release of the kinase inhibitor to the back of the eye, which would potentially reduce the need for frequent IVT injections.

SEGRM Program

Activation of the glucocorticoid receptor, or GR, can result in regulation of gene expression along both the transactivation, or TA, and transrepression, or TR, pathways. There is considerable third-party scientific evidence that the TR pathway alone is likely sufficient for anti-inflammatory and immunomodulatory activity. Furthermore, we believe the TA pathway is likely responsible for the adverse effects associated with ocular and systemic administration of corticosteroids, including elevated IOP, hypertension, and osteoporosis.

SEGRMs are a novel class of compounds designed to selectively regulate gene expression through the TR pathway while avoiding the TA pathway. As a result, we believe our SEGRM program has the potential for anti-inflammatory and immunomodulatory activity comparable to corticosteroids without their associated side effects. Our SEGRM program is currently in the lead optimization stage, and we are aiming to identify a development candidate for the program by the end of 2021.

Surface Targeted Steroid Program (KPI-333)

Although corticosteroids are potent inhibitors of ocular surface inflammation, long-term use is limited due to potential significant adverse effects, including elevated IOP and cataract formation. These adverse events are mediated by steroid exposure to the aqueous humor, trabecular meshwork and lens. A topical steroid that targets the ocular surface only could overcome the safety issues associated with long-term use of steroids.

We are developing KPI-333, an NCE, as a topical steroid that targets the ocular surface. In our preclinical animal studies, KPI-333 shows excellent efficacy without raising IOP. Based on this data, we believe KPI-333 may have the potential to address the significant unmet need for an effective chronic treatment of ocular surface inflammation associated with diseases such as dry eye.

Strategy

Our goal is to become a leading biopharmaceutical company focused on the discovery, development and commercialization of innovative therapies primarily for diseases of the front and back of the eye. Key elements of our strategy include:

- ***Successfully launch, and maximize the commercial potential of, EYSUVIS for the short-term treatment of dry eye disease.*** EYSUVIS is the first and only FDA-approved prescription product with an indication for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease. EYSUVIS was approved in October 2020, and we commenced a full promotional launch in January 2021. We estimate that approximately 17.2 million people in the United States have been diagnosed with dry eye disease. We believe that EYSUVIS' broad mechanism of action, rapid onset of relief of both signs and symptoms, favorable tolerability profile and potential to be complementary to existing therapies, offers a favorable profile for the management dry eye associated conditions that would benefit from short-term treatment. We further believe that EYSUVIS could become the preferred first-line prescription therapy for treating dry eye flares, which affect the vast majority of dry eye patients. We plan to commercialize EYSUVIS with our specialty sales force which includes 91 TSMs, 14 RSLs, two ASLs and three DNAs. In 2021, we plan to increase our sales force from 91 TSMs to approximately 125 TSMs, pending the status of the COVID-19 pandemic.

- ***Maximize the commercial potential of INVELTYS for post-operative inflammation and pain***. INVELTYS is the first and only FDA approved ocular corticosteroid product with a twice-a-day dosing regimen for the treatment of post-operative inflammation and pain following ocular surgery. Other approved topical ocular corticosteroid products for this indication are dosed three or four times a day. In January 2019, we began to commercialize INVELTYS in the United States with our own focused, specialty sales force, which promotes both EYSUVIS and INVELTYS.

- ***Advance our pipeline of preclinical development programs.*** We are also progressing our pipeline of proprietary preclinical development programs targeting front and back of the eye diseases. These programs, all of which contain NCEs, include our rTKI compounds that inhibit the VEGF pathway, for the treatment of retinal diseases, including Wet AMD, our SEGRMs, which are a novel class of therapies designed to modify the downstream activity of the receptors to exhibit the anti-inflammatory and immunomodulatory properties without side effects associated with corticosteroids, and our novel surface targeting steroid designed to target the ocular surface and thus have the potential to have fewer side effects compared to traditional topical steroids. We own all intellectual property and worldwide rights to these preclinical development programs. Prior to initiating IND-enabling studies, we may consider potential collaborative partnership opportunities to advance product candidates we develop, including through these programs. We may also evaluate additional opportunities to address significant unmet medical needs by leveraging our proprietary AMPPLIFY technology.

- ***Business development through selective acquisitions and licensing***. We plan to pursue value-driven business development opportunities as they arise in order to enhance our business and product pipeline through strategically acquiring clinical or commercial-ready product candidates or approved revenue-generating products with growth potential, particularly in the ophthalmic area. We will also continue to assess the addition of other specialty therapeutic areas through both product/portfolio acquisitions or other business development activity with a similar focus on opportunities that we anticipate are or will become revenue generating and accretive.

Our AMPPLIFY Technology

Opportunities in Drug Delivery across Eye and other Mucosal Barriers

The body is surrounded by boundary tissues that play the important physiological role of preventing foreign bodies from penetrating into the body. The mucus that coats these tissues, the eyes, lung, cervical/vaginal tract and gastrointestinal tract, for example, serves as a protective barrier to trap and eliminate particulate matter, such as viruses, bacteria and allergens, before these agents can enter the underlying tissues and cause infections or elicit reactions. However, in playing this pivotal role of protection, mucus can also hinder medical treatments by limiting the penetration of medications to mucus-protected tissues, thereby reducing their therapeutic effect.

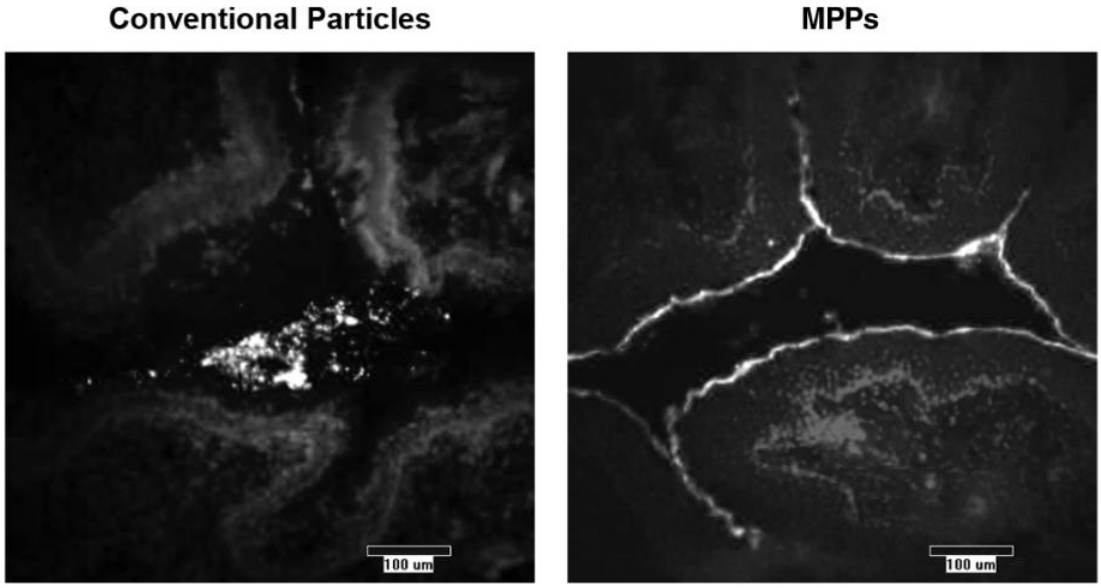
Mucus also makes it difficult to treat many ophthalmic diseases. The body can rapidly eliminate drugs delivered to the eye via the tear film protecting the surface of the eye, which can significantly limit the effectiveness of these drugs. This is the case both for drugs designed to treat conditions in the front of the eye, such as dry eye disease and post-operative inflammation and pain, as well as for drugs designed to treat conditions in the back of the eye, such as retinal diseases. We believe that our proprietary MPP technology, which we refer to as our AMPPLIFY technology, has the potential to address this clear unmet medical need for more efficient delivery of drugs. Our AMPPLIFY technology may have applications to other areas of the body that are protected by mucus, such as the lung, cervical/vaginal tract and gastrointestinal tract. We have demonstrated in preclinical studies that AMPPLIFY technology can be used to increase mucus penetration of over 15 classes of drugs.

MPP Technology

Our MPPs are selectively-sized nanoparticles, with average diameters of approximately 330 nanometers, and have non-covalent proprietary coatings. We believe that these two key attributes enable even distribution of drug particles on mucosal surfaces and significantly increase drug delivery to target tissues by enhancing mobility of drug particles through mucus and preventing drug particles from becoming trapped and eliminated by mucus. We believe this enables enhanced efficacy at equal or lower doses as well as less frequent dosing for improved patient convenience and compliance.

In a preclinical study, MPPs or conventional particles in a hypotonic solution were administered intravaginally to mice. Ten minutes after administration, the vaginal tissues were dissected and stained. The image on the left below shows the distribution of the conventional particles and the image on the right below shows the distribution of the MPPs.

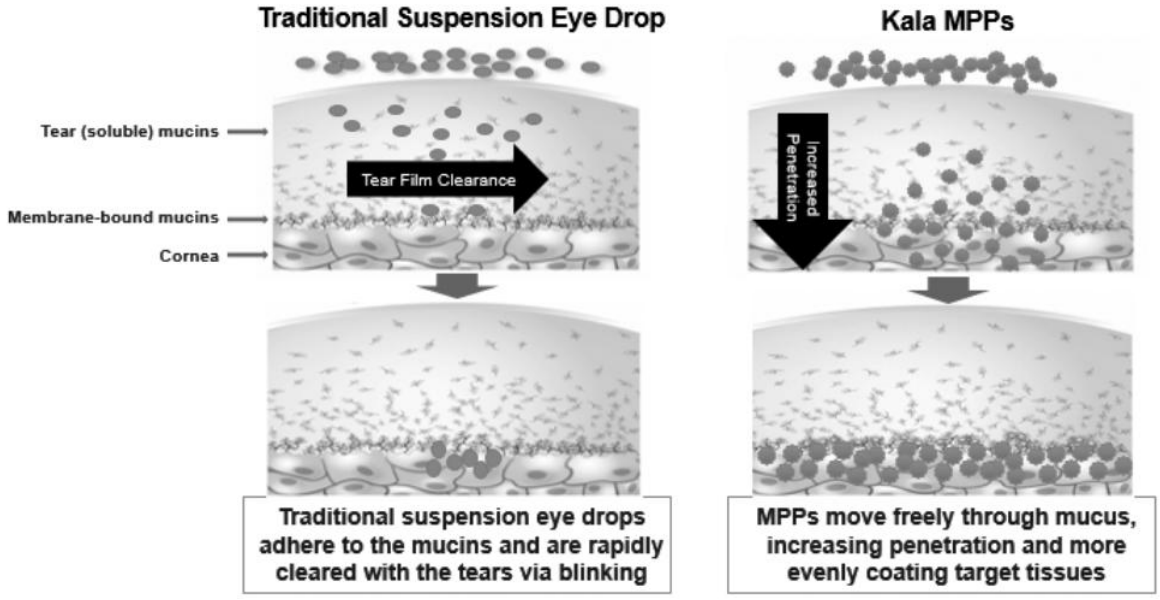
The conventional particles aggregated in the lumenal mucus and did not reach the target tissues. In contrast, the MPPs coated the entire vaginal epithelium, including all the target surfaces.



Source: Laura M. Ensign et al., Mucus-Penetrating Nanoparticles for Vaginal Drug Delivery Protect Against Herpes Simplex Virus, Science Translational Medicine, June 14, 2012.

Also, for ophthalmic applications, while a significant portion of conventionally formulated ophthalmic drugs are rapidly eliminated via the tear film, we have shown that our MPPs are capable of achieving higher concentration on the surface of the eye, thereby enabling the active drug substance to reach cells in the underlying ocular tissue at higher levels.

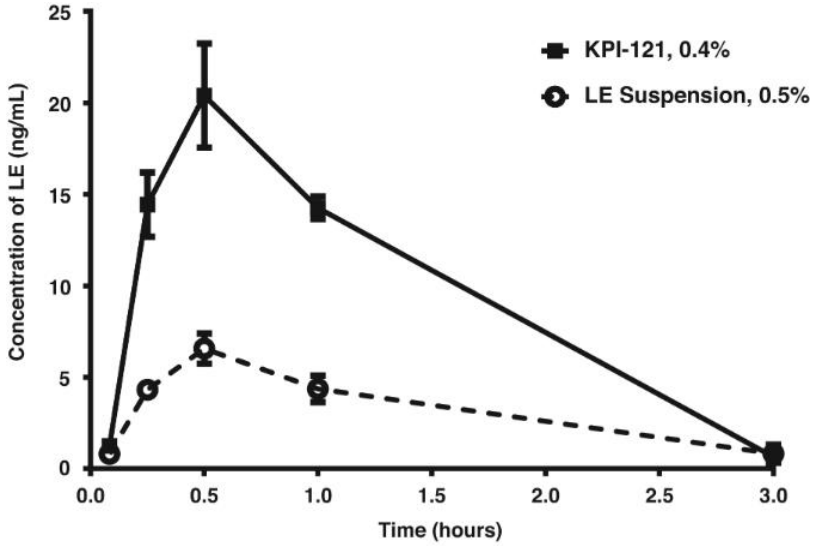
The graphic below illustrates the ability of our MPP drug nanoparticles to penetrate the tear and membrane-bound mucins to reach the ocular surface, as compared to conventional, non-coated particles, which adhere to the mucins in the tear film and are cleared with the tears through blinking.



This graphic is included for illustrative purposes only and is not intended to provide a complete representation of the way in which our MPP drug nanoparticles interact with the ocular surface.

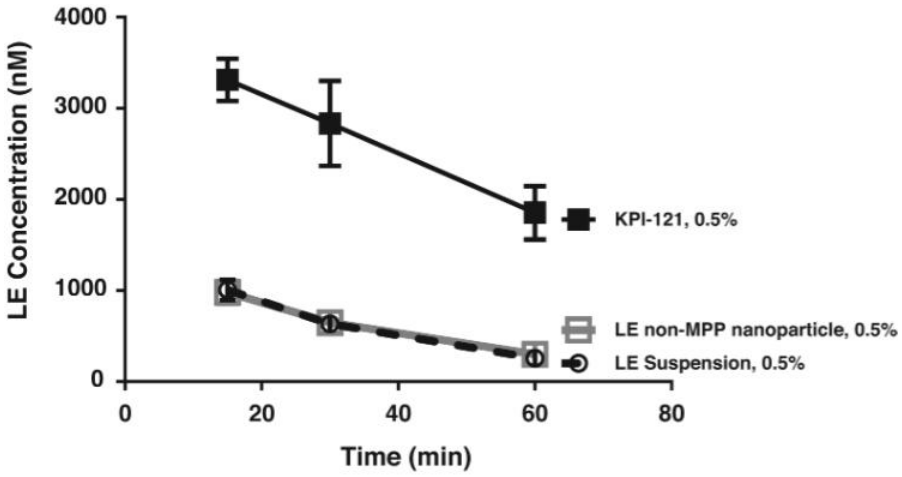
Our primary focus is to leverage our MPP technology, to enhance delivery of drugs into the eye. In preclinical studies, KPI-121 demonstrated favorable pharmacokinetic characteristics and increased drug penetration into ocular tissues as compared to a branded form of LE. In a preclinical study of ocular inflammation in rabbits, KPI-121 0.5% administered four times a day, or QID, showed a larger reduction of inflammation as compared to a branded form of LE 0.5% given QID, as measured by the mean aqueous humor cell counts after intravitreal injection of lipopolysaccharide. We also administered either 0.4% KPI-121 or 0.5% branded LE to the eyes of two groups of rabbits. As illustrated in the line graph below, the concentrations of LE in aqueous humor, a transparent gelatinous fluid that fills the anterior and posterior chambers between the lens and the cornea, of the rabbit eyes treated with KPI-121 were more than three times higher than the rabbit eyes treated with branded LE 30 minutes after dosing, at a 20% lower concentration.

LE in Aqueous Humor



We administered KPI-121 0.5%, LE suspension 0.5%, or 0.5% of an LE non-MPP nanoparticle, to the eyes of three groups of rabbits and measured the amount of LE that was delivered to the cornea. The non-MPP nanoparticle was similar in size to our MPP nanoparticles but lacked the proprietary surface coating used in our MPP nanoparticles. As illustrated in the line graph below, concentrations of LE in the cornea of the rabbit eyes treated with KPI-121 were more than three times higher than the concentrations in rabbits treated with branded LE between 20 and 40 minutes after dosing. In addition, the rabbit eyes treated with the non-MPP nanoparticles had concentrations of LE similar to that in the rabbit eyes treated with branded LE and did not display the improved drug bioavailability properties observed with KPI-121. We believe these results highlight the importance of our proprietary MPP technology and show that KPI-121's improved pharmacokinetic profile has the potential to reduce the dosing strength and/or frequency of administration of LE with KPI-121 as compared to LE suspension 0.5%.

LE in Cornea



We also have demonstrated the potential of our MPP nanoparticles to increase the mucus penetration of over fifteen classes of drugs. While our primary focus is in ophthalmology, in preclinical studies, our MPP technology has been effective in delivering drugs to the lungs, cervical/vaginal tract, gastrointestinal tract and other mucus-protected tissues. We have the ability to vary the rate of drug release as appropriate for the targeted disease state and tissue. As a result, drugs can be delivered either in rapid release formulations or as sustained release formulations that slowly release drug over a time period that ranges from hours to days.

Eye Disease

The human eye is often segmented into two sections—the front and back of the eye. The front of the eye consists of tissues and structures responsible for the protection and maintenance of the eye (including the cornea, conjunctiva and tear film), for providing nutrition to the various tissues of the eye (aqueous humor) and for facilitating the optimal transfer and focusing of light to the retina (including the cornea, iris and lens). Front-of-the-eye diseases include ocular inflammation, dry eye disease, infection, allergy and refractive disorders. Clinicians typically treat diseases that affect the front of the eye with topically applied eye drops. A major limitation of these treatments is that the eye rapidly eliminates topically applied medications via the tear film, limiting the penetration of drugs into the ocular tissue.

The back of the eye contains the retina, which is the light sensing layer of tissue, the choroid, which is a key vascular layer of the eye, the vitreous humor, which is a transparent gel that fills the vitreous chamber between the lens and the retina, and the optic nerve, which transmits visual information from the retina to the brain. Common retinal diseases include AMD, Diabetic Retinopathy, or DR, Diabetic Macular Edema, or DME, and Retinal Vein Occlusion, or RVO. These diseases frequently result in damage to the vasculature of the eye, leading to poor function and/or leaking of existing vessels and often leading to proliferation of new, abnormal and leaky blood vessels in the back of the eye. These conditions can lead to retinal damage, scarring and irreversible loss of vision. The most common treatments for these diseases involve administration of biologic agents that block the VEGF pathway and prevent or retard the blood vessel leakage and/or proliferation. Unfortunately, clinicians must inject these biologic agents directly into the vitreous of the eye via frequent intravitreal injections, or IVTs, to maintain vision. An effective therapeutic to treat retinal diseases with improved dosing regimen would bring significant benefits to patients.

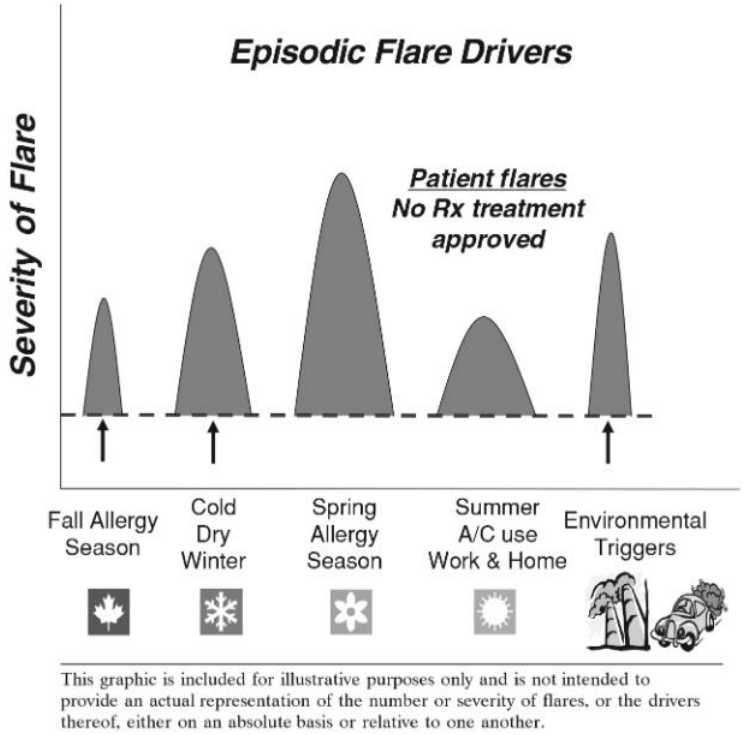
Our Products

EYSUVIS for Dry Eye Disease

Dry Eye Disease Overview

Dry eye disease is a chronic, episodic, multifactorial disease affecting the tears and ocular surface that can result in tear film instability, inflammation, discomfort, visual disturbance and ocular surface damage. While the precise cause of dry eye disease is not fully understood, it often involves impairment of the lacrimal unit, which consists of the lacrimal glands, ocular surface and the sensory and motor nerves that connect them, and has a significant inflammatory component. There is significant published research that suggests that inflammation plays a major role in the development of dry eye disease. Dry eye disease can have a significant impact on quality of life and can potentially cause long-term damage to the ocular surface. Due to the impact of dry eye disease on tear film dynamics, the condition can affect performance of common vision-related activities such as reading, using a computer and driving, and can lead to complications associated with visual impairment. Dry eye disease is commonly treated by ophthalmologists and optometrists.

A significant number of dry eye disease patients experience acute, episodic exacerbations of their symptoms, which we refer to as flares, at various times throughout the year that can cause significant discomfort and disability. A dry eye flare is defined as a rapid onset, inflammation-driven response to a variety of triggers that typically cannot be adequately managed with the patient's ongoing therapy. As illustrated in the graphic below, these flares can be triggered by numerous factors, such as environmental stimuli related to exposure to allergens, pollution, wind and low humidity. Intense visual concentration, such as watching television or working at a computer, can also trigger flares. Other potential triggers include contact lens wear, smoking and sleep deprivation, which cause ocular surface inflammation and impact tear production and/or tear film stability.



This graphic is included for illustrative purposes only and is not intended to provide an actual representation of the number or severity of flares, or the drivers thereof, either on an absolute basis or relative to one another.

We estimate dry eye disease affects approximately 38 million people in the United States. Based on third-party academic research, we believe dry eye disease results in approximately $55 billion in direct and indirect costs in the United States each year, of which approximately $3.8 billion are direct medical costs. The exact prevalence of dry eye disease is unknown due to the difficulty in defining the disease and the lack of a single diagnostic test to confirm its presence. The Beaver Dam Offspring Study, a major epidemiological study published in 2014 in the *American Journal of Ophthalmology*, reported that in a cohort of over 3,000 patients, dry eye disease was self-reported by 14.5% of the patients. The prevalence of dry eye disease increases with age, and we expect that the number of dry eye disease cases will increase as the U.S. population continues to age. Epidemiology and market research commissioned by us indicate that there are an estimated 17.2 million patients with a diagnosis of dry eye disease in the United States. The vast majority of dry eye patients experience acute exacerbations of their symptoms, which are commonly referred to as flares, at various times throughout the year.

The most commonly used treatments for dry eye disease in the United States are over-the-counter eye drops, often referred to as "artificial tears," and three prescription pharmaceutical products, Restasis, Xiidra and Cequa. Artificial tears are palliative in nature and intended to supplement insufficient tear production or improve tear film instability, but do not treat the underlying inflammation in dry eye disease. Restasis and Cequa both increase tear production and Xiidra treats the signs and symptoms of dry eye disease, however, Restasis, Cequa and Xiidra are typically used chronically for dry eye patients who have continuous symptoms. As each of Restasis, Cequa and Xiidra

have a relatively long onset of action, they are not generally used for the short-term treatment of episodic dry eye flares. We believe there is a larger proportion of dry eye patients whose symptoms are primarily episodic as opposed to chronic, and for whom a chronic therapy is not necessary and EYSUVIS, an FDA-approved therapy for short-term use, can address a significant unmet need.

Limitations of Existing Treatments for Dry Eye Disease

Initial treatment for dry eye disease in the United States frequently consists of over-the-counter artificial tear/lubricating eye drops. Most over-the-counter artificial tears are palliative and typically provide only short term or temporary relief by lubricating the eyes and helping to maintain moisture on the outer surface of the eye. These products do not treat the underlying inflammatory components of dry eye disease.

In addition to over-the-counter artificial tears, Restasis, Xiidra and Cequa are sometimes prescribed as a chronic therapy for the treatment of dry eye disease. We believe that less than 15% of patients diagnosed with dry eye disease in the United States use a chronic therapy to treat their disease. Restasis and Cequa are topically applied, ophthalmic formulation of the immuno-suppressant cyclosporine. Restasis and Cequa are not approved for the treatment of the signs and symptoms of dry eye disease, but rather for increasing tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with dry eye disease. Restasis frequently causes burning upon instillation, and, according to the package insert, 17% of patients in clinical trials of Restasis reported ocular burning upon instillation. Cequa frequently causes pain upon instillation, and, according to the package insert, 22% of patients in clinical trials of Cequa reported pain upon instillation of drops. Xiidra is a topically applied ophthalmic formulation of lifitegrast, a small molecule LF1a antagonist, which was approved by the FDA in July 2016 for the treatment of the signs and symptoms of dry eye disease and was commercially launched in the United States in August 2016. Xiidra, like Restasis and Cequa, is typically used chronically. Due to each of Restasis, Cequa and Xiidra having a relatively long onset of action, they are not generally used for the short-term treatment of dry eye flares.

EYSUVIS Opportunity in Dry Eye Disease

We believe that EYSUVIS has a favorable profile for the management of dry eye disease flares, including the following attributes:

- *Broad mechanism of action.* LE is a corticosteroid. Corticosteroids are known for their broad anti-inflammatory properties.

- *Rapid onset of relief.* In our Phase 2 and Phase 3 clinical trials, patients treated with EYSUVIS reported reductions in ocular discomfort within days of initiation of treatment.

- *Favorable safety and tolerability profile.* LE is one of the safest topical ocular steroids available due to its unique pharmacokinetics. LE was designed to be metabolized after exerting its anti-inflammatory action in the eye. The metabolism of LE to inactive metabolites reduces exposure of the trabecular meshwork, an area of tissue located in the anterior chamber that is responsible for draining the aqueous humor from the eye, to active steroid, thus reducing the risk of an increase in IOP relative to other steroids. EYSUVIS was well-tolerated across four clinical trials, with adverse events and IOP increases comparable to that observed with vehicle.

- *Specifically targeting relief of episodic dry eye flares.* The mechanism of action and rapid onset of relief of EYSUVIS in dry eye disease is distinct from that of artificial tears and chronic therapies like Restasis, Cequa and Xiidra. Therefore, we expect it to be used as a stand-alone short course therapy to provide rapid relief of dry eye flares by improving ocular discomfort (a dry eye symptom) and reducing ocular redness (a dry eye sign).

- *Potentially complementary to existing therapies.* We believe that patients on chronic therapies also experience dry eye flares and could potentially benefit from using EYSUVIS in addition to their maintenance therapy.

We believe that these attributes make EYSUVIS attractive to prescribing clinicians for treating patients that suffer from dry eye flares.

EYSUVIS Clinical Development Program

EYSUVIS was evaluated in four clinical trials. In January 2018, we announced topline results from two completed Phase 3 clinical trials, which we refer to as STRIDE 1 and STRIDE 2 (STRIDE - **S**hort **T**erm **R**elief **I**n **D**ry **E**ye), evaluating the safety and efficacy of EYSUVIS versus vehicle (placebo) in patients with dry eye disease. In STRIDE 1, statistical significance was achieved for the primary sign endpoint of conjunctival hyperemia and the primary symptom endpoint of ocular discomfort severity change from baseline to day 15 in the intent to treat, or ITT, population; in addition, statistical significance was also achieved in STRIDE 1 for a second pre-specified primary symptom endpoint of ocular discomfort severity change from baseline to day 15 in patients with more severe baseline ocular discomfort. In STRIDE 2, statistical significance was achieved for the primary sign endpoint of conjunctival hyperemia, but statistical significance was not achieved for the primary symptom endpoint of ocular discomfort severity. EYSUVIS was generally well tolerated in both STRIDE 1 and STRIDE 2, with no clinically significant treatment-related adverse events observed during the course of either trial, and with elevations in interocular pressure, or IOP, in both trials similar to placebo.

In October 2018, we submitted a New Drug Application, or NDA, to the FDA for EYSUVIS. In August 2019, we announced that we received a complete response letter, or CRL, from the FDA regarding this NDA. The FDA indicated that efficacy data from an additional clinical trial would be needed to support a resubmission of the NDA. Based upon the previous recommendation of the FDA, we had initiated an additional Phase 3 clinical trial, STRIDE 3, in the third quarter of 2018. In March 2020, we announced top line results from STRIDE 3, achieving statistical significance the pre-specified primary endpoints of change from baseline to day 15 in ocular discomfort severity in the overall ITT population and in a pre-defined subgroup of patients with more severe baseline ocular discomfort. In addition, statistical significance was achieved for conjunctival hyperemia at day 15. Consistent with prior clinical experience, EYSUVIS was well-tolerated in STRIDE 3, with adverse events and intraocular pressure increases comparable to vehicle.

The positive results from STRIDE 3 for both signs and symptoms of dry eye disease, along with the positive data from the previous clinical trials of EYSUVIS, served as the basis for our NDA resubmission in April 2020. EYSUVIS received FDA approval for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease in October 2020 utilizing a two-week course of therapy administered four times a day. We commenced our full promotional launch of EYSUVIS in January 2021.

EYSUVIS Customer Concentration

Three customers comprised 10% or more of our revenue attributable to EYSUVIS during the year ended December 31, 2020. These customers comprised 35%, 32% and 29% of our revenue attributable to EYSUVIS, respectively. There were no sales of EYSUVIS during the year ended December 31, 2019.

INVELTYS for Post-Operative Inflammation and Pain

Post-Operative Inflammation and Pain Overview

Ocular inflammation and pain are common complications following ocular surgery. According to Marketscope, in 2019 there were approximately 8.6 million ocular surgeries in the United States. Marketscope also projected that there would be approximately 10.1 million ocular surgeries in the United States in 2024. Commonly performed ocular surgeries include cataract, cornea, refractive, oculoplastic and glaucoma procedures. Tissue damage caused by ocular surgery leads to the production of prostaglandins and increases in blood flow to the affected area, which contribute to inflammation. The standard of care for post-operative inflammation and pain includes anti-inflammatory drugs such as corticosteroids, which improve patient comfort and accelerate recovery through disruption of the inflammatory cascade. Commonly used topical ocular corticosteroid products for the treatment of post-operative inflammation and pain are

approved for dosing four times a day. This dosing regimen can be burdensome for patients as they are taking multiple eye drops following surgery, and three or four-times-a-day dosing is believed to reduce patient compliance.

INVELTYS was approved by the FDA on August 22, 2018. INVELTYS is the first and only twice-daily ocular corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

Limitations of Treatments for Post-Operative Inflammation and Pain

LE is a unique steroid that was designed to limit side effects, such as increases in IOP and cataract formation, that are associated with other ocular steroids. The first LE containing product, Lotemax®, was approved by the FDA in 1998. Subsequent gel and ointment formulations of Lotemax were approved by the FDA for the treatment of post-operative inflammation and pain following ocular surgery. Durezol® is a topical steroid approved by the FDA for the treatment of inflammation and pain associated with ocular surgery. Durezol eye drops are dosed four times a day for two weeks followed by dose tapering based on patient response.

The most commonly used ocular steroids, including Lotemax products and Durezol, are approved for the treatment of post-operative inflammation and pain with a three or four-times-a-day dosing regimen. This dosing regimen can be burdensome for patients as they are taking multiple eye drops following surgery, and three or four-times-a-day dosing may reduce patient compliance with the prescribed medication. Other than INVELTYS, there is currently no marketed ocular steroid product with an approved twice-a-day dosing regimen.

INVELTYS Opportunity in Post-Operative Inflammation and Pain

We believe that INVELTYS has a favorable profile for the treatment of post-operative inflammation and pain following ocular surgery, including the following attributes:

- *Twice daily dosing.* INVELTYS is the first and only twice-daily ocular corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery. All other ocular corticosteroid products for the treatment of post-operative inflammation and pain are approved for dosing three or four times a day. Given the generally accepted view that less frequent dosing leads to higher patient compliance, we believe the ability to achieve a significant reduction in inflammation and pain following surgery with a twice-a-day product is a key differentiating attribute of INVELTYS.

- *Favorable safety and tolerability profile.* LE is one of the safest topical ocular steroids available due to its unique pharmacokinetics. LE was designed to be metabolized after exerting its anti-inflammatory action in the eye. The metabolism of LE to inactive metabolites reduces exposure of the trabecular meshwork to the active steroid, thus reducing risk of IOP increase relative to other steroids. In our completed Phase 3 clinical trials, INVELTYS had a tolerability profile comparable to placebo, with no treatment-related serious adverse events observed during the course of either Phase 3 trial.

Our current estimates of potential future revenue from sales of INVELTYS are based, in part, on current prescription trends, anticipated changes in payer coverage, market growth assumptions and physician market research data we have commissioned that examines intent to prescribe. These estimates may be impacted by the current COVID-19 pandemic. The extent of the impact of COVID-19 on our commercialization efforts will depend on the length and severity of this pandemic and the impact on our customers, employees, vendors and government agencies, which is uncertain and cannot be predicted.

INVELTYS Customer Concentration

Three customers comprised 10% or more of our revenue attributable to INVELTYS during the years ended December 31, 2020 and 2019. These customers comprised 40%, 28% and 28% of our revenue, respectively, during the year ended December 31, 2020 and 39%, 33% and 26% of revenue, respectively, during the year ended December 31, 2019.

Preclinical Development Programs

rTKI Program

Retinal Disease

There are a range of retinal diseases and conditions that adversely affect vision.

Age-Related Macular Degeneration (AMD)

AMD is a degeneration of the macula of the retina that leads to impairment and loss of central vision. There are two categories of AMD: "Dry" AMD, which involves slow deterioration of the retina with submacular drusen, atrophy, loss of macular function and central vision impairment; and "Wet" AMD, which involves growth of abnormal blood vessels under the retina and macula, resulting in edema, tissue damage and rapid loss of central vision. If untreated, neovascularization in Wet AMD patients typically results in significant vision loss and the formation of a scar under the macular region of the retina. Most cases begin as Dry AMD, which can progress to Wet AMD. Wet AMD is a leading cause of blindness in people over the age of 55 in the United States and the European Union. The incidence of Wet AMD increases substantially with age, and we expect that the number of cases of Wet AMD will increase with growth of the elderly population in the United States.

The current standard of care for Wet AMD is intravitreal injection of drugs that target VEGF, one of the key proteins involved in neovascularization.

Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME)

DR is an ocular complication of diabetes involving changes of retinal blood vessels that lead to significant visual impairment. These changes include dysfunction of retinal vasculature (nonproliferative retinopathy), with vascular occlusion and increased permeability, leading to retinal hypoxia and DME. The disease can further progress to proliferative retinopathy with retinal neovascularization, hemorrhage and retinal detachment.

Among an estimated 19.8 million adults in the United States aged forty years and older known to have diabetes, the prevalence rate for DME is 3.8%, or approximately 746,000 people. DME is the leading cause of visual impairment and blindness in Americans between 20 and 74 years old.

Retinal Vein Occlusion (RVO)

RVO is a blockage of the small veins that carry blood away from the retina. The disease can cause sudden blurring or vision loss in all or part of one eye. RVO has been estimated to affect 16 million people worldwide.

Limitations of Existing Treatments for Retinal Disease

VEGF is a protein that plays a critical role in the formation of new blood vessels and increased permeability, two pathological processes that contribute to the vision loss associated with certain retinal diseases. Several tyrosine kinase inhibitors have been investigated in AMD patients in clinical trials. These inhibitors have been administered in a variety of ways, including intravitreal injection, oral administration and topical dosing. To date, no tyrosine kinase inhibitors have been approved in the United States for the treatment of ocular diseases. We believe that there is a substantial market opportunity for a safe and effective VEGF tyrosine kinase inhibitors to treat various retinal diseases, such as AMD, DR, DME, RVO and related neovascular diseases.

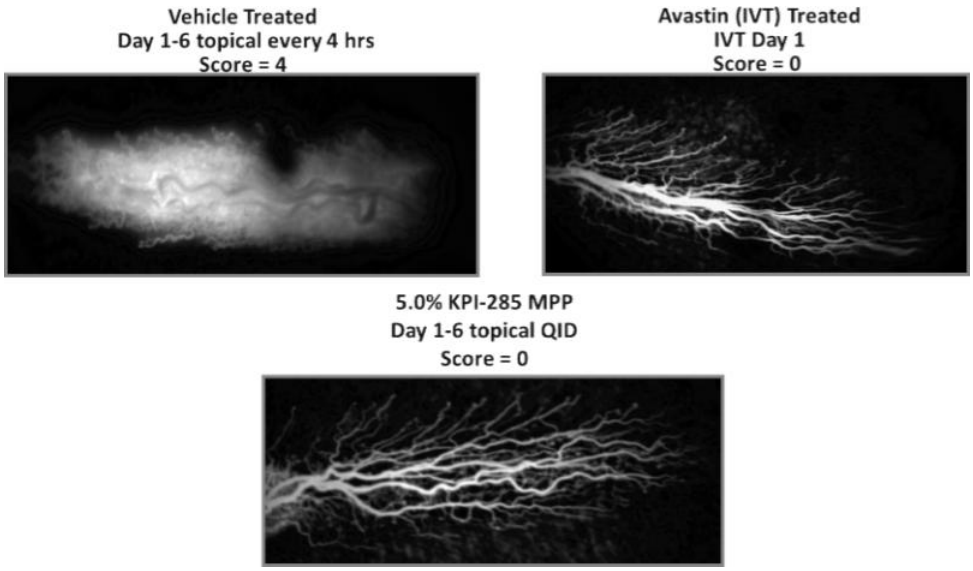
The most common treatments for retinal diseases involve administration of biologic agents that block the VEGF pathway and prevent or retard the blood vessel leakage and/or proliferation. Unfortunately, clinicians must inject these biologic agents directly into the eye via frequent IVTs to maintain vision. Sales of the two leading IVT biologic agents used to treat eye diseases associated with abnormal blood vessel proliferation, Genentech's Lucentis® and Regeneron's Eylea®, were $1.7 billion and $4.1 billion, respectively, in the United States in 2018. A new biologic form of Novartis'

Beovu® was approved in October 2019. An effective therapeutic to treat retinal diseases with improved dosing regimen would bring significant benefits to patients.

rTKI Program for the Potential Treatment of Wet AMD, DR, DME and RVO

Through our rTKI program we have developed several novel, potent, selective rTKIs, including K0066, which can inhibit the VEGF pathway. In vitro assays show that K0066 has a sub-nanomolar potency against the VEGF receptor-2 kinase and good selectivity against other growth factor receptor kinases, cell cycle kinases and other off-target receptors. We are assessing K0066 in two formulations, topical (KPI-285) and injectable depot (KPI-286)-for the treatment of various retinal diseases.

In preclinical rabbit studies, topical administration of KPI-285 achieved concentrations in tissues in the back of the eye well above the concentrations required for *in vitro* inhibition of 50% of the VEGF-2 receptor kinase activity. In addition, in a rabbit model of VEGF induced vascular leakage, topically applied KPI-285 reduced leakage to an extent similar to that achieved with an IVT injection of Genentech's Avastin®, a recombinant human monoclonal antibody that binds to VEGF. In this model, vascular leakage of fluorescein was induced by IVT injections of VEGF. The extent of fluorescein leakage observed in various treatment groups was scored in a blinded fashion on a scale from 0 to 4, with 0 being no leakage and 4 being heavy leakage. As shown in the photographs below, the magnitude of the effect achieved with topical administration of KPI-285 5.0% was similar to that observed with IVT injection of Avastin.



We believe that an effective therapy with an improved delivery for patients with retinal diseases such as AMD, DR, DME and RVO will be a significant advancement in the treatment of these diseases and could increase patient compliance and reduce treatment burden in patients suffering from these sight threatening diseases.

SEGRM Program

Activation of the glucocorticoid receptor can result in regulation of gene expression along both the transactivation, or TA, and transrepression, or TR, pathways. There is considerable third-party scientific evidence that the TR pathway alone may be sufficient for anti-inflammatory and immunomodulatory activity. Furthermore, we believe the TA pathway is likely responsible for the adverse effects associated with ocular and systemic administration of corticosteroids, including elevated IOP, hypertension, and osteoporosis.

SEGRMs are a novel class of compounds designed to selectively regulate gene expression through the TR pathway while avoiding the TA pathway. As a result, we believe our SEGRM program has the potential for anti-inflammatory activity comparable to corticosteroids without their associated side effects. Our SEGRM program is currently in the lead optimization stage, and we are aiming to identify a development candidate for the program by the end of 2021.

Surface Targeted Steroid Program (KPI-333)

Although corticosteroids are potent inhibitors of ocular surface inflammation, long-term use is limited due to potential significant adverse effects, including elevated IOP and cataract formation. These adverse events are mediated by steroid exposure to the aqueous humor, trabecular meshwork and lens. A topical steroid that targets the ocular surface only could overcome the safety issues associated with long-term use of steroids.

We are developing KPI-333, an NCE, as a topical steroid that targets the ocular surface. In our preclinical animal studies, KPI-333 shows excellent efficacy without raising IOP. Based on this data, we believe KPI-333 may have the potential to address the significant unmet need for an effective chronic treatment of ocular surface inflammation associated with diseases such as dry eye.

Potential Applications of AMPPLIFY Technology in Other Diseases

Mucus limits delivery of conventionally formulated drugs to mucosal tissues such as the lung, cervical/vaginal and gastrointestinal tract. While our primary focus is in ophthalmology, our AMPPLIFY technology has been effective in preclinical studies in enhancing drug delivery to these other tissues. We also have demonstrated in preclinical studies that AMPPLIFY technology can be used to increase mucus penetration of over fifteen classes of drugs.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Our products compete, and any product candidates that we successfully develop and commercialize will compete, with existing therapies and new therapies that may become available in the future.

Our competitors include large pharmaceutical and biotechnology companies, and specialty pharmaceutical and generic drug companies. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of EYSUVIS, INVELTYS and any product candidates that we develop are the product or product candidate’s efficacy, safety, method of administration, convenience, price, the

level of generic competition and the availability of insurance coverage and reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than our products. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. In addition, our ability to compete may be affected because in many cases insurers or other third-party payors seek to encourage the use of generic products.

Competition in Dry Eye Disease

The current disease management approaches for dry eye disease in the United States includes non-pharmaceutical therapies and pharmaceutical therapies. Non-pharmaceutical therapies include over the counter artificial tear eye drops, which are palliative and used on an intermittent or chronic basis to provide short-term symptomatic relief of dryness and irritation; hot compresses for the eye and lid hygiene management; devices, such as punctal plugs that are inserted into the tear ducts to inhibit tear drainage, resulting in more moisture on the surface of the eye.

Pharmaceutical therapies for dry eye disease include on label prescription drugs, including Restasis®, Xiidra®, and Cequa™, which are the only prescription pharmaceutical products other than EYSUVIS that are approved in the United States for use in patients with dry eye disease; off label prescription drugs, including topical steroid drops and/or other similar products, which are sometimes prescribed for treatment of dry eye disease; and various drugs that are produced by compounding pharmacies. Generic versions of Restasis are expected to become available in the United States in the near future. Restasis and Cequa are both topical cyclosporine formulations that are approved for increasing tear production in patients whose tear production is presumed to be suppressed due to ocular keratoconjunctivitis sicca. Xiidra is a topical anti-inflammatory therapy approved for treatment of the signs and symptoms of dry eye disease.

EYSUVIS is indicated for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease, which includes dry eye flares. Any product that is developed for the treatment of the signs and/or symptoms of dry eye disease could directly compete with EYSUVIS. There are several product candidates in preclinical and clinical development in the United States for the treatment of dry eye disease. These product candidates are being developed by pharmaceutical, biotechnology, specialty pharmaceutical and generic drug companies of various sizes, such as Oyster Point Pharma's OC-01 nasal spray, for which an NDA was submitted in December 2020 and, if approved, could be launched as early as late 2021, Aldeyra Therapeutics' reproxalap ophthalmic solution, Novaliq's CyclAsol and NOV03, which has been licensed to Bausch Health Companies Inc. and others.

Based on publicly available information, we have identified various other product candidates in clinical development for the chronic treatment of dry eye disease in the United States. If any of these product candidates is approved and such product candidate either effectively treats the signs and symptoms of dry eye disease or reduces the frequency of flares in dry eye patients, it could reduce patient demand for EYSUVIS.

Competition in Inflammation and Pain Following Ocular Surgery

Following ocular surgery, topical steroids are commonly prescribed to manage and prevent complications from post-operative inflammation. Topical steroid drops are the main competition to INVELTYS for the treatment of inflammation and pain following ocular surgery. The current branded market leaders for topical steroids in the United States, based on revenue, are Lotemax® products and Durezol®. Generic topical steroid formulations consist mainly of products containing prednisolone, fluorometholone or dexamethasone. In addition, the first generic formulation of loteprednol suspension 0.5% (Lotemax suspension) was launched in May 2019 and Durezol lost its patent exclusivity in 2019, which could result in a potential generic launch of this product in the near future.

There are also non-topical formulations of ocular steroids that have been approved and/or marketed. Eyepoint Pharmaceutical launched Dexycu®, an intraocular suspension of dexamethasone for the treatment of post-operative inflammation, in July 2019. Also in July 2019, Ocular Therapeutix launched Dextenza®, an intracanalicular insert of dexamethasone, for the treatment of ocular pain and inflammation following ophthalmic surgery. There are also a

number of companies in the United States developing products and therapies in preclinical research and clinical development for the treatment of inflammation and pain following ocular surgery. In addition, there are various formulations of steroids that are produced by compounding pharmacies and that are in drop form or are injected into the eye following ocular surgery.

Competition in Retinal Disease

Several therapies have been developed to block the effects of VEGF by binding to and sequestering the protein. These include Regeneron Pharmaceuticals, Inc.'s Eylea, Genentech, Inc.'s Lucentis and Avastin, and Novatis' Beovu. Avastin is approved as an anti-cancer agent, but is widely used off-label in ophthalmic diseases. All of these therapies are administered by intravitreal injections and must be regularly dosed for optimal efficacy.

In addition to the anti-VEGF therapies, there also are marketed drug delivery systems, or DDS, that are used to treat retinal diseases, notably: Ozurdex®, which releases dexamethasone, a corticosteroid, and is marketed by Allergan; Iluvien®, which releases fluocinolone acetonide, a corticosteroid, and is marketed by Alimera Sciences; and Yutiq™, which releases fluocinolone acetonide, a corticosteroid, and is marketed by Eyepoint.

There are several wet-AMD product candidates in clinical development, including those being developed by F. Hoffmann-La Roche AG, Kodiak Sciences, GrayBug, and Ocular Therapeutix. There are also a number of preclinical research and clinical development programs being conducted by third parties to develop treatments for retinal diseases. We expect that product candidates currently in clinical development, or that could enter clinical development in the near future, may represent significant competition if approved. These product candidates may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies.

Competition in Ocular Surface Disease

Ocular surface conditions, which include dry eye disease, are currently treated with a variety of therapies, including branded and generic corticosteroids and non-steroidal anti-inflammatory drugs. We are developing KPI-333 as alternative to such therapies for the chronic treatment of ocular surface conditions. Corticosteroids are frequently used for the treatment of anterior segment conditions, including dry eye disease and for the treatment of post-surgical inflammation. Corticosteroids are also frequently used for the treatment of wet-AMD and diabetic eye disease as second line to the anti-VEGF therapies. We are developing our SEGRM program to be an alternative to topical and injected corticosteroids for the treatment of a variety of ocular conditions.

Sales and Marketing

In January 2019, we began commercializing INVELTYS in the United States with our own focused, specialty sales force of 57 TSMs, seven RSLs, and three DNAs. During the fourth quarter of 2020, we expanded our sales force to include 91 TSMs, 14 RSLs, and two ASLs. In 2021, we plan to further increase our sales force from 91 TSMs to approximately 125 TSMs, pending the status of the COVID-19 pandemic. Our sales force promotes EYSUVIS and INVELTYS. We believe our sales team is one of the most experienced in our specialty with our RSLs having an average of 9.1 years ophthalmic experience and 5.4 years sales leadership experience and our 91 TSMs having an average of 7.9 years ophthalmic experience and 14.2 years pharmaceutical sales experience as of December 31, 2020.

We expect to explore commercialization of EYSUVIS and potentially other product candidates in certain markets outside the United States, including the EU, utilizing a variety of collaboration, distribution and other marketing arrangements with one or more third parties.

Manufacturing

We utilize our substantial in-house expertise and know-how to develop and scale up our manufacturing processes before these processes are transferred to third-party contract manufacturers, and to understand and establish controls of critical process parameters. We also have personnel with deep product development experience who actively

manage the third-party contract manufacturers producing EYSUVIS and INVELTYS and plan to use such personnel to manage third-party contract manufacturers for any products that we may develop in the future.

EYSUVIS and INVELTYS are currently manufactured at qualified contract manufacturing facilities in compliance with current good manufacturing practice, or cGMP, regulations. Our third-party manufacturers are subject to FDA inspections from time to time.

We have supply agreements in place with these contract manufacturers to support commercial, clinical and registration manufacturing, release testing, registration stability, and labeling and packaging. We also have entered into long term commercial supply agreements with these contract manufacturers to supply drug substance for EYSUVIS and INVELTYS.

Catalent Commercial Supply Agreement. In June 2016, we entered into a Commercial Supply Agreement, or the Catalent Agreement, which we amended in February 2018, March 2020 and December 2020, with Catalent Pharma Solutions, LLC, or Catalent, pursuant to which Catalent has agreed to manufacture and supply to us, and we have agreed to purchase from Catalent, a combined minimum amount of EYSUVIS and INVELTYS for commercial use. The Catalent Agreement had an initial term of eight years from August 22, 2018, which is the date INVELTYS was approved for commercial sale in the United States. Pursuant to the March 2020 amendment, the initial term was extended through June 30, 2030. The Catalent Agreement is subject to three-year automatic renewal periods after the initial term, absent termination by either party in accordance with the terms of the Catalent Agreement. The Catalent Agreement provides for pricing structured on a tiered basis, with the price reduced as the volume of products ordered increases. Prior to the March 2020 amendment, we had annual minimum purchase requirements for each of EYSUVIS and INVELTYS. However, pursuant to the March 2020 amendment, the annual minimum purchase requirements are now determined on an aggregate basis for the two products. We may cancel any purchase order under the Catalent Agreement, subject to our minimum purchase obligations. Each party has the right to terminate the Catalent Agreement for customary reasons such as material breach and bankruptcy. The Catalent Agreement contains provisions relating to compliance by Catalent with cGMP, indemnification, confidentiality, dispute resolution and other customary matters for an agreement of this kind.

Altasciences Commercial Supply Agreement. In October 2017, we entered into an Amended and Restated Master Services Agreement, or the Altasciences Agreement, with Alliance Contract Pharma, LLC, which was assigned to Altasciences company, or Altasciences, pursuant to which Altasciences has agreed to provide to us, and we have agreed to purchase from Altasciences, bulk intermediates. The Altasciences Agreement provides for pricing structured on a tiered basis, with the price reduced as the volume of product ordered increases. Under the Altasciences Agreement, we will provide a forecast of orders for the quantities we believe we will require, and forecasted quantities will become binding at a certain point before the firm delivery date set forth in the forecast. Unless earlier terminated pursuant to its terms, the Altasciences Agreement has an initial term of ten years, after which it continues until terminated. Each party has the right to terminate the Altasciences Agreement for customary reasons such as material breach and bankruptcy. In addition, we have the right to terminate the Altasciences Agreement at any time for any or no reason upon sufficient advance notice, in which case we would owe payment to Altasciences for any firm orders and certain raw materials. The Altasciences Agreement contains provisions relating to compliance by Altasciences with cGMP, indemnification, confidentiality, dispute resolution and other customary matters for an agreement of this kind.

Chemo Iberica Manufacturing and Supply Agreement. In January 2017, we entered into a Manufacturing and Supply Agreement, or the Chemo Agreement, with Chemo Iberica SA, or Chemo, pursuant to which Chemo has agreed to manufacture and supply to us, and we have agreed to purchase from Chemo, bulk supply of lotepredno l, with pricing structured on a per-kilogram basis. Under the Chemo Agreement, we will provide a forecast of orders for the quantities of lotepredno l we believe we will require, and we commit to purchasing 75% of the forecasted quantities. We can alter portions of a forecast at any time, except that, without Chemo's consent, we cannot alter a portion of the forecast less than ninety days before the period to which such portion pertains. Unless earlier terminated pursuant to its terms, the Chemo Agreement has an initial term of seven years, after which it renews in two year increments unless either party gives notice of non-renewal at least one year in advance. Each party has the right to terminate the Chemo Agreement for customary reasons such as material breach and bankruptcy. The Chemo Agreement contains provisions relating to compliance by Chemo with cGMP, indemnification, confidentiality, dispute resolution and other customary matters for an agreement of this kind.

Intellectual Property

Our success depends significantly on our ability to obtain and maintain proprietary protection for our products, product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We seek to protect our proprietary position by, among other methods, filing U.S. and certain foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business, where patent protection is available. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

As of February 1, 2021, we owned 39 U.S. issued patents and 14 U.S. patent applications, as well as 50 foreign issued patents and 97 foreign patent applications (including Patent Cooperation Treaty, or PCT, applications). We exclusively licensed a total of 32 U.S. issued patents and 16 U.S. patent applications, as well as 42 foreign issued patents and 27 foreign patent applications including original filings, continuations and divisional applications. Our patent portfolio includes the following patents and patent applications that we own or exclusively license:

- 13 U.S. patents and six U.S. patent applications, relating to our MPP technology, which we refer to as our AMPPLIFY technology, including those related to EYSUVIS and INVELTYS, in-licensed from The Johns Hopkins University, or JHU, four related foreign patents jointly owned by us and JHU, seven related foreign patent applications jointly owned by us and JHU, 13 related foreign patents owned by us and 28 related foreign patent applications owned by us, which, if granted with respect to the patent applications, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in 2033;

- one U.S. patent and one U.S. patent application relating to our AMPPLIFY technology, and four related foreign patents and seven related foreign patent applications, which are owned by us, and which, if granted with respect to the patent applications, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in 2033;

- 35 U.S. patents and 10 U.S. patent applications, relating to rTKI compounds, including K0066, and their uses, and 24 related foreign patents, and 53 foreign related patent applications, including pending PCT applications, which are owned by us, and which, if granted with respect to the patent applications, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, which are expected to expire beginning in 2034 through 2038;

- two U.S. patents and one U.S. patent application, relating to antibiotic compounds and their uses, and three related foreign patents and two related foreign patent applications, which are owned by us, and which, if granted with respect to the patent applications, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in 2034;

- eight U.S. patents and five U.S. patent applications, relating to methods for treating an eye disease or disorder by injecting or instilling a drug delivery system, and 15 related foreign patents, and 22 related foreign patent applications, which are exclusively sub-licensed from GrayBug Vision, Inc., and which, if granted with respect to the patent applications, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire beginning in 2031 through 2035; and

- 11 U.S. patents and five U.S. patent applications, related to our AMPPLIFY technology, and 27 related foreign patents and five related foreign patent applications, which are exclusively in-licensed from JHU, and which, if granted with respect to the patent applications, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire beginning in 2025 through 2036.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may, in

certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date of a U.S. patent as partial compensation for the length of time the drug is under regulatory review while the patent is in force. A patent term 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 extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. We cannot provide any assurance that any patent term extension with respect to any U.S. patent will be obtained and, if obtained, the duration of such extension.

Similar provisions are available in the European Union and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, if permitted under the applicable laws, regulations, and rules and depending upon the length of the clinical trials for each drug and other factors. The expiration dates referred to above are without regard to potential patent term extension or other market exclusivity that may be available to us. However, we cannot provide any assurances that any such patent term extension of any patent will be obtained and, if obtained, the duration of such extension.

Trade Secrets

In addition to patents, we may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, and obtain and maintain ownership of certain technologies, in part, by confidentiality and invention assignment agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

License Agreements

The Johns Hopkins University

In November 2009, we entered into an exclusive license agreement with JHU, which was amended in November 2012, May 2014, August 2014, June 2018 and July 2020 and amended in part in October 2014 by the JHU settlement agreement described below. We refer to the amended license agreement with JHU as the JHU license agreement. Pursuant to the JHU license agreement, JHU granted us an exclusive, worldwide, sublicensable license under specified patent rights covering various aspects of MPP technology, to research, develop, make, use and sell products and provide services in any field. JHU also granted us a non-exclusive license to use specified know-how with limits on JHU's right to license the know-how to other commercial entities.

Financial Terms

In connection with the JHU license agreement, we paid JHU an upfront license fee in the low tens of thousands of dollars and issued to JHU a low single digit percentage of our common stock. We also reimbursed JHU for the prosecution and maintenance costs incurred by JHU for the licensed patent rights prior to our entering into the JHU license agreement, and we are responsible for all of the ongoing costs relating to the prosecution and maintenance of the JHU patent rights licensed to us. We paid JHU fees in the low tens of thousands of dollars upon entering into certain of the amendments to the JHU license agreement.

In connection with the JHU license agreement and the JHU settlement agreement described below, we are obligated to make certain future payments to JHU. We paid JHU $112,500 in minimum annual royalty and running fees in the aggregate in 2020. We are obligated to pay JHU annual minimum royalties that will not exceed approximately $112,500 per year in the future. In addition, we must pay JHU a tiered royalty rate in the low single-digits on annual net sales by us or our affiliates of products or services covered by a valid issued claim, or certain pending claims, of a

licensed JHU patent right in the country of sale, from which we may, under specified circumstances, offset portions of amounts we must pay as royalties on other patent rights in order to commercialize a licensed product or licensed service up to a maximum reduction of a mid-double digit percentage. We must also pay a percentage, in the high single digits, of certain consideration we or our affiliates receive from sublicensing rights under the licensed JHU intellectual property, subject to specified offsets and deductions. We may offset against each minimum annual payment the royalties and sublicense income that we pay to JHU in the preceding twelve-month period. We are obligated to pay JHU milestone fees not to exceed $750,000 in connection with the commercial sales of EYSUVIS in the U.S., and certain ex-US countries in the aggregate, if certain development and commercial events are achieved. We also are obligated to pay to JHU certain remaining milestone payments for the development of a third and fourth product under the JHU license agreement, which will not exceed approximately $1.7 million in the aggregate, if certain development and commercial events are achieved. The JHU patent rights sublicensed to us by GrayBug under the JHU settlement agreement described below are considered in the same way as the JHU patent rights directly licensed to us by JHU for purposes of determining these payments.

Diligence Obligations

We are required to use commercially reasonable efforts to develop and introduce the licensed products and licensed services to the market, including developing licensed products suitable for different indications, consistent with sound and reasonable business practice and judgment, and, after introducing a licensed product or licensed service into the market, we must endeavor to keep licensed products and licensed services reasonably available to the public consistent with sound and reasonable business practice and judgment.

Term and Termination

The JHU license agreement will expire on a country-by-country basis upon the expiration of the last to expire licensed patent in such country or, if no licensed patent issues in such country, then in November 2029. Either we or JHU may terminate the JHU license agreement for the other party's breach that is not cured within specified time periods or if the other party is subject to certain bankruptcy protections. In addition, we may terminate the JHU license agreement, for any reason, upon 90 days' prior written notice to JHU.

Assignment and Exclusive License

In April 2017 we assigned to JHU certain Kala-owned patent applications and our interest in certain patents and patent applications formerly co-owned by JHU and Kala, unifying ownership of the assigned patent rights in JHU's name. As part of the assignment of these patent rights to JHU, Kala was granted an exclusive, non-royalty bearing, sub-licensable license from JHU under all of the patent rights Kala assigned in this transaction, which will expire upon the expiration of the last to expire licensed patent under the new license. No fees were paid to JHU for this exclusive license.

GrayBug Vision, Inc. and The Johns Hopkins University

A dispute arose between us, JHU, and GrayBug Vision, Inc. (formerly known as GrayBug, LLC and GrayBug, Inc.), or GrayBug, over rights licensed to us and GrayBug under certain patent rights owned by JHU. In October 2014, we, GrayBug, and JHU resolved this matter by entering into a Settlement and License Agreement, which was amended in January 2015, which we refer to as the JHU settlement agreement.

Under the JHU settlement agreement, GrayBug granted us, under specified patent rights that are exclusively licensed to GrayBug by JHU in all fields, an exclusive, worldwide royalty-free sublicense in the field of use of a particle with specified characteristics for delivery of a biologically active material through mucus, mucin, or a mucosal barrier where such delivery does not involve administration via injection to the eye, which we refer to as the Kala sublicense field. In December 2017 and April 2019, GrayBug terminated its exclusive license from JHU as to two patent families among these patent rights. Pursuant to the JHU settlement agreement, these patent rights were to be automatically directly licensed to us under the terms of the JHU license agreement unless we specifically declined to accept such automatic direct license. While we did not accept the automatic direct license to one of the patent families as it does not

directly relate to EYSUVIS, INVELTYS or any other potential drug candidates, we accepted the automatic direct license to the other patent family and are now responsible for all future patent prosecution costs for these patent rights.

In turn, pursuant to the JHU settlement agreement we granted GrayBug, under specified patent rights that are exclusively licensed to us by JHU in all fields, an exclusive, worldwide royalty-free sublicense in the field of use of a particle with specified characteristics for delivery of a biologically active material to the eye via injection, excluding any particle comprising or consisting of loteprednol etabonate, which we refer to as the GrayBug sublicense field.

In addition, JHU granted us, under the terms of the JHU license agreement, an exclusive, sublicensable, worldwide license under certain additional specified patent rights relating to further aspects of MPP technology in the Kala sublicense field. JHU also granted to GrayBug a similar license under these same patent rights in the GrayBug sublicense field. In January 2017, GrayBug terminated its license under all but one patent family in these additional specified patent rights, and in July 2017, GrayBug terminated its license under the remaining patent family. As a result, for those patent rights terminated by GrayBug, we are now licensed in both the Kala sublicense field and the GrayBug sublicense field. JHU also granted us certain rights to obtain a non-exclusive license to certain additional patent rights and, if we obtain such a license, we would have the exclusive right to negotiate for a specified time period an exclusive license under such patent rights in the Kala sublicense field. Under the JHU settlement agreement, we agreed not to exercise our rights under the JHU patent rights licensed or sublicensed to us to use a particular active ingredient. Each party to the JHU settlement agreement may sublicense the rights granted to it pursuant to the JHU settlement agreement, subject to notice requirements and the requirement that any such sublicense must involve some aspect of collaboration, joint research, development, manufacture, partnership or the like. In any event, sublicenses beyond a specified number of tiers are not permitted without the original licensing party's written consent.

We, GrayBug and JHU each released the others, and certain persons affiliated with them, from any claims and losses known to the releasing party as of the effective date of the JHU settlement agreement in connection with the dispute that led to the JHU settlement agreement.

Financial Terms

The JHU settlement agreement also amended certain of our financial obligations under the JHU license agreement, which we have reflected in the description above. Neither we nor GrayBug owe the other any royalties, milestone payments or other payments with respect to the sublicenses and other rights granted to each other. In addition, JHU agreed that we are not responsible for paying to JHU any sublicense fees or other payments due under our JHU license agreement that may otherwise have arisen as a result of our granting GrayBug the sublicenses under the JHU settlement agreement.

For the specified patent rights directly licensed to us by JHU in the Kala sublicense field under the JHU settlement agreement, we reimbursed JHU for a portion of the patent prosecution and maintenance costs incurred prior to entering the JHU settlement agreement, and we are responsible for all of the ongoing prosecution and maintenance costs of any of these JHU patent rights for which there is no other direct licensee of JHU, such as the JHU patent rights licensed to us in both the Kala sublicense field and the GrayBug sublicense field.

Term and Termination

The JHU settlement agreement will expire upon the expiration of all the patent rights that are the subject of the JHU settlement agreement. We may terminate one or more of the licenses or sublicenses granted to us in the JHU settlement agreement on a country-by-country basis for convenience upon 30 days' prior written notice to GrayBug. We or GrayBug may terminate one or more the sublicenses granted to the other party under the JHU patent rights if the other party, or its employees, officers, directors, agents or representatives, takes certain steps to oppose, attempt to invalidate or prevent the issuance of any of the patent rights directly licensed to the terminating party by JHU.

Government Regulation and Product Approvals

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, pricing, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of biopharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Approval and Regulation of Drugs in the United States

In the United States, drug products are regulated under the U.S. Federal Food, Drug and Cosmetics Act, or the FDCA, and applicable implementing regulations and guidance. The failure of an applicant to comply with the applicable regulatory requirements at any time during the product development process, including non-clinical testing, clinical testing, the approval process or post-approval process, may result in delays to the conduct of a study, regulatory review and approval and/or administrative or judicial sanctions.

An applicant seeking approval to market and distribute a new drug in the United States generally must satisfactorily complete each of the following steps before the product candidate will be approved by the FDA:

- preclinical testing including laboratory tests, animal studies and formulation studies, which must be performed in accordance with the FDA's good laboratory practice, or GLP, regulations and standards;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency and purity of the product candidate for each proposed indication, in accordance with current good clinical practices, or GCP;
- preparation and submission to the FDA of an NDA for a drug product which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labelling for one or more proposed indication(s);
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities, including those of third parties, at which the product candidate or components thereof are manufactured 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 any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCP and the integrity of clinical data in support of the NDA;
- payment of user fees and securing FDA approval of the NDA to allow marketing of the new drug product; and

- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct any post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, must be submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

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 and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. 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 product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee, or DSMB. This group provides recommendations as to whether or not a trial may 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.

Information about clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator 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 clinical trial 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.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after approval.

Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or in patients. During Phase 1 clinical trials, information about the investigational drug product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.

Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are well controlled, closely monitored and conducted in a limited patient population.

Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 clinical trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a drug: such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to further document a clinical benefit in the case of drugs approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Progress reports detailing the status and a brief description of available results of the clinical trials must be submitted at least annually to the FDA 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 product; 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 completed at all. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

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

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, an application or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the 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. 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 Food and Drug Administration Safety and Innovation Act, or FDASIA. The FDA maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. Congress amended the FDA Reauthorization Act of 2017, or FDARA. Previously, drugs that had been granted orphan drug designation were exempt from the requirements of the Pediatric Research Equity Act. Under the amended section 505B, beginning on August 18, 2020, the submission of a pediatric assessment, waiver or deferral will be required for certain molecularly targeted cancer indications with the submission of an application or supplement to an application.

Review and Approval of an NDA

In order to obtain approval to market a drug product in the United States, a marketing application must be submitted to the FDA that provides sufficient data establishing the safety, purity and potency of the proposed drug product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the drug product to the satisfaction of the FDA.

The NDA is a vehicle through which applicants formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new drug product candidate must be the subject of an approved NDA before it may be commercialized in the United States. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2021 is $2,875,842 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2021 is $336,432. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of an NDA, the FDA conducts a preliminary review of the application generally 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 whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept the application 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 in the review process of NDAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which the FDA accepts the application 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 products 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 and the PDUFA goal date 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.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including component manufacturing, finished 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.

Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

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.

The FDA may refer an application for a novel product 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, Priority Review and Regenerative Advanced Therapy 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 referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy 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 products, 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 application 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 application 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.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, 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.

Third, the FDA may designate a product for priority review if it is a product 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 product 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 product 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.

With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

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

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

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 product's clinical benefit. As a result, a product 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 initiate expedited proceedings to withdraw approval of the product. All promotional materials for product 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 application 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, or CRL. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL 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 new product, it may limit the approved indications for use of the product. The agency may also 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, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe use, or ETASU. ETASU can 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 patent registries. 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 Regulation

If regulatory approval for marketing of a new product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA may have imposed as part of the approval process. The sponsor will be required to report, among other things, certain adverse reactions and manufacturing problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements 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 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, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or

- injunctions or the imposition of civil or criminal penalties.

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 generally 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 Department of Justice, 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 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, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drug samples at the federal level, and set minimum standards for the regulation of distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. 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 were 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 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the 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.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, 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, or RLD.

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, the strength of the drug and the conditions of use of the drug. 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. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug product containing a new chemical entity. For the purposes of this provision, a 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 responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA 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 often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ''competitor generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

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 applicant files its application with the FDA, the applicant is required to certify 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. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

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 applicant is not seeking approval).

If the ANDA 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 once the ANDA has been accepted for filing by the FDA. 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 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.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Pediatric Exclusivity

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. 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. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which a generic (ANDA or 505(b)(2) NDA) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by a proposed generic product.

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 product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must seek orphan drug designation before submitting an NDA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation 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 drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different conditions. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug 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. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, 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 on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. 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 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 products for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

FDA approval and regulation of companion diagnostics

If safe and effective use of a therapeutic depends on an in vitro diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and in vitro companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling.

If the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population.

The guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a biologic product candidate generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a product are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE. In July 2016, the FDA issued a draft guidance document intended to further assist sponsors of therapeutic products and sponsors of *in vitro* companion diagnostic devices on issues related to co-development of these products.

Under the FDCA, in vitro diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval, or PMA approval.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. For federal fiscal year 2021, the standard fee is $365,657 and the small business fee is $91,414. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Once granted, PMA approval may be withdrawn by the FDA if

compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

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

Health care Law and Regulation

Health care providers 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, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, 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 health care program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program or making false statements relating to health care 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, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute, which 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 health care benefits, items or services;

- the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical

supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as 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, which may apply to health care items or services that are reimbursed by non-government third-party payors, including private insurers.

Further, 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 manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. 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.

Pharmaceutical Insurance Coverage and Health Care Reform

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. 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. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

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 marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party 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.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States. In March 2010,

President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2030 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These 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.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020. On February 10, 2021, the Biden Administration withdrew DOJ's support for this lawsuit. A ruling by the Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal 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. To those ends, President Trump issued five executive orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these orders will remain in force under the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Review and Approval of Medicinal 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 products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union ("EU") generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on Good Clinical Practice, or GCP, and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the EU. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will become directly applicable to and binding in all 28 EU Member States without the need for any national implementing legislation. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the EU. 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 Regulation was published on June 16, 2014 but has not yet become effective. As of January 1, 2020, the website of the European Commission reported that the implementation of the Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020. In late 2020, the EMA indicated that it plans to focus on the findings of a system audit; improving the usability, quality and stability of the clinical trial information system; and knowledge transfer to prepare users and their organizations for the new clinical trial system. The EMA has indicated that the system will go live in December 2021.

As in the US, parties conducting certain clinical trials must post clinical trial information in the European Union at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the EU

In March 2016, the European Medicines Agency, or EMA, launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products (CHMP) or Committee for Advanced Therapies (CAT) are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level.

Pediatric Studies

Companies developing a new medicinal product must agree upon a Pediatric Investigation Plan, or PIP, with the EMA's pediatric committee, or PDCO, and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies (e.g., because the relevant disease or condition occurs only in adults). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The marketing authorization application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted by the PDCO of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults, in which case the pediatric clinical trials must be completed at a later date.

Marketing Authorization

To obtain a marketing authorization for a product under EU regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EU. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (i.e. the EU as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, ATMPs and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may at the request of the applicant also be used in certain other cases. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

Under the centralized procedure, the CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to

questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related "droit de regard". The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called "marketing authorization under exceptional circumstances". Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

The European Commission may also grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the

centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

The EU medicines rules expressly permit the EU Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the national laws in certain EU Member States may prohibit or restrict us from commercializing our future products, if these future products contain, consist of or are derived from such a human or animal cell, even if they have been granted an EU marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the EU Member States of the marketing authorization of a medicinal product by the competent authorities of other EU Member States. The holder of a national marketing authorization may submit an application to the competent authority of an EU Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU Member State.

Regulatory Data Protection in the EU

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited

period. Any authorization which is not followed by the actual placing of the medicinal product on the EU n market (in case of centralized procedure) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Pediatric Exclusivity

Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) even where the trial results are negative. In the case of orphan medicinal products, a two year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) 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 (2) 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.

Once authorized, orphan medicinal products are entitled to 10 years of market exclusivity in all EU Member States and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the 10-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.

- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.

- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly

regulated in the EU notably under Directive 2001/83EC, as amended, and EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the EU on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable by up to two years). On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the UK, as the UK legislation now has the potential to diverge from EU legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the UK in the long-term. The MHRA has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the UK's regulatory position on medicinal products evolves over time.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the European Union's General Data Protection Regulation, or GDPR, has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the European Economic Area, or EEA, to the United Kingdom will remain lawful under GDPR. The Trade and Cooperation Agreement provides for a transitional period during which the United Kingdom will be treated like an European Union member state in relation to processing and transfers of personal data for four months from January 1, 2021. This may be extended by two further months. After such period, the United Kingdom will be a "third country" under the GDPR unless the European Commission adopts an adequacy decision in respect of transfers of personal data to the United Kingdom. The United Kingdom has already determined that it considers all of the EU 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the EU/EEA remain unaffected.

Pricing Decisions for Approved Products

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

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Human Capital

Our ability to sustain and grow our business requires us to hire, retain and develop a highly skilled workforce. As of December 31, 2020, we had a total of 188 full time employees. During 2020, we added 65 new employees, largely as a result of the increase in our sales force due to the recent FDA approval of EYSUVIS. We expect to continue to add additional employees, with a focus on expanding our sales force, pending the status of the COVID-19 pandemic. We continually evaluate our business needs and opportunities and balance in house expertise and capacity with outsourced expertise and capacity.

Recruiting, motivating and retaining qualified employees is critical to our success. We monitor our compensation programs and aim to provide our employees a competitive mix of cash compensation and medical insurance benefits, as well as the opportunity to participate in our equity programs. We believe that our philosophy of providing competitive compensation, along with opportunities for career growth and development, encourage a high level of corporate employee tenure and low level of voluntary turnover. A large majority of our employees have obtained advanced degrees in their professions. Our employees are supported with training and development opportunities to pursue their careers and to ensure compliance with our policies. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

We value the health, safety and wellbeing of our employees and their families. In response to the COVID-19 pandemic, we have implemented significant changes that we determined were in the best interest of our employees, as well as the communities in which we operate, and which comply with government regulations. This includes allowing our corporate employees to work remotely, as appropriate, while implementing significant safety measures designed to protect the health of all those entering our office.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in July 2009. Our office is located at 490 Arsenal Way, Suite 120, Watertown, MA 02472, and our telephone number is (781) 996-5252. Our website address is www.kalarx.com. The information on our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be a part of this Annual Report on Form 10-K. Our website address is included in this Annual Report on Form 10-K as an inactive technical reference only.

Available Information

Through our website, we make available free of charge our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, or the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission, or the SEC. You can review our electronically filed reports and other information

that we file with the SEC on the SEC's web site at http://www.sec.gov. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors & Media," as a source of information about us.

The information on our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be a part of this Annual Report on Form 10-K. Our website address is included in this Annual Report on Form 10-K as an inactive technical reference only.

Item 1A RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10-K, including our financial statements and the related notes appearing at the end of this Annual Report on Form 10-K, before deciding to invest in our common stock. These risks, some of which have occurred and any of which may occur in the future, can have a material adverse effect on our business, prospects, operating results and financial condition. In such event, the trading price of our common stock could decline and you might lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business, prospects, operating results and financial condition.

Risks Related to Our Financial Position and Need For Additional Capital

We have incurred significant losses from operations and negative cash flows from operations since our inception. We expect to incur additional losses and may never achieve or maintain profitability.

Since inception, we have incurred significant losses from operations and negative cash flows from operations. Our net losses were $104.3 million for the year ended December 31, 2020 and $94.3 million for the year ended December 31, 2019. As of December 31, 2020, we had an accumulated deficit of $399.8 million. In January 2019, we launched our first product, INVELTYS® (loteprednol etabonate ophthalmic suspension) 1% for the treatment of post-operative inflammation and pain following ocular surgery. On October 26, 2020, the U.S. Food and Drug Administration, or FDA, approved our second product, EYSUVIS™ (loteprednol etabonate ophthalmic suspension) 0.25% for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease. We began shipping EYSUVIS to wholesalers in the United States in late December 2020 and commenced a full promotional launch in early January 2021. We have had limited revenues to date from product sales. We have financed our operations primarily through proceeds from our initial public offering, or IPO, follow-on public offerings of common stock and sales under our at-the-market offering facility, or the ATM Offering, private placements of preferred stock, borrowings under credit facilities, convertible promissory notes and warrants. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials, and engaging in activities to launch and commercialize EYSUVIS and INVELTYS. Although we expect to continue to generate revenue from sales of INVELTYS and began to generate revenue from sales of EYSUVIS in late December 2020, there can be no assurance as to the amount or timing of any such revenue, and we expect to continue to incur significant expenses and operating losses. We may never achieve or maintain profitability. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year.

We anticipate that our expenses will increase substantially as compared to prior periods as we continue to commercialize INVELTYS in the United States and execute our commercial launch plan for EYSUVIS, as a result of increased headcount, including management personnel to support our clinical, manufacturing and commercialization activities, expanded infrastructure, increased legal, compliance, accounting and investor and public relations expenses associated with being a public company and increased insurance premiums, among other factors. The anticipated increase in expenses from an increase in headcount includes the expansion of our sales force from 56 territory sales managers, or TSMs, to 91 TSMs, which occurred in the fourth quarter of 2020, and our plan to further increase our sales force from 91 TSMs to approximately 125 TSMs in 2021, pending the status of the COVID-19 pandemic.

Our expenses will also increase if and as we:

- continue to grow our sales, marketing and distribution capabilities in connection with the commercialization of EYSUVIS, INVELTYS and any product candidates, for which we may submit for and obtain marketing approval;
- continue to scale up our manufacturing processes and capabilities to support commercialization of EYSUVIS and INVELTYS;

- seek regulatory approval for EYSUVIS and INVELTYS outside of the United States;
- progress our current and any future preclinical development programs;
- in license or acquire the rights to other products, product candidates or technologies;
- conduct clinical trials and other development activities and/or seek marketing approval for future product candidates;
- leverage our proprietary AMPPLIFY technology to seek to advance additional therapeutics into preclinical and clinical development;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control, scientific, manufacturing, commercial and management personnel;
- expand our operational, financial and management systems; and
- increase our product liability insurance coverage as we expand our commercialization efforts for EYSUVIS and INVELTYS.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses will increase from what we anticipate if:

- we elect or are required by the FDA or non-U.S. regulatory agencies to perform clinical trials or studies in addition to those expected;
- there are any delays in enrollment of patients in or completing our clinical trials or the development of our product candidates;
- we in-license or acquire rights to other products, product candidates or technologies; or
- there are any third-party challenges to our intellectual property portfolio, or the need arises to defend against intellectual property-related claims or enforce our intellectual property rights.

Our ability to become and remain profitable depends on our ability to generate revenue. While we began to generate revenue from the sales of EYSUVIS and INVELTYS in late December 2020 and January 2019, respectively, there can be no assurance as to the amount or timing of any future revenue from EYSUVIS and INVELTYS, and we may not achieve profitability. Achieving and maintaining profitability will require us to be successful in a range of challenging activities, including:

- successfully launching EYSUVIS and growing EYSUVIS revenues;
- successfully growing INVELTYS revenues;
- achieving an adequate level of market acceptance, and obtaining and maintaining coverage and adequate reimbursement from third-party payors for EYSUVIS, INVELTYS and any other products we commercialize;
- manufacturing at commercial scale, marketing, selling and distributing EYSUVIS and INVELTYS;

- maintaining regulatory and marketing approvals for EYSUVIS and INVELTYS;
- discovering, developing and successfully seeking marketing approval and commercialization of additional product candidates;
- hiring and building a full commercial organization required for marketing, selling and distributing those products for which we obtain marketing approval;
- obtaining, maintaining and protecting our intellectual property rights; and
- adapting our business in response to the current pandemic health event resulting from COVID-19 and its collateral consequences.

EYSUVIS and INVELTYS are our only products that have been approved for sale, and they have only been approved in the United States. We plan to seek approval in other jurisdictions, but may not do so successfully, or at all. Further, the successful commercialization of EYSUVIS and INVELTYS in the United States is subject to many risks. As a company, we have limited experience commercializing products, and we may not be able to do so successfully. There are numerous examples of unsuccessful product launches and failures to meet expectations of market potential, including by pharmaceutical companies with more experience and resources than us. Our revenue from sales of EYSUVIS and INVELTYS alone may not be sufficient for us to become profitable in the near future, if at all.

In addition, our recent commercialization efforts have been hampered by the operational restrictions on our sales force from quarantines, travel restrictions and bans and other governmental restrictions related to COVID-19. As a result of these restrictions, we previously suspended our sales force from substantially all in-person interactions with physicians and customers and were limited to conducting educational and promotional activities virtually. However, our sales force has resumed substantially all in-person interactions in the field. To the extent we restrict, or are restricted from, in-person interactions with physicians and customers, we are limited to conducting educational and promotional activities virtually, which has hampered, and may continue to hamper, our ability to market INVELTYS and could adversely affect our ability to launch and market EYSUVIS. In addition, government restrictions have at times led to moratoria on elective ocular surgeries in many jurisdictions, which has significantly reduced, and may in the future continue to significantly reduce, the demand for INVELTYS, which is indicated for the treatment of post-operative inflammation and pain following ocular surgery. The extent of the impact of COVID-19 on our commercialization efforts will depend on the length and severity of this pandemic, including the extent any resurgence of the COVID-19 virus and any variant strains of the virus, the availability and effectiveness of vaccines, and the impact of the foregoing on our customers, employees, vendors and government agencies, which is uncertain and cannot be predicted.

We may never succeed in these activities and may never generate revenue that is sufficient to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

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

We are an early-stage commercial company. Our operations to date have been limited to organizing and staffing our company, acquiring rights to intellectual property, business planning, raising capital, developing EYSUVIS and INVELTYS and conducting other research and development activities, and commercially launching EYSUVIS and INVELTYS. We are in the process of transitioning from a company solely with a research and development focus to a company engaging in commercial activities. We may not be successful in such a transition. We only launched INVELTYS in January 2019 and are still in the process of executing our commercial launch plan for EYSUVIS, have no prior history of commercializing products, and, to date, have generated limited revenue from the sale of EYSUVIS and INVELTYS. In addition, our commercial operations and INVELTYS sales have been and continue to be negatively

impacted by COVID-19 and its collateral consequences. The effects of COVID-19 may also disrupt the launch and commercialization of EYSUVIS. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating and commercialization history.

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

We may need substantial additional funding. 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 to devote substantial financial resources to our ongoing and planned activities, particularly as we commercialize EYSUVIS and INVELTYS, and as we advance our preclinical activities for our product candidates. We also expect to incur significant additional expenses if and as we conduct further research and development activities, and potentially initiate clinical trials of, and seek regulatory approval for, any product candidates that we identify and advance, including product candidates from our rTKI program, our STS program and the novel SEGRM program.

Our expenses have increased relative to prior periods in connection with our launch and commercialization of EYSUVIS and INVELTYS, including costs associated with the addition and subsequent expansion of our specialty sales force and increased marketing, distribution and manufacturing capabilities. For example, with the approval of EYSUVIS, we increased our sales force from 56 TSMs to 91 TSMs and from seven RSLs to 14 RSLs during the fourth quarter of 2020, and plan to further increase our sales force to approximately 125 TSMs in 2021, pending the status of the COVID-19 pandemic. Accordingly, we may need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any current or future commercialization efforts.

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

- the costs and timing of commercialization activities for EYSUVIS and INVELTYS, including the costs and timing of expanding our sales force and establishing additional product sales, marketing, medical affairs, distribution and outsourced manufacturing capabilities;
- our ability to successfully commercialize and sell EYSUVIS and INVELTYS in the United States and the amount of revenue received from commercial sales;
- the progress, costs and results of any clinical activities for regulatory review of, and our success seeking approval and/or commercializing, EYSUVIS and INVELTYS outside of the United States;
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements;
- the scope, progress, results and costs of any product candidates that we may develop;
- the extent to which we successfully advance and/or in-license or acquire rights to other products, product candidates or technologies; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims.

We expect to continue to incur significant expenses and operating losses. Net losses may fluctuate significantly from quarter-to-quarter and year-to-year. We expect that our cash, cash equivalents, and short-term investments of $153.5 million as of December 31, 2020, along with anticipated revenue from INVELTYS and the $18.2 million net proceeds raised under the ATM Offering program in January 2021, will enable us to fund our operations, lease and debt

service obligations, and capital expenditure requirements into at least the fourth quarter of 2022. We expect anticipated revenue generated from sales of EYSUVIS to provide additional cash runway. We have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. As a result, we could deplete our available capital resources sooner than we currently expect.

Commercializing products is a time-consuming, expensive and uncertain process. Although we commercially launched INVELTYS in early 2019, began shipping EYSUVIS to wholesalers in the United States in late December 2020 and commenced a full promotional launch of EYSUVIS in early January 2021, our revenue from product sales of EYSUVIS and INVELTYS may not be sufficient for us to become profitable in the near future, if at all. In addition, other than our approved products, EYSUVIS and INVELTYS, all of our other development efforts are in the early stages of preclinical development. Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete. Completion dates and completion costs can vary significantly for each product candidate and are difficult to predict. We may never generate the necessary data or results required to obtain marketing approval and achieve product sales from our preclinical development programs. Also, even if we successfully identify and develop product candidates from our preclinical development programs and those are approved, we may not achieve commercial success with them. Accordingly, we will need to rely on the commercial success of EYSUVIS and INVELTYS to generate product revenue for the foreseeable future.

We may require additional financing to achieve our business objectives. In addition, we may opportunistically raise additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. Adequate additional financing may not be available to us on acceptable terms, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more of our product candidates or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize EYSUVIS and INVELTYS, or any product candidates for which we obtain approval.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, royalty agreements, and marketing and distribution arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include pledging of assets as collateral, covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our pledge of our assets as collateral to secure our obligations under our credit facility with Athyrium Opportunities III Acquisition LP, or Athyrium Credit Facility, may limit our ability to obtain additional debt financing. Under the Athyrium Credit Facility, we are also restricted from paying dividends on our common stock and limited with respect to certain other uses of our cash without the lenders' consent.

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

Our substantial indebtedness may limit cash flow available to invest in the ongoing needs of our business.

We have a substantial amount of indebtedness. As of December 31, 2020, we had $75.0 million of outstanding borrowings under the Athyrium Credit Facility. Amounts outstanding under the Athyrium Credit Facility bear interest at a rate of 9.875% per annum. The Athyrium Credit Facility provides for quarterly interest-only payments for 48 months.

Beginning on September 30, 2022, we will be required to make principal and interest payments through October 1, 2024, the date of maturity. Our obligations under the Athyrium Credit Facility are secured by substantially all of our assets. We could in the future incur additional indebtedness beyond our borrowings under our Athyrium Credit Facility.

Our debt combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate a substantial portion of cash flow from operations or cash on hand to the payment of interest on, and principal of, our debt, which will reduce the amounts available to fund working capital, capital expenditures, product development efforts and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and our industry; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our existing cash and anticipated product revenue. Nonetheless, we may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our existing debt and funds from external sources may not be available on acceptable terms, if at all. In addition, a failure to comply with the covenants under our Athyrium Credit Facility could result in an event of default and acceleration of amounts due. If an event of default occurs and the lender accelerates the amounts due under our Athyrium Credit Facility, we may not be able to make accelerated payments, and the lender could seek to enforce security interests in the collateral securing such indebtedness.

If our estimates or judgments relating to our critical accounting policies, or any of our projections, prove to be inaccurate or financial reporting standards or interpretations change, our results of operations could be adversely affected.

The preparation of financial statements in conformity with generally accepted accounting principles in the United States requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses. Such estimates and judgments include revenue recognition, inventory, the present value of lease liabilities and the corresponding right-of-use assets, the fair value of warrants, stock-based compensation, accrued expenses and the recoverability of our net deferred tax assets and related valuation allowance. We base our estimates and judgments on historical experience, expected future experience and on various other assumptions that we believe to be reasonable under the circumstances. In addition, from time to time, we may rely on projections regarding our expected future performance that represent our management's then-current estimates. However, any of these estimates, judgments or projections, or the assumptions underlying them, may change over time or may otherwise prove to be inaccurate. Our results of operations may be adversely affected if our estimates, assumptions or projections change or if actual circumstances differ from those in our estimates or assumptions, which could cause our results of operations to fall below the expectations of securities analysts and investors, resulting in a decline in the trading price of our common stock.

For example, we rely on third-party data providers to collect and report estimates of prescription information and pipeline inventory levels as components of our estimations for revenue recognition. There is a limited amount of information available to such data providers to determine the actual number of total prescriptions for prescription products during such periods. Their estimates are based on a combination of data received from pharmacies and other distributors, and historical data when actual data is unavailable. Their calculations of changes in prescription levels

between periods can be significantly affected by lags in data reporting from various sources or by changes in pharmacies and other distributors providing data. Such methods can from time to time result in significant inaccuracies in information when ultimately compared with actual results. Further, data for a single and limited period may not be representative of a trend or otherwise predictive of future results.

Additionally, we regularly monitor our compliance with applicable financial reporting standards and review new pronouncements and drafts thereof that are relevant to us. As a result of new standards, changes to existing standards and changes in their interpretation, we might be required to change our accounting policies, alter our operational policies and implement new or enhance existing systems so that they reflect new or amended financial reporting standards, or we may be required to restate our published financial statements. Such changes to existing standards or changes in their interpretation may have an adverse effect on our reputation, business, financial position, and profit.

Risks Related to the Commercialization of EYSUVIS, INVELTYS and our Product Candidates

The ongoing novel coronavirus pandemic and the efforts to prevent its spread have adversely impacted our operations and the market for INVELTYS, could impact the launch and commercialization of EYSUVIS and may continue to adversely affect our business, results of operations and financial condition.

The ongoing novel coronavirus pandemic, commonly referred to as COVID-19, which began in December 2019, has spread worldwide, causing federal, state and local governments to implement measures to slow the spread of the outbreak through quarantines, strict travel restrictions and bans, heightened border scrutiny and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services has fallen significantly.

In particular, from time to time moratoria have been put in place on routine medical appointments and elective surgeries in many jurisdictions, including ocular surgeries, which have adversely affected, and may adversely affect in the future, the market for INVELTYS, which is indicated for the treatment of inflammation and pain following ocular surgery, resulting in a significant reduction in the demand for INVELTYS. The COVID-19 pandemic has negatively impacted revenues from INVELTYS and we expect it to continue to do so until surgeries return to and remain at historical levels. Shelter-in-place orders and other mandated local travel and social interaction prohibitions have also restricted the activities of our sales force. We previously suspended substantially all in-person interactions with physicians and customers and were limited to conducting educational and promotional activities virtually. However, our sales force has resumed substantially all in-person interactions in the field. To the extent we restrict, or are restricted from, in-person interactions with eye care professionals and customers, we are limited to conducting educational and promotional activities virtually, which has hampered, and may continue to hamper, our ability to market INVELTYS and could adversely affect our ability to launch and market EYSUVIS. Furthermore, while the majority of our day-to-day operations are continuing as our employees are working remotely, our laboratory facilities that support our early-stage research activities were partially limited, and may be limited again in the future, as a result of COVID-19.

Additionally, while we currently are not experiencing interruptions in our manufacturing of EYSUVIS or INVELTYS, quarantines, travel restrictions and other measures may significantly impact the ability of employees of our third-party suppliers to get to their places of work to manufacture and deliver future supplies if and when needed.

The COVID-19 pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could impact our ability to raise additional funds through public offerings and may also impact the volatility of our stock price and trading in our stock. Moreover, the significant ongoing impact of the pandemic on economies worldwide could result in more extensive adverse effects on our business and operations. The extent of the impact of COVID-19 on our commercialization efforts will depend on the length and severity of this pandemic, the timing and extent of any resurgence of the COVID-19 virus and any variant strains of the virus, the availability and effectiveness of vaccines, and the impact of the foregoing on our customers, employees, vendors and government agencies, which is uncertain and cannot be predicted. We cannot be certain what the overall impact of the

COVID-19 pandemic will be on our business and it has the potential to significantly and adversely affect our business, financial condition, results of operations and prospects.

EYSUVIS, INVELTYS or any of our product candidates that receive marketing approval may fail to achieve market acceptance by clinicians and patients, or adequate formulary coverage, pricing or reimbursement by third-party payors and others in the medical community, and the market opportunity for these products may be smaller than we estimate.

EYSUVIS, INVELTYS or any product candidate that we develop that receives marketing approval may fail to gain sufficient market acceptance by clinicians, patients, third-party payors and others in the medical community. While there are no drugs other than EYSUVIS currently approved in the United States for the short-term treatment of the signs and symptoms of dry eye disease, current treatments that are used in the United States for dry eye disease include over-the-counter artificial tears, Restasis®, Xiidra®, Cequa™, off-label use of corticosteroids and various drugs that are produced by compounding pharmacies. Generic versions of Restasis are also expected to become available in the United States in the near future. Our current expectations regarding market potential for EYSUVIS are based, in part, on market research data we have commissioned which indicated that interest in prescribing EYSUVIS is high among surveyed eye care professionals, or ECPs. However, it is possible that ECPs may continue to rely on other existing treatments rather than EYSUVIS. In addition, generic versions of any products that compete with any of our product candidates would likely be offered at a substantially lower price than we expect to offer for our product candidates, if approved. As a result, clinicians, patients and third-party payors may choose to rely on such products rather than our product candidates.

Common treatments in the United States for inflammation and pain following ocular surgery include corticosteroids. Our current estimates of potential future revenue from sales of INVELTYS are based, in part, on market research data we have commissioned which indicated that a majority of surveyed ophthalmologists were likely to prescribe INVELTYS. However, doctors may continue to rely on ocular steroids other than INVELTYS and other treatments rather than INVELTYS. In addition, there are also non-topical formulations of ocular steroids that have been recently approved and/or marketed. It is also possible that other therapeutics will be approved for treatment of inflammation and pain following ocular surgery with twice a day or less frequent dosing.

The market opportunity for EYSUVIS and INVELTYS may be further impacted by extraordinary events such as the current pandemic health event resulting from COVID-19 and its collateral consequences. For example, from time to time moratoria have been put in place on routine medical appointments and elective surgeries in many jurisdictions, including ocular surgeries such as cataract and refractive, which have adversely affected, and may adversely affect in the future, the market for INVELTYS, which is indicated for the treatment of post-operative inflammation and pain following ocular surgery, resulting in a significant reduction in the demand for INVELTYS. Shelter-in-place orders and other mandated local travel prohibitions have also restricted the activities of our sales force. We previously suspended substantially all in-person interactions with physicians and customers and were limited to conducting educational and promotional activities virtually. However, our sales force has resumed substantially all in-person interactions in the field. To the extent we restrict, or are restricted from, in-person interactions with physicians and customers, we are limited to conducting educational and promotional activities virtually, which has hampered, and may continue to hamper, our ability to market INVELTYS and could adversely affect our ability to successfully launch and market EYSUVIS.

Our assessment of the potential market opportunity for EYSUVIS, INVELTYS and our product candidates is based on industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties, some of which we commissioned. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data. The potential market opportunity for the treatment of dry eye disease in particular is difficult to precisely estimate. The results from our physician and patient surveys may be less reflective of the dry eye disease population as a whole than a survey conducted with a larger sample size. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of our

assumptions or estimates, or these publications, research, surveys or studies prove to be inaccurate, then the actual market for EYSUVIS, INVELTYS or any of our product candidates may be smaller than we expect, and as a result our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability. The uncertainty with respect to the future progression of the COVID-19 pandemic and its long-term effects may adversely impact the accuracy of such estimates and our potential market opportunity for EYSUVIS and INVELTYS.

If EYSUVIS, INVELTYS or any of our product candidates for which we obtain marketing approval do not achieve adequate levels of acceptance, formulary coverage, pricing or reimbursement, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of EYSUVIS, INVELTYS or any product candidates for which we obtain marketing approval, will depend on a number of factors, including:

- the efficacy and potential advantages of our product or our product candidates compared to alternative treatments, including the existing standard of care;
- our ability to offer our products for sale at competitive prices, particularly in light of the lower cost of alternative treatments;
- the availability of third-party formulary coverage and adequate reimbursement, particularly by Medicare in light of the prevalence of dry eye disease and cataracts in persons over age 55;
- the clinical indications for which the product is approved;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of clinicians to prescribe these therapies;
- the strength of our marketing and distribution support;
- the timing of market introduction of competitive products;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

Even if we are able to successfully commercialize EYSUVIS, INVELTYS or any product candidate that we may develop, the products may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

Our ability to successfully commercialize EYSUVIS, INVELTYS or any of our product candidates that we may develop successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers, managed care plans and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for EYSUVIS, INVELTYS or any product candidate that we commercialize and, even if they are available, the level of reimbursement may be limited or not satisfactory.

Inadequate reimbursement may adversely affect the demand for, or the price of, EYSUVIS, INVELTYS or any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our

products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize EYSUVIS, INVELTYS or any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, such as EYSUVIS, and coverage may be more limited than the indications for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop would compromise our ability to generate revenues and become profitable.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

There can be no assurance that EYSUVIS, INVELTYS or our product candidates, even if such product candidates are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors, or that coverage and an adequate level of reimbursement will be available or that third-party payors' reimbursement policies will not adversely affect our ability to sell EYSUVIS, INVELTYS or our product candidates profitably.

If we are unable to maintain our sales, marketing and distribution capabilities, establish additional capabilities if and when necessary, or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing EYSUVIS, INVELTYS or any of our product candidates that we may develop if and when they are approved.

We established our sales and marketing infrastructure for the commercial launch of INVELTYS, our first product, and EYSUVIS, and, as a company, we have limited experience in the sales, marketing and distribution of therapeutic products. To achieve commercial success for any product for which we obtained marketing approval, we may need to establish additional sales, marketing and distribution capabilities, either ourselves or through collaborations or other arrangements with third parties.

In 2019, we completed the initial buildout of our specialty sales, marketing and distribution infrastructure in the United States to commercialize INVELTYS, which included a sales force of 57 TSMs, seven RSLs, and three directors of national accounts. During the fourth quarter of 2020, we expanded our sales force to include 91 TSMs, 14 RSLs, and two new area sales leaders. In 2021, we plan to increase, pending the status of the COVID-19 pandemic, our sales force

from 91 TSMs to approximately 125 TSMs, who will promote both EYSUVIS and INVELTYS. There are risks involved with establishing, maintaining and expanding our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any future product launch. Further, we may underestimate the size of the sales force required for a successful product launch, including with respect to the launch of EYSUVIS, and may need to expand our sales force earlier and at a higher cost than we anticipated. If the commercial launch of any of our product candidates for which we establish additional commercial infrastructure is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize EYSUVIS, INVELTYS or any product candidates for which we receive marketing approval on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- our inability to obtain and maintain coverage, adequate pricing, and adequate reimbursement from third-party payors, including government payors;
- the inability of sales personnel to obtain access to clinicians, including as a result of limitation on office visits as a result of COVID-19 or other health concerns, or persuade adequate numbers of clinicians to prescribe our products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with maintaining and expanding an independent sales, marketing and distribution organization.

While we cannot be certain when, if ever, we will seek and/or receive marketing approval to commercialize any of our product candidates outside the United States, we may seek marketing approval and explore commercialization of EYSUVIS in certain markets outside the United States, including the European Union, utilizing a variety of collaboration, distribution and other marketing arrangements with one or more third parties. Our product revenues and our profitability, if any, under any such third-party collaboration, distribution or other marketing arrangements are likely to be lower than if we were to market, sell and distribute EYSUVIS ourselves. We may also consider seeking marketing approval outside the United States for other product candidates in the future. If we decide to seek regulatory approval for any of our product candidates outside the United States, we may need to seek additional patent approvals, seek licenses to patents held by third parties and/or face claims of infringing third-party patent rights.

In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute EYSUVIS, INVELTYS or any of our product candidates or we may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market effectively EYSUVIS, INVELTYS or any of our product candidates for which we obtain marketing approval. If we do not maintain our sales, marketing and distribution capabilities successfully, or do not establish additional capabilities if and when needed successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing EYSUVIS, INVELTYS or any of our product candidates for which we obtain marketing approval.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do. Our competitors include major pharmaceutical companies with significantly greater financial resources. EYSUVIS, INVELTYS and our product candidates will also compete with existing branded, generic and off-label products.

The development and commercialization of new drug products is highly competitive. We face competition with respect to EYSUVIS, INVELTYS and will face competition with respect to any product candidates that we may seek to

develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Our products and product candidates target markets that are already served by a variety of competing products. Many of these existing products have achieved widespread acceptance among clinicians, patients and payors. In addition, many of these products are available on a generic basis, and our products or our product candidates may not demonstrate sufficient additional clinical benefits to clinicians, patients or payors to justify a higher price compared to generic products. In many cases, insurers or other third-party payors, particularly Medicare, seek to encourage the use of generic products.

The current disease management approaches for dry eye disease in the United States includes non-pharmaceutical therapies and pharmaceutical therapies. Non-pharmaceutical therapies include over the counter artificial tear eye drops, which are palliative and used on an intermittent or chronic basis to provide short-term symptomatic relief of dryness and irritation; hot compresses for the eye and lid hygiene management; and devices, such as punctal plugs that are inserted into the tear ducts to inhibit tear drainage, resulting in more moisture on the surface of the eye.

Pharmaceutical therapies for dry eye disease include on label prescription drugs, including Restasis, Xiidra, and Cequa, which are the only prescription pharmaceutical products other than EYSUVIS that are approved in the United States for use in patients with dry eye disease; and off label prescription drugs, including topical steroid drops and/or other similar products, which are sometimes prescribed for treatment of dry eye disease. Generic versions of Restasis are expected to become available in the United States in the near future. Restasis and Cequa are both topical cyclosporine formulations that are approved for increasing tear production in patients whose tear production is presumed to be suppressed due to ocular keratoconjunctivitis sicca. Xiidra is a topical anti-inflammatory therapy approved for treatment of the signs and symptoms of dry eye disease.

EYSUVIS is indicated for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease, which includes dry eye flares. Any product that is developed for the treatment of the signs and/or symptoms of dry eye disease could directly compete with EYSUVIS. There are several product candidates in preclinical and clinical development in the United States for the treatment of dry eye disease. If any of these product candidates is approved and such product candidate either treats the signs and/or symptoms of dry eye disease or reduces the frequency of flares in dry eye patients, it could reduce the overall market opportunity for EYSUVIS. These product candidates are being developed by pharmaceutical, biotechnology, specialty pharmaceutical and generic drug companies of various sizes, such as Oyster Point Pharma's OC-01 nasal spray, for which an NDA was submitted in December 2020 and, if approved, could be launched as early as late 2021, Aldeyra Therapeutics' reproxalap ophthalmic solution, Novaliq's CyclAsol and NOV03, which have been licensed to Bausch Health Companies Inc., and others.

Following ocular surgery, topical steroids are commonly prescribed to manage and prevent complications from post-operative inflammation. Topical steroid drops are the main competition to INVELTYS for the treatment of inflammation and pain following ocular surgery. The current branded market leaders for topical steroids in the United States, based on revenue, are Lotemax® products and Durezol®. Generic topical steroid formulations consist mainly of products containing prednisolone, fluorometholone or dexamethasone. In addition, the first generic formulation of loteprednol suspension 0.5% (Lotemax suspension) was launched in May 2019 and Durezol lost its patent exclusivity in 2019, which could result in a potential generic launch of this product at any time.

There are also non-topical formulations of ocular steroids that have been recently approved and/or marketed. Eyepoint Pharmaceutical launched Dexycu®, an intraocular suspension of dexamethasone for the treatment of post-operative inflammation, in July 2019. Also in July 2019, Ocular Therapeutix launched Dextenza®, an intracanalicular insert of dexamethasone, for the treatment of ocular pain following ophthalmic surgery. There are also a number of companies in the United States developing products and therapies in preclinical research and clinical development for the treatment of inflammation and pain following ocular surgery. In addition, there are various formulations of steroids that are produced by compounding pharmacies and that are in drop form or are injected into the eye following ocular surgery.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than our products. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

In addition, our ability to compete may be affected in many cases by insurers or other third-party payors, particularly Medicare, seeking to encourage the use of generic products. Generic products are currently being used for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years.

Many of the companies against which we are competing or which we may compete against in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Given that EYSUVIS and INVELTYS utilize a known FDA-approved corticosteroid, these products and any similar product candidates, if approved, may face competition from generic and branded versions of existing drugs based on corticosteroids that are administered in a different manner.

If our contracted manufacturing facilities experience production issues for any reason, we may be unable to manufacture commercial quantities of our products or product candidates for a substantial amount of time, which could have a material adverse effect on our business.

We rely on third-party contract manufacturers to manufacture commercial supplies of EYSUVIS and INVELTYS. Specifically, we rely on the following: Catalent Pharma Solutions, LLC, or Catalent, to manufacture and supply to us a minimum amount of EYSUVIS and INVELTYS bottles for commercial use; Altasciences company, or Altasciences, for manufacturing bulk intermediates; and Chemo Iberica SA, or Chemo Iberica, to manufacture and supply to us a bulk supply of loteprednol etabonate, or LE. We expect to rely on third parties to manufacture clinical supplies of any other product candidates and commercial supplies of any other products, if and when approved for marketing by applicable regulatory authorities, as well as for packaging, serialization, storage, distribution and other production logistics. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or manufacture our products or our product candidates in accordance with regulatory requirements, if there are disagreements between us and such parties, or if such parties are unable to expand capacities to support commercialization of our products or any of our product candidates for which we obtain marketing approval, we may not be able to compete, or may be delayed in producing sufficient product or product candidates to meet our supply requirements. These facilities may also be affected by natural disasters, such as floods or fire, epidemics or pandemics, such as COVID-19, or such facilities could face manufacturing issues, such as contamination or regulatory concerns following a regulatory inspection of such facility. In such instances, we may need to locate an appropriate replacement third-party relationship, which may not be readily available or on acceptable terms, or at all, which would cause additional delay and increased expense, including as a result of additional required FDA approvals, and may have a material adverse effect on our business.

Our third-party manufacturers are subject to inspection and approval by the FDA before we can commence the manufacture and sale of any of our products or product candidates, and thereafter subject to FDA inspection from time to time. Failure by our third-party manufacturers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our products or product candidates may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses. Depending on the severity of any potential regulatory action, our clinical or commercial supply could be interrupted or limited, which could have a material adverse effect on our business.

We or our third-party manufacturers may also encounter shortages in the raw materials or active pharmaceutical ingredient, or API, necessary to produce our product candidates in the quantities needed for our clinical trials or, our products or our product candidates if approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or API, including shortages caused by the purchase of such raw materials or API by our competitors or others and shortages related to epidemics or pandemics, such as the COVID-19 pandemic. The failure of us or our third-party manufacturers to obtain the raw materials or API necessary to manufacture sufficient quantities of our products or product candidates, may have a material adverse effect on our business.

Product liability lawsuits against us could divert our resources and could cause us to incur substantial liabilities and limit commercialization of EYSUVIS, INVELTYS and any other products that we may develop.

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

- decreased demand for EYSUVIS, INVELTYS and any other products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced time and attention of our management to pursue our business strategy; and
- the inability to successfully commercialize EYSUVIS, INVELTYS and any other products that we may develop.

We currently hold $15 million in product liability insurance coverage in the aggregate, with a per incident limit of $15 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage if and as we commence commercialization of EYSUVIS or any product candidates for which we obtain marketing approval. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Product Development

We are dependent on the success of EYSUVIS, INVELTYS and any product candidates for which we receive marketing approval. If we are unable to successfully commercialize our products and product candidates, our business will be materially harmed.

We have devoted a significant portion of our financial resources and business efforts to the development of INVELTYS for the post-operative treatment of inflammation and pain following ocular surgery and EYSUVIS for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease. There is a significant risk that we will fail to successfully commercialize EYSUVIS and INVELTYS. Our ability to generate meaningful product revenues will depend on our successful commercialization of EYSUVIS and INVELTYS.

The success of our products EYSUVIS and INVELTYS and any product candidates for which we receive marketing approval will depend on many factors, including the following:

- successful commercialization of EYSUVIS and INVELTYS in the United States, including maintaining sales, marketing, manufacturing and distribution capabilities for EYSUVIS and INVELTYS;
- acceptance of EYSUVIS and INVELTYS and any product candidates we develop by patients, the medical community and third-party payors;
- obtaining and maintaining coverage, adequate pricing, and adequate reimbursement from third-party payors, including government payors;
- successfully developing and applying for and receiving marketing approvals from applicable regulatory authorities for any product candidates;
- maintaining regulatory approval of our manufacturing processes and our third-party manufacturers' facilities from applicable regulatory authorities and maintaining adequate supply of our products;
- maintaining a workforce of experienced scientists and others with experience in AMPPLIFY technology and eye diseases to continue to develop our product candidates;
- leveraging our sales, marketing and distribution capabilities for our current products and expanding upon these capabilities if and when appropriate;
- establishing additional sales, marketing and distribution capabilities for, and successfully launching commercial sales of any other product candidates for which we obtain marketing approval, whether alone or in collaboration with others;
- effectively competing with other therapies;
- maintaining an acceptable safety profile of our products following approval;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- protecting our rights in our intellectual property portfolio; and
- not infringing, misappropriating or otherwise violating others' intellectual property rights.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize EYSUVIS, INVELTYS or our product candidates, which would materially harm our business. In addition, other than our approved products, EYSUVIS and INVELTYS, all of our other development efforts are in the early stages of preclinical development. We may never identify any product candidates or advance any product candidates to clinical-stage development from these preclinical development programs. Therefore, our ability to generate product revenue will depend heavily on the successful commercialization of EYSUVIS and INVELTYS, as the development and eventual commercialization of product candidates from our preclinical development programs may never occur.

If clinical trials of any product candidate that we develop fail to demonstrate safety and efficacy to the satisfaction of the FDA or other regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidate.

All of our current development efforts are in the early stages of preclinical development. The risk of failure in developing product candidates is high. It is impossible to predict when or if any product candidate would prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. Furthermore, the failure of any product candidates to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of our other product candidates and/or cause the FDA or other regulatory authorities to require additional testing before approving any of our product candidates. For example, we previously conducted a Phase 2 clinical trial of EYSUVIS for the treatment of meibomian gland dysfunction which did not achieve its primary endpoint. The failure of this trial may have an adverse impact on the perceived safety or efficacy of EYSUVIS in treating dry eye disease or other indications or of INVELTYS.

In January 2018, we announced that we had completed two Phase 3 clinical trials evaluating EYSUVIS, STRIDE 1 and STRIDE 2, evaluating the safety and efficacy of EYSUVIS versus placebo in patients with dry eye disease. In STRIDE 1, statistical significance was achieved for both primary endpoints. However, in STRIDE 2 we did not achieve statistical significance for the primary symptom endpoint of ocular discomfort severity. In August 2019, we announced that we received a complete response letter, or CRL, from the FDA indicating that positive efficacy data from an additional clinical trial will be needed to support a resubmission of our new drug application, or NDA. On March 9, 2020, we announced that our Phase 3 clinical trial of EYSUVIS, which we refer to as STRIDE 3, met both of its primary symptom endpoints and its key secondary sign endpoint, and on April 30, 2020, we resubmitted our NDA with the positive data from STRIDE 3. On October 26, 2020, we received approval from the FDA to market EYSUVIS in the United States. Our Phase 3 clinical trials of EYSUVIS may not be sufficient to support an application for marketing approval outside the United States. Further, if regulatory authorities outside the United States do not accept the data from any trial we conduct in the United States, in particular if the European Union does not allow us to utilize the results from our Phase 3 clinical trials of EYSUVIS pursuant to the Article 10(3) submission pathway or otherwise, we will likely need to conduct additional trials to obtain marketing approval in such jurisdiction, which would be costly and time-consuming and could delay or permanently halt our ability to commercialize the applicable product candidates in the applicable jurisdictions.

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

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or

- have the product removed from the market after obtaining marketing approval.

If we experience any of a number of possible unforeseen events in connection with our clinical trials, potential marketing approval or commercialization of our product candidates could be delayed or prevented, and our competitors could bring products to market before we do.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize any product candidates that we may develop, including:

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may recommend or require us, to conduct additional clinical trials or abandon product development programs;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;

- our third-party contractors may fail to comply with regulatory requirements or meet their obligations to us in a timely manner, or at all;

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;

- we may decide, or regulators or institutional review boards may require us, to suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

- we may be subject to additional post-marketing testing requirements to maintain regulatory approval;

- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate;

- the cost of clinical trials of our product candidates may be greater than we anticipate;

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate or may be delayed;

- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate trials;

- ongoing or future restrictions resulting from the COVID-19 pandemic and its collateral consequences may result in internal and external operational delays and limitations; and

- regulatory authorities may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a modified Risk Evaluation and Mitigation Strategy.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods

during which we may have the exclusive right to commercialize our product candidates or allow our competitors, such as those developing treatments for dry eye disease, to bring products to market before we do and impair our ability to successfully commercialize our product candidates.

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 product candidates we develop 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 United States.

Patient enrollment is affected by a variety of factors, including:

- the prevalence and severity of the disease or condition under investigation;
- the patient eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate under study;
- the existence of existing treatments for the indications for which we are conducting clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of clinicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients;
- the conducting of clinical trials by competitors for product candidates that treat the same indications as our product candidates;
- the impact of public health epidemics, such as the ongoing COVID-19 pandemic; and
- the lack of adequate compensation for prospective patients.

For example, we experienced a delay in patient enrollment for STRIDE 3, which evaluated EYSUVIS for the short-term treatment of the signs and symptoms of dry eye disease. There were a number of factors that may have impacted the delay, including increased competition for eligible patients from competitors that were developing product candidates to treat similar indications and the limited number of patients who fit the eligibility criteria for STRIDE 3. Our inability to locate and enroll a sufficient number of patients for our clinical trials could result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If serious adverse or unacceptable side effects are identified during the development or commercialization of our products or product candidates, we may need to abandon or limit our commercialization efforts for our products or development of such product candidates.

If EYSUVIS, INVELTYS or any of our product candidates are associated with serious adverse events or undesirable side effects in clinical trials or following approval and/or commercialization, or if our products or product candidates have characteristics that are unexpected, we may need to abandon their development or limit development or marketing to narrower uses or subpopulations in which the serious adverse events, undesirable side effects or other

characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. The most common adverse effects to date in trials evaluating the safety and efficacy of EYSUVIS and INVELTYS have been eye pain, instillation site pain, blurred vision and photophobia, which is discomfort or pain due to exposure to light. There have been no serious adverse events related to the administration of EYSUVIS and INVELTYS reported in any of our clinical trials to date. Increases in IOP and cataract formation are additional adverse effects associated with the use of corticosteroids in general. We have no clinical safety data on or patient exposure to either EYSUVIS or INVELTYS for longer than 28 days. Our understanding of the relationship between our products and these adverse effects may change as we gather more information, and additional unexpected adverse effects may occur. Compounds that initially show promise in clinical or earlier stage testing for treating ophthalmic disease or other diseases may later be found to cause side effects that prevent further development and commercialization of the compound. In addition, adverse events which had initially been considered unrelated to the study treatment may later, even following approval and/or commercialization, be found to be caused by the study treatment. Moreover, incorrect or improper use of our products or our product candidates (including use of EYSUVIS or INVELTYS more frequently than is prescribed) by patients could cause increases in IOP and may result in additional unexpected side effects or adverse events. There can be no assurance that our products or our product candidates will be used correctly, and if used incorrectly, such misuse could hamper commercial adoption or market acceptance of our products or product candidates, if approved, at the rate we currently expect.

We may not be successful in our efforts to develop new product candidates based on our AMPPLIFY technology or expand the use of our AMPPLIFY technology for treating additional diseases and conditions.

We are currently directing a portion of our development efforts towards applying our AMPPLIFY technology to develop new product candidates that are designed to diffuse through the mucus layer and enable the active drug substance to reach cells in the underlying target tissue. We have product candidates at various stages of development for treatment of eye diseases and may explore the potential use of our AMPPLIFY technology in other diseases. Our existing product candidates and any other potential product candidates that we identify may not be suitable for continued preclinical or clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize our product candidates that we develop based upon our AMPPLIFY technology, we will not be able to obtain substantial product revenues in future periods.

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

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We may in the future conduct clinical trials for product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations.

We may in the future choose to conduct one or more of our clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and be performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and

regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

Risks Related to Our Dependence on Third Parties

We contract with third parties for the manufacture of EYSUVIS and INVELTYS and plan to contract with third parties for clinical and commercial supply of any future product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our products and product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities for the production of commercial quantities of EYSUVIS, INVELTYS or any product candidates. We rely on Catalent to manufacture and supply to us a minimum amount of EYSUVIS and INVELTYS bottles. We also rely on Altasciences for manufacturing bulk intermediates, and Chemo Iberica to manufacture and supply to us a bulk supply of LE. We expect to rely on third-party manufacturers to manufacture commercial supplies of all of our products and clinical supplies of any other product candidates if and when approved for marketing by applicable regulatory authorities. Our current and anticipated future dependence upon others for the manufacture of EYSUVIS, INVELTYS and any other product or product candidate that we develop may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis. In addition, certain of our third-party manufacturers have in the past, and may in the future, experience performance issues that result in lower than expected yields. Any performance failure on the part of our existing or future manufacturers could delay clinical development, marketing approval or the supply and sale of any product of ours that has been approved for commercial use.

To date, we have obtained materials for our clinical trials and the commercialization of EYSUVIS and INVELTYS from third-party manufacturers, including Catalent and Altasciences. We have supply agreements in place with these contract manufacturers to provide commercial supply. We obtain the API for EYSUVIS and INVELTYS from Chemo Iberica, a third-party API manufacturer. While we have long-term commercial supply agreements with these third-party manufacturers, if these suppliers do not perform as we expect, we may be required to replace one or more suppliers. Although we believe that there are a number of potential long-term replacements to our suppliers, we may incur added costs and delays in identifying and qualifying any such replacements.

The FDA maintains strict requirements governing the manufacturing process. When a manufacturer seeks to modify or make even seemingly minor changes to that process, the FDA may require the applicant to conduct a comparability study that evaluates the potential differences in the product resulting from the change in the manufacturing process. The FDA has issued several rounds of guidance on this point. In connection with any application for approval to market product candidates in the United States, we may be required to conduct a comparability study if the product we intend to market is supplied by a manufacturer different from the one who supplied the product evaluated in our clinical studies. Delays in designing and completing this study to the satisfaction of the FDA could delay or preclude our development and commercialization plans and thereby limit our revenues and growth.

Reliance on third-party manufacturers entails additional risks, including:

- EYSUVIS, INVELTYS and any other product that we develop may compete with other product candidates and products for access to a limited number of suitable manufacturing facilities that operate under current good manufacturing practices, or cGMP, regulations;
- reliance on the third-party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third-party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and

- the possible termination or nonrenewal of the agreement by the third-party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products and harm our business and results of operations.

Any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. We were previously required to change our third-party manufacturer when the manufacturer was purchased by a third-party and exited the contract manufacturing business. The process of changing manufacturers can cause substantial time delays, and if we are required to change our manufacturer again in the future, it may delay our planned clinical trials or development timeline.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for bulk drug substances. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement. Additionally, while we currently are not experiencing interruptions in our manufacturing of EYSUVIS or INVELTYS, quarantines, travel restrictions and bans and other governmental restrictions related to COVID-19 may significantly impact the ability of employees of our third-party suppliers to get to their places of work to manufacture and deliver future supply if and when needed.

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

We may enter into collaborations with third parties for the development or commercialization of our products and product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these products and product candidates.

We expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to develop and commercialize EYSUVIS, INVELTYS or any of our product candidates for which we seek or obtain marketing approval in markets outside the United States. We also may enter into arrangements with third parties to perform these services in the United States to enhance our own sales, marketing and distribution capabilities in the United States or if we determine that such third-party arrangements are otherwise beneficial. We also may seek third-party collaborators for development and commercialization of our product candidates. For example, we may consider potential collaborative partnership opportunities prior to initiating IND-enabling studies on KPI-285, KPI-286, KPI-333 or any other product candidates we develop, including our SEGRMs. Our likely collaborators for any sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangement. However, if we do enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our products and product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Collaborations that we enter into may pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development of our product candidates or may elect not to continue or renew development programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may not pursue commercialization of our product candidates that receive marketing approval or may elect not to continue or renew commercialization programs based on changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own products or product candidates, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our products or product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would divert management attention and resources, be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of products or product candidates in the most efficient manner, or at all. If any collaborations that we enter into do not result in the successful development

and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed, and we may need additional resources to develop our product candidates. All of the risks relating to product development, regulatory approval and commercialization described herein also apply to the activities of our collaborators.

Additionally, subject to its contractual obligations to us, if a collaborator of ours were to be involved in a business combination, it might de-emphasize or terminate the development or commercialization of any product or product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be harmed.

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We rely on third parties, such as clinical research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, in conducting our clinical trials and expect to continue to rely on such parties to conduct clinical trials of any product candidate that we develop. We or these third parties may terminate their engagements with us at any time for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that could delay our product development activities.

Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

If we are not able to establish collaborations, we may have to alter our development and commercialization plans and our business could be adversely affected.

For some of our product candidates, we may decide to collaborate with pharmaceutical or biotechnology companies for the development of our product candidates and the commercialization of our products or the potential commercialization of our product candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the

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

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay the commercialization of a product or a product candidate or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform.

Risks Related to Our Intellectual Property

We may be unable to obtain and maintain patent protection for our technology, products and product candidates, or the scope of the patent protection obtained may not be sufficiently broad or enforceable, such that our competitors could develop and commercialize technology, products and product candidates similar or identical to ours, and our ability to successfully commercialize our technology, products and product candidates may be impaired.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology, products and product candidates. We have sought to protect our proprietary position by filing in the United States and in certain foreign jurisdictions patent applications related to our novel technologies, products and product candidates.

The patent prosecution process is expensive and time-consuming, and we may not have filed, maintained, or prosecuted and may not be able to file, maintain and prosecute all necessary or desirable patents or patent applications at a reasonable cost or in a timely manner. We may also fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of pharmaceutical, biotechnology, and medical device companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may fail to result in issued patents in the United States or in other foreign countries which protect our technology, products or product candidates, or which effectively prevent others from commercializing competitive technologies and products. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, and the standards applied by the U.S. Patent and Trademark Office and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, unlike patent law in the United States, European patent law precludes the patentability of methods of treatment of the human body and imposes substantial restrictions on the scope of claims it will grant if broader than specifically disclosed embodiments. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain whether we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. Databases for patents and publications, and methods for searching them, are inherently limited so we may not know the full scope of all issued and pending patent applications. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology, products or product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies, products and product candidates. In particular, during prosecution of any patent application, the issuance of any patents based on the application may depend upon our ability to generate additional preclinical or clinical data that support the patentability of our proposed claims. We may not be able to generate sufficient additional data on a timely basis, or at all. Moreover,

changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection for our proprietary technology, products and product candidates, prevent competitors from competing with us, or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies, products or product candidates in a non-infringing manner. In particular, a competitor may develop an approach to deliver drugs through the mucus layer to the underlying target tissue that uses a different approach than our AMPPLIFY technology, and therefore may not infringe on our patent rights.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity, or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology, products or product candidates, or limit the duration of the patent protection of our technology, products and product candidates. Given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we are not able to obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for our products or product candidates, our business may be materially harmed.

Depending upon the timing, duration, and specifics of FDA marketing approval of our product candidates, one of the U.S. patents covering each of such product candidates or the use thereof may be eligible for up to five years of patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Also, the regulatory review period of an FDA-approved product may not serve as a basis for a patent term extension if the active ingredient of such product was subject to regulatory review and approval in an earlier product approved by the FDA. We do not expect the U.S. patents covering EYSUVIS and INVELTYS to be eligible for patent term extension due to this limitation. Patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Nevertheless, we may not be able to seek or be granted patent term extension either in the United States or in any foreign country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration sooner, and our revenue could be reduced, possibly materially.

It is possible that we will not obtain patent term extension under the Hatch-Waxman Act for a U.S. patent covering products or one of our product candidates even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought. Further, for our licensed patents, we may not have the right to control prosecution, including filing with the U.S. Patent and Trademark Office, a petition for patent term extension under the Hatch-Waxman Act. Thus, if one of our licensed patents is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether a petition to obtain a patent term extension is filed, or obtained, from the U.S. Patent and Trademark Office.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If one of our product candidates is approved and a patent covering that product candidate is not listed in the Orange Book, with respect to the patent, a manufacturer of generic drugs would not have to provide advance notice to us of any Abbreviated New Drug Application filed with the FDA to obtain permission to sell a generic version of such product candidate.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our owned and licensed patents, trade secrets, or other intellectual property. As a result, to counter infringement, misappropriation or unauthorized use, we may be required to file infringement or misappropriation claims or other intellectual property related proceedings, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents or that our asserted patents are invalid. In addition, in a patent infringement or other intellectual property related 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 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. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, and could put any of our patent applications at risk of not yielding an issued patent. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information or trade secrets could be compromised by disclosure during this type of litigation.

We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in other contested proceedings such as opposition, derivation, reexamination, *inter partes* review, post-grant review, or interference proceedings in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology, products or product candidates 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 product candidates.

In the United States, the FDA does not prohibit clinicians from prescribing an approved product for uses that are not described in the product's labeling. Although use of a product directed by off-label prescriptions may infringe our method-of-treatment patents, the practice is common across medical specialties, particularly in the United States, and such infringement is difficult to detect, prevent, or prosecute.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability to develop, manufacture, market, and sell EYSUVIS, INVELTYS and our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and other proprietary rights of third parties. There is a considerable amount of intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, infringement litigation claims regarding our products, product candidates and technology, including claims from competitors or from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may have no deterrent effect. Moreover, we may become party to future adversarial proceedings or litigation regarding our patent portfolio or the patents of third parties. Such proceedings could also include contested

post-grant proceedings such as oppositions, *inter partes* review, reexamination, interference, or derivation proceedings before the U.S. Patent and Trademark Office or foreign patent offices.

The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. The risks of being involved in such litigation and proceedings may increase as our product candidates commence commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. We may not be aware of all such intellectual property rights potentially relating to our products or product candidates and their uses. Thus, we do not know with certainty that EYSUVIS, INVELTYS or any of our product candidates or our development and commercialization thereof, do not and will not infringe or otherwise violate any third-party's intellectual property.

If we are found to infringe, misappropriate or otherwise violate a third-party's intellectual property rights, we could be required to obtain a license from such third-party to continue developing, manufacturing, marketing and selling our products, product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us and could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease commercializing the infringing technology, products or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent and could be forced to indemnify our customers or collaborators. A finding of infringement could also result in an injunction that prevents us from commercializing our products or product candidates or forces us to cease some of our business operations, which could materially harm our business. In addition, we may be forced to redesign our product candidates, seek new regulatory approvals and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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

Periodic maintenance, renewal and annuity fees on any issued patent must be paid to the U.S. Patent and Trademark Office and foreign patent agencies in several stages or annually over the lifetime of our owned and licensed patents and patent applications. The U.S. Patent and Trademark Office and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In certain circumstances, we rely on our licensing partners to pay these fees to, or comply with the procedural and documentary rules of, the relevant patent agency. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, it would have a material adverse effect on our business.

EYSUVIS, INVELTYS and certain aspects of our AMPPLIFY technology are protected by patents exclusively licensed from other companies or institutions. If these third parties terminate their agreements with us or fail to maintain or enforce the underlying patents, or we otherwise lose our rights to these patents, our competitive position and our market share in the markets for any of our approved products will be harmed.

A substantial portion of our patent portfolio is in-licensed. As such, we are a party to license agreements and certain aspects of our business depend on patents and/or patent applications owned by other companies or institutions. In particular, we hold exclusive licenses for patent families relating to EYSUVIS, INVELTYS and our product candidates and some aspects of our AMPPLIFY technology. While we control patent prosecution of the licensed patent families

relating to EYSUVIS and INVELTYS, for the remainder of the patent families subject to our exclusive license agreement with The Johns Hopkins University, or JHU, that relate to our AMPPLIFY technology, JHU retains control of patent prosecution. Our rights with respect to in-licensed patents and patent applications may be lost if the applicable license agreement expires or is terminated. We are likely to enter into additional license agreements to in-license patents and patent applications as part of the development of our business in the future, under which we may not retain control of the preparation, filing, prosecution, maintenance, enforcement and defense of such patents. If we are unable to maintain these patent rights for any reason, our ability to develop and commercialize our products or product candidates could be materially harmed.

Our licensors may not successfully prosecute certain patent applications, the prosecution of which they control, under which we are licensed and on which our business depends. Even if patents issue from these applications, our licensors may fail to maintain these patents, may decide not to pursue litigation against third-party infringers, may fail to prove infringement, or may fail to defend against counterclaims of patent invalidity or unenforceability.

Risks with respect to parties from whom we have obtained intellectual property rights may also arise out of circumstances beyond our control. In spite of our best efforts, our licensors might conclude that we have materially breached our intellectual property agreements and might therefore terminate the intellectual property agreements, thereby removing our ability to market products covered by these intellectual property agreements. If our intellectual property agreements are terminated, or if the underlying patents fail to provide the intended market exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products similar or identical to ours. Moreover, if our intellectual property agreements are terminated, our former licensors and/or assignors may be able to prevent us from utilizing the technology covered by the licensed or assigned patents and patent applications. This could have a material adverse effect on our competitive business position and our financial condition, results of operations and our business prospects.

Some intellectual property which we own or have licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for United States industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-U.S. manufacturers.

Some of the intellectual property rights we own or have licensed have been generated through the use of United States government funding and may therefore be subject to certain federal regulations. For example, certain aspects of our AMPPLIFY technology as well as certain aspects of our patents that use LE as an active ingredient were developed using United States government funds. As a result, the United States government may have certain rights to intellectual property embodied in our current or future products and product candidates based on our AMPPLIFY technology or that use LE as an active ingredient pursuant to the Bayh-Dole Act of 1980. These United States government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the United States government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third-party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The United States government also has the right to take title to these inventions if we fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. In addition, the United States government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the United States government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for United States manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. Any

exercise by the government of any of the foregoing rights could harm our competitive position, business, financial condition, results of operations and prospects.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

Our license agreement with JHU, under which we license certain of our patent rights and a significant portion of the technology for EYSUVIS, INVELTYS and our product candidates imposes royalty and other financial obligations on us and other substantial performance obligations. We also may enter into additional licensing and funding arrangements with third parties that may impose diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under current or future license and collaboration agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product or product candidate that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could diminish the value of our products or product candidates. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

In addition, it is possible that JHU may conclude that we have materially breached the JHU licensing agreement and might therefore terminate the agreement, thereby removing our ability to market products covered by our license agreement with JHU. If the JHU licensing agreement is terminated, or if the underlying patents fail to provide the intended market exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products similar or identical to ours. Moreover, if our license agreement with JHU is terminated, JHU and/or its assignors may be able to prevent us from utilizing the technology covered by the licensed or assigned patents and patent applications. If we breach the agreement (including by failing to meet our payment obligations) and do not adequately cure such breach, the rights in the technology licensed to us under the JHU license agreement will revert to JHU at no cost to JHU. This could have a material adverse effect on our competitive business position, our financial condition, our results of operations and our business prospects.

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

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

Filing, prosecuting, and defending patents on our products and product candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection or licenses, but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to

biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our and our licensors' employees and contractors were previously employed at other biotechnology, medical device or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Furthermore, we are unable to control whether our licensors have obtained similar assignment agreements from their own employees and contractors. Our and their assignment agreements may not be self-executing or may be breached, and we or our licensors may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we or our licensors fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel which could have a material adverse effect on our competitive business position and prospects. Such intellectual property rights could be awarded to a third-party, and we could be required to obtain a license from such third-party to commercialize our technology or products, which may not be available on commercially reasonable terms or at all. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation or other legal proceedings relating to intellectual property could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

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

more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace.

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

In addition to seeking patents for our technology, our products and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Detecting the disclosure or misappropriation of a trade secret and enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

If we are not able to obtain required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate significant revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate.

Other than EYSUVIS and INVELTYS, we have not received approval to market any product candidate from regulatory authorities in any jurisdiction. We may never generate the necessary data or results required to obtain regulatory approval of any other products with the market potential sufficient to enable us to achieve profitability. We have only limited experience in submitting and supporting the applications necessary to gain marketing approvals and have relied on, and expect to continue to rely on, third-party consultants and vendors to assist us in this process. 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 product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA or other regulatory authorities may determine that any product candidate that we develop is not effective, is only moderately effective, is not safe or has undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate.

In addition, disruptions at the FDA and other agencies may prolong the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. The Trump Administration also took several executive actions that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities.

If we experience delays in obtaining approval or if we fail to obtain approval of any product candidate that we develop, the commercial prospects for such product candidate may be harmed and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad.

In order to market and sell EYSUVIS, INVELTYS or our product candidates in the European Union and many other jurisdictions, we or our potential third-party collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. Our Phase 3 clinical trials of EYSUVIS, INVELTYS or any product candidate may not be sufficient to support an application for marketing approval outside the United States.

The time required to obtain approval outside of the United States may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be sold in that country. We or our potential collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in other countries. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market, which could significantly and materially harm our business.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. On December 24, 2020, the United Kingdom and European Union entered into a trade and cooperation agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for EYSUVIS, INVELTYS or our product candidates, which could significantly and materially harm our business.

The terms of approvals, ongoing regulations and post-marketing restrictions for our products may limit how we manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any potential collaborators we may have in the future, must therefore comply with requirements concerning advertising and promotion for EYSUVIS, INVELTYS or for any of our products for which we obtain marketing approval. Promotional communications with respect to drug products and medical devices are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we are limited to promoting EYSUVIS and INVELTYS in accordance with

their approved labels and the accompanying label may limit the approved use of any other product for which we obtain marketing approval, which could limit sales of such product.

The FDA may also impose requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product, including the adoption and implementation of risk evaluation and mitigation strategies. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling and regulatory requirements. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not restrict the marketing of our products only to their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDCA relating to the promotion of prescription drugs or the promotion or manufacturing of drug products or medical devices may lead to investigations by the FDA, Department of Justice and state Attorneys General alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may have various consequences, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions and warnings in the labeling and marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- exclusion and debarment from federal healthcare reimbursement programs; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with European Union requirements or laws of other countries regarding safety monitoring or pharmacovigilance can also result in significant financial penalties. Similarly, failure to comply with the European Union's or other countries' requirements regarding the protection of personal information can lead to significant penalties and sanctions.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs

applicable to drug manufacturers or quality assurance standards applicable to medical device manufacturers, 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, any contract manufacturers we may engage in the future, our future collaborators and their contract manufacturers will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to clinicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a risk evaluation and mitigation strategy.

We may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products.

Our relationships with customers and third-party payors may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers, clinicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription and use of EYSUVIS and INVELTYS, and will play a primary role in the recommendation and prescription and use of any product candidates for which we obtain marketing approval. Our arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute EYSUVIS and INVELTYS and any products for which we obtain marketing approval. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which 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, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which impose criminal and civil penalties, including civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which 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 of 2009, and their respective implementing regulations, which imposes obligations, including mandatory contractual terms, on covered healthcare providers, health plans and healthcare clearinghouses, as well as their business associates, with respect to safeguarding the privacy, security and transmission of individually identifiable health information; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise

restrict payments that may be made to healthcare providers, state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to clinicians and other healthcare providers or marketing expenditures, and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, individual imprisonment, integrity obligations, and the curtailment or restructuring of our operations. Any penalties, damages, fines, individual imprisonment, integrity obligations, exclusion from funded healthcare programs, or curtailment or restructuring of our operations could adversely affect our financial results. Our corporate compliance program is designed to ensure that we will develop, market and sell our products and product candidates in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may 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, including, without limitation, damages, fines, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the clinicians or other healthcare providers or entities with whom we do or expect to do business is found to be not in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government funded healthcare programs.

Recently enacted and future legislation may affect our ability to commercialize and the prices we obtain for any products that are approved in the United States or foreign jurisdictions.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could affect our ability to profitably sell or commercialize EYSUVIS, INVELTYS or any product candidate for which we obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and have been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA approved product.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for clinician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. The Budget Control Act of 2011, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2029 unless

additional congressional action is taken. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, which was enacted on March 27, 2020, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030. The American Taxpayer Relief Act of 2012, 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 EYSUVIS, INVELTYS and for any of our product candidates for which we may obtain regulatory approval or the frequency with which EYSUVIS, INVELTYS or any product candidate is prescribed or used.

We expect that additional healthcare reforms may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for EYSUVIS, INVELTYS or any other approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our 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 ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the 2017 Tax Act, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which required most Americans to carry a minimal level of health insurance, became effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. The Trump Administration also took executive actions to undermine or delay implementation of the ACA, but those were rescinded by the Biden Administration. In addition, the Centers for Medicare & Medicaid Services has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Biden Administration have stated that they will address such costs through new legislative and administrative measures. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

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

If we or any third-party manufacturers we engage fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur significant costs.

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

Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We hold $3.0 million of environmental liability insurance for claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. These limits, both in the aggregate and per incident, may not be adequate to cover all liabilities that we may incur.

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

Further, with respect to the operations of any future third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, be precluded from developing manufacturing and selling certain products outside the United States or be required to develop and implement costly compliance programs, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act, or FCPA, the U.K. Bribery Act 2010, or Bribery Act, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The FCPA, Bribery Act and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. Compliance with the FCPA, in particular, is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

We may in the future operate in jurisdictions that pose a high risk of potential FCPA or Bribery Act violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA, Bribery Act or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted. If we expand our operations outside of the United States, we will need to dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws. In addition, various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA, the Bribery Act or other legal requirements, including Trade Control laws. If we are not in compliance with the FCPA, Bribery Act and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Any investigation of any potential violations of the FCPA, the Bribery Act, other anti-corruption laws or Trade Control laws by U.S., U.K. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2020, we had federal net operating loss, or NOL, carryforwards of $243.2 million, which may be available to offset future federal tax liabilities and expire at various dates beginning in 2030. As of December 31, 2020, we also had state NOL carryforwards of $215.0 million, which may be available to offset future state income tax liabilities and expire at various dates beginning in 2030, and federal and state research and development credit carryforwards of approximately $2.4 million, which begin to expire in 2039 (federal) and 2034 (state). These NOL carryforwards could expire unused and be unavailable to offset our future income tax liabilities.

In general, under Sections 382 and 383 of the Code, the amount of benefits from our NOL and research and development tax credit carryforwards, respectively, may be impaired or limited if we incur an "ownership change," generally defined as a greater than 50% change (by value) in our equity ownership by certain stockholders, over a three-year period. We may have experienced ownership changes in the past and may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. As a result, our use of federal NOL and research and development tax credit carryforwards could be limited. State NOL and research and development tax credit carryforwards may be similarly limited. Any such limitations may result in greater tax liabilities than we would incur in the absence of such limitations and increased liabilities could adversely affect our business, results of operations, financial position and cash flows. If our ability to use our historical NOL and research and development tax credit carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs and research and development tax credit carryforwards could expire or otherwise become unavailable to offset future income tax liabilities. As described below in "Changes in tax laws or in their implementation or interpretation could adversely affect our business and financial condition," the 2017 Tax Act, as amended by the CARES Act, includes changes to U.S. federal tax rates and the rules governing NOL carryforwards that may significantly impact our ability to utilize our NOLs to offset taxable income in the future. In addition, state NOLs generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on the research and development, clinical, business development and commercialization expertise of Mark Iwicki, our President and Chief Executive Officer, Todd Bazemore, our Chief Operating Officer, Mary Reumuth, our Chief Financial Officer, Kim Brazzell, Ph.D., our Chief Medical Officer, Hongming Chen, Sc.D., our Chief Scientific Officer, and Eric Trachtenberg, our General Counsel, Chief Compliance Officer and Corporate Secretary, as well as the other principal members of our management, scientific, clinical and commercial teams. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We have expanded and may continue to expand our development, regulatory, commercial and manufacturing capabilities and are continuing to implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We have experienced and expect to continue experiencing significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs, manufacturing, sales, marketing and distribution. For example, in the fourth quarter of 2020, we increased our sales force from 56 TSMs to 91 TSMs, from seven RSLs to 14 RSLs and added two new area sales leaders. In 2021, we plan to further increase our sales force from 91 TSMs to approximately 125 TSMs, pending the status of the COVID-19. To manage our recent, planned and potential future growth, we must continue to implement and improve our managerial, operational and financial systems, and may further expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and our limited experience in managing such growth, we may not be able to effectively manage our recently expanded operations, planned sales force expansion or any future expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Furthermore, operational and other restrictions related to COVID-19 may further hamper our ability to grow as needed, including our planned sales force expansion, and/or to manage our growth. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our internal computer systems, or those of our vendors, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs and commercialization of our products.

Despite the implementation of security measures, our internal computer systems and those of our current and any future vendors, contractors or consultants, including any collaborator, are vulnerable to damage from cyber-attacks,

computer viruses, worms and other destructive or disruptive software, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Cyber incidents or attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber incidents also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. System failures, accidents, cyberattacks or security breaches could cause interruptions in our operations, it could result in a material disruption of our development programs, the commercialization of our products and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential, personal or proprietary information, we could incur liability, including civil fines and penalties under the General Data Protection Regulation (EU) 2016/679, HIPAA and other relevant state and federal privacy laws in the United States and abroad, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

While we have not experienced any material losses relating to cyber-attacks, we have been the subject of a successful phishing attempt. We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties may attempt to penetrate our systems or those of our vendors, contractors or consultants or fraudulently induce our employees or employees of our vendors, contractors or consultants to disclose sensitive information in order to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and viruses, and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our vendors, contractors or consultants occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

Risks Related to Our Common Stock

Our executive officers and directors and their affiliates, if they choose to act together, will continue to have the ability to significantly influence all matters submitted to stockholders for approval.

As of December 31, 2020, our executive officers and directors and their affiliates in the aggregate, owned shares representing approximately 28.27% of our capital stock, based on the most recent institutional stockholder ownership filings with the SEC. As a result, if these stockholders were to choose to act together, they may be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of voting power may:

- delay, defer or prevent a change in control;
- entrench our management and our board of directors; or

- delay or prevent a merger, consolidation, takeover or other business combination involving us on terms that other stockholders may desire.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors are responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- provide for a classified board of directors such that only one of three classes of directors are elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- provide for advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three-years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

An active trading market for our common stock may not be sustained.

Our shares of common stock began trading on The Nasdaq Global Select Market on July 20, 2017. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price for our common stock and thereby affect your ability to sell your shares. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price you paid for such common stock. The market price for our common stock may be influenced by many factors, including:

- our success in commercializing EYSUVIS, INVELTYS and other product candidates;
- results of clinical trials of any of our product candidates;
- results of clinical trials of product candidates of our competitors;
- changes in the structure of healthcare payment systems;
- the success of competitive products or technologies;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key scientific, commercial or management personnel;
- the level of expenses related to the commercialization of EYSUVIS, INVELTYS and clinical development programs for any of our product candidates;
- the results of our efforts to discover, develop, acquire or in-license additional products, product candidates or technologies for the treatment of diseases or conditions, the costs of commercializing any such products and the costs of development of any such product candidates or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- market conditions in the pharmaceutical and biotechnology sectors;
- the societal and economic impact of public health epidemics, such as the ongoing COVID-19 pandemic;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation has often been instituted against that company. We also may face securities class-action litigation if we fail to successfully commercialize EYSUVIS, INVELTYS or our product candidates. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources.

Sale of a substantial number of shares of our common stock into the market could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of February 24, 2021, we had outstanding 61,552,352 shares of common stock. Shares of our common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act, or to the extent such shares have already been registered under the Securities Act and are held by non-affiliates of ours. Persons who were our stockholders prior to our initial public offering continue to hold a substantial number of shares of our common stock. If such persons sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. Moreover, holders of a substantial number of shares of our common stock, including shares of our common stock issuable upon exercise of outstanding warrants and options, have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have filed or intend to file registration statements registering all shares of common stock that we may issue under our equity compensation plans or pursuant to equity awards made to newly hired employees outside of equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until December 31, 2022, although if the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th or if we have annual gross revenues of $1.07 billion or more in any fiscal year, we would cease to be an emerging growth company as of December 31 of the applicable year. We also would cease to be an emerging growth company if we issue more than $1 billion of non-convertible debt over a three-year period.

We are also a "smaller reporting company," as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended. We would cease to be a smaller reporting company if we have a public float in excess of $250 million or have annual revenues in excess of $100 million and a public float in excess of $700 million, determined on an annual basis.

As an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

In addition to the above reduced disclosure requirements applicable to emerging growth companies, as a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not smaller reporting companies. These exemptions include:

- being permitted to provide only two years of audited financial statements in our annual report on Form 10-K, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to furnish a contractual obligations table in "Management's Discussion and Analysis of Financial Condition and Results of Operations"; and
- not being required to furnish a stock performance graph in our annual report.

We cannot predict whether investors will find our common stock less attractive as a result of our reliance on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs relative to prior years and will make some activities more time-consuming and costly.

For as long as we remain an emerging growth company or a smaller reporting company, we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies or smaller reporting companies as described in the preceding risk factor.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of our Athyrium Credit Facility preclude us from paying dividends without the lenders' consent, and any future debt agreements that we

may enter into may preclude us from paying dividends without the lenders' consent or at all. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Our certificate of incorporation designates the state courts in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors, officers and employees.

Our certificate of incorporation provides that, unless we consent 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 derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws or as to which the General Corporation Law of the State of Delaware confers jurisdiction on the Court of Chancery of the State of Delaware, or any action asserting a claim against us governed by the internal affairs doctrine. We do not expect this choice of forum provision will apply to suits brought to enforce a duty or liability created by the Securities Act, the Exchange Act, or any other claim for which federal courts have exclusive jurisdiction.

This exclusive forum provision may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find the choice of forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition and operating results.

General Risk Factors

Changes in tax laws or in their implementation or interpretation could adversely affect our business and financial condition.

Changes in tax law may adversely affect our business or financial condition. On December 22, 2017, President Trump signed into law the 2017 Tax Act, which significantly revised the Internal Revenue Code of 1986, as amended, or the Code. The 2017 Tax Act, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), the limitation of the deduction for net operating losses arising in taxable years ending after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress's response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, the CARES Act was enacted on March 27, 2020 and COVID relief provisions were included in the Consolidated Appropriations Act, 2021, or CAA, which was enacted on December 27, 2020. All contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of net operating losses, which was enacted as part of the 2017 Tax Act. It also provides that net operating losses arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30% to 50% of adjusted taxable income.

Regulatory guidance under the 2017 Tax Act, the FFCR Act, the CARES Act and the CAA is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial

condition. It is also possible that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the 2017 Tax Act, the FFCR Act, the CARES Act or the CAA.

Patent reform legislation under Leahy-Smith America Invents Act could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The United States Patent Office has been developing new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. The first to file provisions limit the rights of an inventor to patent an invention if not the first to file an application for patenting that invention, even if such invention was the first invention. Although it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, which could have a material adverse effect on our business, financial condition, results of operations and prospects. For example, the Leahy-Smith Act provides a new administrative tribunal known as the Patent Trial and Appeals Board, or PTAB, that provides a venue for companies to challenge the validity of competitor patents at a cost that is much lower than district court litigation and on timelines that are much faster. Although it is not clear what, if any, long term impact the PTAB proceedings will have on the operation of our business, the initial results of patent challenge proceedings before the PTAB since its inception in 2013 have resulted in the invalidation of many U.S. patent claims. The availability of the PTAB as a lower-cost, faster and potentially more potent tribunal for challenging patents could therefore increase the likelihood that our own patents will be challenged, thereby increasing the uncertainties and costs of maintaining, defending and enforcing them.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our principal facilities consist of office and laboratory space. On February 28, 2018, we entered into a lease, our Watertown Lease, for our current corporate headquarters located in Watertown, Massachusetts, which consists of 66,052 rentable square feet. We began to occupy this space on January 28, 2019. The Watertown Lease has an initial term of eight years and an option to extend for an additional term of five years.

Item 3. Legal Proceedings

We are not currently subject to any material legal proceedings.

Item 4. Mine Safety Disclosures

None.

Part II

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

Our common stock has been publicly traded on the Nasdaq Global Select Market under the symbol "KALA" since July 20, 2017 in connection with our initial public offering, or IPO. Prior to that time, there was no public market for our common stock.

Holders

As of February 24, 2021, there were approximately 9 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividend policy

We have not declared or paid any cash dividends on our common stock since our inception. We intend to retain all available funds and any future earnings to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. In addition, our ability to pay cash dividends is currently restricted by the terms of our Athyrium Credit Facility, and future debt financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Information about our equity compensation plans

The information required by this item will be set forth in our Proxy Statement for the 2021 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

Recent sales of unregistered securities.

Set forth below is information regarding shares of our common stock issued and stock options granted by us for the twelve months ended December 31, 2020 that were not registered under the Securities Act of 1933, as amended, or the Securities Act and that have not otherwise been described in a Quarterly Report on Form 10-Q or a Current Report on Form 8-K.

On October 15, 2020, we granted stock options to four new employees to purchase an aggregate of 42,000 shares of our common stock at an exercise price of $8.20 per share. On November 13, 2020, we granted stock options to four new employees to purchase an aggregate of 34,500 shares of our common stock at an exercise price of $7.42 per share. On December 15, 2020, we granted stock options to 46 new employees to purchase an aggregate of 233,500 shares of our common stock at an exercise price of $7.63 per share. These options were inducement grants made outside of our 2017 Equity Incentive Plan in accordance with Nasdaq Listing Rules 5635(c)(4) and Section 4(a)(2) of the Securities Act of 1933, as amended. The options have a ten-year term and vest over four years, with 25% of the shares underlying each option award vesting on the one-year anniversary of the applicable employee's new hire date and the remaining 75% of the shares underlying each award vesting monthly thereafter for three years. Vesting of each option is subject to the option holders continued service with our company through the applicable vesting dates. We intend to file a registration statement on a Form S-8 to register the shares of common stock underlying these inducement grants prior to the time at which these options become exercisable.

Purchase of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. Selected Financial Data

You should read the following selected consolidated financial data together with our consolidated financial statements and accompanying notes appearing elsewhere in this Annual Report on Form 10-K and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this Annual Report on Form 10-K. We have derived the selected consolidated statement of operations data for the years ended December 31, 2020 and 2019, and the selected consolidated balance sheet data as of December 31, 2020 and 2019 from our audited consolidated financial statements appearing at the end of this Annual Report on Form 10-K. The selected consolidated statement of operations data for the years ended December 31, 2018, 2017 and 2016 and balance sheet data as of December 31, 2018, 2017 and 2016 set forth below have been derived from the audited financial statements for such years not included in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of the results that may be expected in any future period.

	Year Ended December 31,				
	2020	2019	2018	2017	2016
Statement of Operations Data:	(in thousands, except share and per share amounts)				
Product revenues, net	$ 6,362	$ 6,074	$ —	$ —	$ —
Costs and expenses:					
Cost of product revenues	3,173	2,008	—	—	—
Selling, general and administrative	81,068	65,015	35,431	10,867	7,640
Research and development	18,352	27,275	29,290	29,008	25,029
Total costs and expenses	102,593	94,298	64,721	39,875	32,669
Loss from operations	(96,231)	(88,224)	(64,721)	(39,875)	(32,669)
Other income (expense)					
Interest income	493	2,357	1,687	527	147
Interest expense	(8,589)	(8,480)	(3,314)	(1,019)	(767)
Loss on extinguishment of debt	—	—	(390)	—	—
Change in fair value of warrant liability	—	—	—	(1,844)	122
Net loss attributable to common stockholders	$ (104,327)	$ (94,347)	$ (66,738)	$ (42,211)	$ (33,167)
Net loss per share attributable to common stockholders—basic and diluted	$ (1.99)	$ (2.76)	$ (2.49)	$ (3.71)	$ (28.07)
Weighted average shares outstanding—basic and diluted	52,377,526	34,209,756	26,753,906	11,375,000	1,181,429

	As of December 31,				
	2020	2019	2018	2017	2016
Balance Sheet Data:			(in thousands)		
Cash, cash equivalents and short-term investments	$ 153,540	$ 85,449	$ 170,898	$ 114,565	$ 45,472
Total assets	221,606	154,323	220,966	116,546	46,329
Working capital(1)	149,154	80,710	160,018	100,341	40,080
Long-term debt—less current portion	72,243	71,184	70,226	11,987	9,098
Other long-term liabilities	27,143	28,673	28,752	8	17
Total stockholders' equity (deficit)	99,995	29,692	104,978	89,679	(87,762)

(1) We define working capital as current assets less current liabilities.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes thereto appearing at the end of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. See "Special Note Regarding Forward-Looking Statements and Industry Data." Because of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of innovative therapies for diseases of the eye. We have worldwide rights to a portfolio of innovative products and product candidates that include two marketed therapies utilizing our proprietary mucus penetrating particle, or MPP, drug delivery technology, which we refer to as our AMPPLIFY® Technology, to address medical needs for the front of the eye, and a pipeline of proprietary new chemical entities, or NCEs, targeted to address front and back of the eye diseases.

Our two marketed products are EYSUVIS™ (loteprednol etabonate ophthalmic suspension) 0.25%, for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease, and INVELTYS® (loteprednol etabonate ophthalmic suspension) 1%, a topical twice-a-day ocular steroid for the treatment of post-operative inflammation and pain following ocular surgery. Both products apply our AMPPLIFY technology to loteprednol etabonate, or LE, a corticosteroid designed for ocular applications. The AMPPLIFY® technology, uses selectively sized nanoparticles that each have a proprietary coating. We believe that these two key attributes enable even distribution of drug particles on mucosal surfaces and significantly increase drug delivery to target tissues by enhancing mobility of drug particles through mucus and preventing drug particles from becoming trapped and eliminated by mucus.

We have retained worldwide commercial rights for EYSUVIS, INVELTYS and our preclinical development programs. Starting with FDA approval of INVELTYS, we have built a commercial infrastructure with our own focused, specialty sales force which now includes 91 territory sales managers, or TSMs, 14 regional sales leaders, two area sales leaders and three directors of national accounts. In 2021, we plan to increase our sales force from 91 TSMs to approximately 125 TSMs, pending the status of the COVID-19 pandemic. Our sales representatives promote both EYSUVIS and INVELTYS. We expect to commercialize in the United States any of our product candidates that receive marketing approval as well. We also expect to explore commercialization of EYSUVIS for the treatment of dry eye disease in certain markets outside the United States, including the European Union, or EU, utilizing a variety of collaboration, distribution and other marketing arrangements with one or more third parties.

Since the initial public offering of our common stock, or IPO, we have financed our operations primarily through common stock offerings pursuant to a shelf registration statement on Form S-3 that was declared effective by the SEC on August 27, 2018, or the 2018 Shelf Registration, and sales of our common stock pursuant to a sales agreement, or the 2018 Sales Agreement, with Jefferies, LLC, or Jefferies, under which we were able to issue and sell, from time to time, common stock in at-the-market offerings, or the ATM Offering, through Jefferies, as a sales agent. On March 10, 2020, we notified Jefferies that we were suspending and terminating the prospectus related to the 2018 Sales Agreement. Under the 2018 Shelf Registration, we have issued an aggregate of 30,549,976 shares of common stock, including under the ATM Offering, resulting in aggregate gross proceeds to us of $231.7 million.

On May 7, 2020, we filed a shelf registration statement on Form S-3 with the SEC, which was declared effective on May 19, 2020, or the 2020 Shelf Registration. Under the 2020 Shelf Registration, we may offer and sell up to $350.0 million of a variety of securities including common stock, preferred stock, warrants, depositary shares, debt securities or units during the three-year period that commenced upon the 2020 Shelf Registration becoming effective. In connection with the filing of the 2020 Shelf Registration, we entered into an amended and restated sales agreement with Jefferies pursuant to which we may issue and sell, from time to time, up to an aggregate of $75.0 million of our common stock under our ATM Offering through Jefferies, as a sales agent. During the fourth quarter of 2020, we issued an

aggregate of 2,821,059 shares of our common stock under the ATM Offering, resulting in net proceeds to us of $20.6 million. In January 2021, we issued and sold an additional 2,552,457 shares of our common stock under our ATM Offering, resulting in net proceeds to us of $18.2 million. As of the date of this Annual Report on Form 10-K, there was $35.0 million of shares of common stock remaining under the ATM Offering that we may issue and sell in the future and, excluding the funds designated to be offered under our ATM Offering, there was $275.0 million of securities available to be issued under the 2020 Shelf Registration.

We also have an aggregate principal amount of $75.0 million of indebtedness outstanding under our credit facility, or the Athyrium Credit Facility, with Athyrium Opportunities III Acquisition LP, or Athyrium.

Since inception, we have incurred significant losses from operations and negative cash flows from operations. Our net losses were $104.3 million for the year ended December 31, 2020 and $94.3 million for the year ended December 31, 2019. As of December 31, 2020, we had an accumulated deficit of $399.8 million. As we commenced a full promotional launch of EYSUVIS in early January 2021 and commercially launched our first product, INVELTYS, in January 2019, we have had only limited revenues to date from product sales and have financed our operations primarily through proceeds from our IPO, follow-on public common stock offerings and sales of our common stock under our ATM Offerings, private placements of preferred stock, borrowings under credit facilities convertible promissory notes and warrants. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials and engaging in activities to commercialize EYSUVIS and INVELTYS. Although we expect to continue to generate revenue from sales of EYSUVIS and INVELTYS, there can be no assurance as to the amount or timing of any such revenue, and we expect to continue to incur significant expenses and operating losses. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year.

Business Impact of COVID-19 Pandemic

The ongoing COVID-19 pandemic, which began in December 2019, has spread worldwide, causing federal, state and local governments to implement measures to slow the spread of the pandemic through quarantines, strict travel restrictions and bans, heightened border scrutiny and other measures. In order to safeguard the health of our employees, we follow, and will continue to follow, recommendations from the U.S. Centers for Disease Control and Prevention, as well as federal, state, and local governments, regarding working-from-home practices for non-essential employees. As a result, all office-based personnel have been instructed to work from home, and our laboratory facilities, that support our early-stage research activities, are being utilized as necessary. In addition, we previously suspended our sales force from substantially all in-person interactions with physicians and customers and were limited to conducting educational and promotional activities virtually. However, our sales force has resumed substantially all in-person interactions in the field. To the extent we restrict, or are restricted from, in-person interactions with physicians and customers in the future, we are limited to conducting educational and promotional activities virtually, which has hampered, and may continue to hamper, our ability to market INVELTYS. The effects of COVID-19 may also disrupt the full promotional launch and commercialization of EYSUVIS.

In addition, government restrictions have at times led to moratoria on elective ocular surgeries in many jurisdictions, which has significantly reduced, and may in the future continue to significantly reduce, the demand for INVELTYS, which is indicated for the treatment of post-operative inflammation and pain following ocular surgery. The extent of the impact of COVID-19 on our commercialization efforts of EYSUVIS and INVELTYS and our operational and financial performance will depend on certain developments, including the length and severity of this pandemic and the impact on our customers, employees, vendors, and government agencies, all of which are uncertain and cannot be predicted.

Management is actively monitoring the COVID-19 pandemic and its possible effects on our financial condition, liquidity, operations, customers, sales force, contractors, and workforce. For additional information on risks posed by the COVID-19 pandemic, please see Part I, Item 1A – “Risk Factors” of this Annual Report on Form 10-K, including the risk factor entitled “The ongoing novel coronavirus pandemic and the efforts to prevent its spread have adversely impacted our operations and the market for INVELTYS, could impact the launch and commercialization of EYSUVIS and may continue to adversely affect our business, results of operations and financial condition.”

Financial Operations Overview

Product Revenues, Net

We commenced generating product revenues from sales of INVELTYS in January 2019, and commenced generating revenue from EYSUVIS upon the shipment to wholesalers in the United States in late December 2020. We commenced the full promotional launch of EYSUVIS in early January 2021. Our product revenues are recorded net of provisions relating to estimates for (i) trade discounts and allowances, such as discounts for prompt payment and other discounts and distributor fees, (ii) estimated rebates, chargebacks and co-pay assistance program, and (iii) reserves for expected product returns. These estimates reflect current contractual and statutory requirements, known market events and trends, industry data and forecasted customer buying and payment patterns. Actual amounts may ultimately differ from these estimates. If actual results vary, estimates may be adjusted in the period such change in estimate becomes known, which could have an impact on earnings in the period of adjustment. Beginning in March 2020 and continuing through most of the second quarter of 2020, prescriptions of INVELTYS and revenue had been adversely affected by the ongoing COVID-19 pandemic as federal, state and local governments implemented restrictions on elective procedures, which included most ocular surgeries. While many deferred ocular surgeries have been rescheduled as individual states have released restrictions on elective procedures, and INVELTYS prescriptions have returned to quarterly growth, we are unable to project the specific timing or potential impact on future revenues given the continued uncertainty around the impact and duration of the restrictions related to COVID-19. We also cannot project the potential impact that COVID-19 may have on the full promotional launch and commercialization of EYSUVIS.

Cost of Product Revenues

Cost of product revenues consists primarily of materials, third-party manufacturing costs, freight and distribution costs, royalty expense, allocation of labor, quality control and assurance, reserves for defective inventory, reserves for excess and obsolete inventory and other manufacturing overhead costs. We expensed cost of product revenues related to INVELTYS as research and development expenses prior to U.S. regulatory approval, which we received on August 22, 2018. We expensed cost of product revenues related to EYSUVIS as research and development expenses prior to the determination that FDA approval was probable and before the future economic benefit was expected to be realized. With respect to the ongoing COVID-19 pandemic, we expect that the cost of product revenues will be impacted consistent with the negative impact to product revenues, net. However, we are unable to predict the specific timing or specific impact on cost of product revenues given the continued uncertainty around the impact and duration of the restrictions related to COVID-19.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries, benefits, commissions, stock-based compensation and travel expenses related to our commercial infrastructure and our executive, finance, human resources, legal, information technology and business development functions. Selling, general and administrative expenses also includes external costs related to marketing, costs to manufacture sample units and professional fees for auditing, tax, information technology, consultants, legal services and allocated facility-related costs not otherwise included in research and development expenses.

We anticipate that our selling, general and administrative expenses will increase in the future as we continue to build our commercial infrastructure to support the full promotional launch and commercialization of EYSUVIS and the commercialization of INVELTYS or of any product candidates for which we obtain marketing approval. We also anticipate that our selling, general and administrative expenses will increase if and as we increase our administrative headcount to support our continued research activities and development of our product candidates. With respect to the ongoing COVID-19 pandemic, certain selling, general and administrative expenses were favorably impacted during the year ended December 31, 2020 by the restrictions including those on the activities of our sales force, which had previously suspended substantially all in-person interactions with physicians and customers. Our sales force has resumed substantially all in-person interactions in the field. If we are forced to suspend all or some in-person sales force interactions again in the future as a result of the COVID-19 pandemic, selling, general and administrative expenses could again be favorably impacted by a reduction in certain expenses associated with the restriction in activities for our sales

force and other employees. We are unable to predict the specific amount of this impact if we are forced to resume such restrictions.

Research and Development Expenses

Research and development expenses consist of costs associated with our research activities, including compensation and benefits for full-time research and development employees, an allocation of facilities expenses, overhead expenses and other outside expenses. Our research and development expenses include:

- employee-related expenses, including salaries, related benefits, travel and stock-based compensation;
- expenses incurred for the preclinical and clinical development of our product candidates and under agreements with contract research organizations, or CROs, including costs of manufacturing product candidates prior to the determination that FDA approval of a drug candidate is probable and before the future economic benefit of the drug is expected to be realized; and
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and supplies.

We expense research and development costs as they are incurred. We expense costs relating to the production of inventory for our product candidates, as research and development expenses within our consolidated statements of operations and comprehensive loss in the period incurred, unless we believe regulatory approval and subsequent commercialization of the product candidate is probable and we expect the future economic benefit from sales of the drug to be realized. Research and development costs that are paid in advance of performance are capitalized as a prepaid expense until incurred. We track outsourced development costs by development program but do not allocate personnel costs, payments made under our license agreements or other costs to specific product candidates or development programs. These costs are included in Employee-related costs and Other research and development costs in the line items in the tables under "Results of Operations".

We expect that our total research and development costs will decrease in 2021 as compared to the year ended December 31, 2020 as a result of the completion of our Phase 3 clinical trial of EYSUVIS, or STRIDE 3, and as a result of the capitalization of EYSUVIS manufacturing costs as inventory beginning in the third quarter of 2020. We expect that research and development costs will increase if and as we continue to advance our preclinical development programs, identify product candidates and conduct preclinical studies and clinical trials. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time-consuming. We may never succeed in obtaining marketing approval for any of our product candidates. The probability of success for each product candidate may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability. With respect to the ongoing COVID-19 pandemic, we may incur reduced research and development costs resulting from any limitations that may be placed on our laboratory facilities that support our early-stage research. However, we are unable to predict the specific amount of this impact, nor are we able to predict the additional costs, if any, associated with personnel safely resuming their full activities.

Our research and development programs are at the early stage of development. Successful development and completion of preclinical studies and clinical trials is uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each product candidate and future product candidate and are difficult to predict. We will continue to make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to the scientific and clinical success of each product candidate as well as ongoing assessments as to the commercial potential of product candidates and our ability to enter into collaborations with respect to each product candidate. We may need to raise additional capital and may seek collaborations in the future to advance our various product candidates. Additional private or public financings may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a material adverse effect on our financial condition and our ability to pursue our business strategy.

Interest Income

Interest income consists of interest earned on our cash, cash equivalents and short-term investments.

Interest Expense

Interest expense primarily consists of contractual coupon interest, amortization of debt discounts and debt issuance costs recognized on our debt facility.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. We believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as critical because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we make the estimate, and different estimates—which also would have been reasonable—could have been used. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

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

Revenue

We account for revenue in accordance with Accounting Standards Codification ("ASC") Topic 606, *Revenue from Contracts with Customers*. Under ASC Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to be entitled in exchange for those goods or services. We perform the following five steps to recognize revenue under ASC Topic 606: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only recognize revenue when it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services that will be transferred to the customer.

Product revenues, net

We sell EYSUVIS and INVELTYS primarily to wholesalers in the United States, or Customers. These Customers subsequently resell our products to specialty and other retail pharmacies. In addition to agreements with Customers, we enter into arrangements with third-party payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts for the purchase of our products.

The goods promised in our product sales contracts represent a single performance obligation. We recognize revenue from product sales at the point the Customer obtains control of the product, which occurs upon delivery. The transaction price ("net sales price") that is recognized as revenue for product sales includes the selling price to the Customer and an estimate of variable consideration. Components of variable consideration include prompt pay and other discounts, product returns, government rebates, third-party payor rebates, coverage gap rebates, incentives such as patient co-pay assistance, and other fees paid to Customers and other third-party payors where a distinct good or service is not received. Variable consideration is recorded on the consolidated balance sheet as either a reduction of accounts receivable, if payable to a Customer, or as a current liability, if payable to a third-party other than a Customer. We consider all relevant information when estimating variable consideration such as assessment of our current and

anticipated sales and demand forecasts, actual payment history, information from third parties regarding the payor mix for products, information from third parties regarding the units remaining in the distribution channel, specific known market events and trends, industry data and current contractual and statutory requirements that are reasonably available. We include estimated amounts for such variable consideration in the net sales price to the extent it is determined probable that a significant reversal of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is resolved.

Payment terms with Customers do not exceed one year and, therefore, we do not account for a significant financing component in our arrangements. We expense the incremental cost of obtaining a contract with a Customer when incurred as the period of benefit is generally less than one year.

Reserves for Variable Consideration:

Trade Discounts and Allowances

We provide our Customers with certain trade discounts and allowances including discounts for prompt payments and other discounts and fees paid for distribution, data and administrative services. These discounts and fees are based on contractually-determined percentages and are recorded as a reduction of revenue and accounts receivable in the period in which the related product revenue is recognized.

Chargebacks

Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These components of variable consideration are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable. Reserves for chargebacks consist of credits we expect to issue for units that remain in the distribution channel at the end of each reporting period and that we expect will be sold to qualified healthcare providers, as well as chargebacks that Customers have claimed, but for which we have not yet issued a credit.

Product Returns

Consistent with industry practice, we have a product returns policy that provides Customers right of return for product purchased within a specified period prior to and subsequent to the product's expiration date. We estimate the amount of products that may be returned and present this amount as a reduction of revenue in the period the related product revenue is recognized, in addition to establishing a liability. Our estimates for product returns are based upon available industry data and our own sales information, including our visibility into the inventory remaining in the distribution channel as well as historical returns, which develop over time.

Commercial Payor and Medicare Part D Rebates

We contract with certain third-party payors, primarily pharmacy benefit managers, or PBM's, and health plans, or Plans, for the payment of rebates with respect to utilization of our product. These rebates are based on contractual percentages applied to the amount of product prescribed to patients who are covered by the PBMs or the Plans with which it contracts. We estimate rebates for commercial and Medicare Part D payors based on the contractual discount percentage, the various payor mix for EYSUVIS and INVELTYS as well as future rebates that will be made for product that has been recognized as revenue but remains in the distribution channel at the end of each reporting period. We also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. Such estimates are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Government Rebates

We are subject to discount obligations under Medicaid and other government programs. For Medicaid, reserves are based on actual payment history, and estimates of future Medicaid beneficiary utilization applied to the Medicaid unit rebate formula established by the Centers for Medicaid and Medicare Services. Our liability for these rebates consists of estimates of claims for the current period and estimated future claims that will be made for product that has been recognized as revenue but remains in the distribution channel at the end of each reporting period. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Co-pay Assistance Program

We offer a co-pay assistance program (the "co-pay program"), which is intended to provide financial assistance to patients who may or may not be covered by commercial insurance or who opt out of Medicare Part D programs. The calculation of accruals for the co-pay program is based on actual claims processed during the period as well as an estimate of the number and cost per claim that we expect to receive associated with product that has been recognized as revenue but remains in the distribution channel at the end of each reporting period. Allowances for estimated co-pay claims are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Inventory

Inventory is stated at the lower of cost or net realizable value, on a first-in, first-out method. Costs include amounts related to third party manufacturing, transportation, internal labor and overhead. We capitalize pre-launch inventory when we believe regulatory approval and subsequent commercialization of the product candidate is probable and expect the future economic benefit of the drug to be realized. In doing so, we consider a number of factors in order to determine the amount of inventory to be capitalized, including the historical experience of achieving regulatory approvals for our similar products, the amount of inventory that is likely to be used in commercial production, receipt and analysis of positive Phase 3 clinical trial results for the underlying product candidate, results from meetings with the relevant regulatory authorities prior to the filing of regulatory applications and the compilation of the regulatory application. We also monitor the status of the product within the regulatory review and approval process, including all relevant communication with regulatory authorities. For inventories capitalized in preparation for product launch, anticipated future sales, expected shelf life and expected approval date are taken into account when evaluating realizability. The shelf life of a product is determined as part of the regulatory approval process; however, in assessing whether to capitalize pre-launch inventory, we consider the product stability data of all of the pre-launch inventory procured or produced to date to determine whether there is adequate shelf life. If management is aware of any specific material risks or contingencies other than the normal regulatory review and approval process, or if the criteria for capitalizing inventory produced prior to regulatory approval are otherwise not met, we would not capitalize such inventory costs, choosing instead to recognize such costs as a research and development expense in the period incurred. For INVELTYS, capitalization of costs as inventory began upon U.S. regulatory approval. For EYSUVIS, capitalization of costs as inventory began in the third quarter of 2020 when we believed regulatory approval and subsequent commercialization of the product candidate was probable and expected the future economic benefit of the drug to be realized.

We perform an assessment of the recoverability of capitalized inventory during each reporting period, including quality control and assurance reserves for defective inventories, and we also write-down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded within cost of product revenues, unless associated with our samples inventory, in which case the charges are recorded to selling, general and administrative expense. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required which would be recorded as a cost of product revenues in the consolidated statements of operations and comprehensive loss.

Shipping and handling costs for product shipments are recorded as incurred in costs of revenues along with costs associated with manufacturing the product, and any inventory write-downs. Inventory produced that will be used in a promotional sample program is expensed to selling, general and administrative expense when it is designated as a sample. Long-term inventory includes raw materials, work-in-progress and/or finished goods inventory with an anticipated consumption or sale beyond one year from the balance sheet date based on our forecasted expectations.

Stock-based Compensation

We measure stock options and other stock-based awards granted to employees and directors based on the fair value of the award on the date of the grant and recognize the corresponding compensation expense of those awards using the straight-line method, over the requisite service period, which is generally the vesting period of the respective award, and account for the effect of forfeitures as they occur. For performance awards whose vesting is contingent upon a specified event, we recognize stock-based compensation expense over the derived service period, based on the probability of achievement of the specified event.

We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield.

Emerging Growth Company Status

In April 2012, the Jumpstart Our Business Startup Act, or JOBS Act, was enacted by the federal government. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Results of Operations

Comparison of the Years ended December 31, 2020 and 2019

The following table summarizes the results of our operations for the years ended December 31, 2020 and 2019:

	Year Ended December 31,		
	2020	2019	Change
	(in thousands)		
Product revenues, net	$ 6,362	$ 6,074	$ 288
Costs and expenses:			
Cost of product revenues	3,173	2,008	1,165
Selling, general and administrative	81,068	65,015	16,053
Research and development	18,352	27,275	(8,923)
Total costs and expenses	102,593	94,298	8,295
Loss from operations	(96,231)	(88,224)	(8,007)
Other income (expense)			
Interest income	493	2,357	(1,864)
Interest expense	(8,589)	(8,480)	(109)
Net loss	$ (104,327)	$ (94,347)	$ (9,980)

Product revenues, net

Product revenues, net was $6.4 million for the year ended December 31, 2020 compared to $6.1 million for the year ended December 31, 2019. The increase in product revenues, net of $0.3 million is primarily the result of the first sales of EYSUVIS, which we began shipping to wholesalers in the United States in late December 2020, as well as a higher per unit gross selling price of INVELTYS. These increases were partially offset by higher estimated reserves per unit related to the year ended December 31, 2020 as compared to those estimated during the year ended December 31, 2019 and a decrease in the total units of INVELTYS sold in the year ended December 31, 2020 as compared to those sold during the year ended December 31, 2019, which we attribute to the reductions in elective surgeries as a result of the restrictions related to COVID-19. We expect product revenues to increase if and as we increase our market share and obtain and maintain coverage and adequate reimbursement for EYSUVIS and INVELTYS from third-party payors; however, revenues could continue to be negatively impacted in 2021 as a result of the COVID-19 pandemic.

Cost of product revenues

Cost of product revenues was $3.2 million for the year ended December 31, 2020, a $1.2 million increase compared to $2.0 million for the year ended December 31, 2019. The primary drivers of this increase were a reserve for excess INVELTYS inventory of $1.0 million during the year ended December 31, 2020 due to COVID-19 and the cost of product revenues attributable to EYSUVIS of $0.3 million which included $0.1 million related to the write-off of certain units that did not pass quality inspection. The cost per unit for INVELTYS increased as a result of the units sold during the year ended December 31, 2019 being further manufactured prior to FDA approval and previously expensed as research and development expenses as compared to those units sold during the year ended December 31, 2020, but the increase was more than offset by a decrease in total INVELTYS units sold compared to the year ended December 31, 2019, for a net decrease of $0.1 million. We expect cost of product revenues to increase as we continue to commercialize INVELTYS and as a result of the launch of EYSUVIS, which we began shipping to wholesalers in the United States in late December 2020 and for which we commenced a full promotional launch in early January 2021.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $81.1 million for the year ended December 31, 2020 compared to $65.0 million for the year ended December 31, 2019, an increase of $16.1 million. Selling, general and administrative expenses for the year ended December 31, 2020 include a $7.5 million increase in external sales and marketing costs related to preparation for the launch of EYSUVIS. External sales and marketing costs incurred during the year ended December 31, 2019 primarily related to the commercial launch of INVELTYS. Also contributing to the increase in selling, general and administrative expenses for the year ended December 31, 2020 was a $3.4 million increase in costs for administrative and professional service fees, a $3.3 million increase in stock-based compensation costs, of which $2.9 million was a result of the issuance of restricted stock units and performance-based restricted stock units in June 2020, a $1.1 million increase in employee-related expenses primarily due to increased incentive compensation and increased recruiting costs related to hiring efforts as we prepared for the launch of EYSUVIS, partially offset by reduced travel due to COVID-19, and a $0.8 million increase in other selling, general and administrative costs, which includes facility related costs and certain medical affairs costs. We anticipate that our selling, general and administrative expenses will increase in the future as we continue to commercialize EYSUVIS and INVELTYS and if and as we increase our administrative headcount to support our continued research and development activities and seek marketing approval for our product candidates.

Research and Development Expenses

The following table summarizes the research and development expenses incurred during the years ended December 31, 2020 and 2019:

	Year Ended December 31,		
	2020	2019	Change
	(in thousands)		
KPI-121 development costs	$ 4,686	$ 12,323	$ (7,637)
Employee-related costs	10,607	11,333	(726)
Other research and development costs	3,059	3,619	(560)
Total research and development	$ 18,352	$ 27,275	$ (8,923)

Research and development expenses were $18.4 million for the year ended December 31, 2020 compared to $27.3 million for the year ended December 31, 2019, a decrease of $8.9 million. The decrease was primarily the result of a $7.6 million decrease in EYSUVIS development costs related to a decrease in external spend on STRIDE 3, our Phase 3 clinical trial of EYSUVIS, a $0.7 million decrease in employee-related costs largely due to reduced travel due to COVID-19 and the decrease in the allocation of employee time dedicated to research and development and a $0.6 million decrease in other research and development costs, which include other facility related costs, preclinical studies, certain medical affairs and associated regulatory costs. We expect research and development costs to increase if and as we advance our development programs and conduct any necessary preclinical studies and clinical trials and other development activities for product candidates.

Interest Income

Interest income was $0.5 million for the year ended December 31, 2020, compared to $2.4 million for the year ended December 31, 2019, a decrease of $1.9 million. Interest income consists of interest earned on our cash, cash equivalents and short-term investments. The decrease was attributable to lower interest rates during the year ended December 31, 2020.

Interest Expense

Interest expense was $8.6 million for the year ended December 31, 2020, compared to $8.5 million for the year ended December 31, 2019, an increase of $0.1 million. Interest expense was comprised of the contractual coupon interest expense and the amortization of the debt discount associated with our Athyrium Credit Facility during the year ended December 31, 2020 and 2019. During the years ended December 31, 2020 and 2019, $75.0 million of indebtedness was outstanding under the Athyrium Credit Facility.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. As we commercially launched our first product, INVELTYS, in January 2019, and commenced a full promotional launch of our second product, EYSUVIS, in early January 2021, we have had limited revenues to date from product sales and have financed our operations primarily through proceeds from our IPO, follow-on public common stock offerings and sales of our common stock under our ATM Offerings, private placements of preferred stock, borrowings under credit facilities, convertible promissory notes and warrants.

In July 2017, we completed an IPO pursuant to which we issued and sold 6,900,000 shares of our common stock, which included 900,000 shares sold pursuant to the exercise of the underwriters' option to purchase additional shares, at a price of $15.00 per share. We received net proceeds of $94.0 million after deducting underwriting discounts and commission of $7.3 million and offering costs of $2.2 million.

On August 9, 2018, we filed our 2018 Shelf Registration under which we could initially offer and sell up to $250.0 million of a variety of securities including common stock, preferred stock, warrants, depositary shares, debt securities, purchase contracts, purchase units or any combination of such securities during the three-year period that commenced upon the 2018 Shelf Registration becoming effective. Under the 2018 Shelf Registration, we may periodically offer one or more types of securities in amounts, at prices and on terms announced, if and when the securities are ever offered.

On October 1, 2018, we entered into the Athyrium Credit Facility with Athyrium for up to $110.0 million. The Athyrium Credit Facility provided for a Term Loan A in the aggregate principal amount of $75.0 million, and a Term Loan B in the aggregate principal amount of $35.0 million. On October 1, 2018, we borrowed the entire principal amount of the Term Loan A. We did not satisfy the conditions to draw down any of the Athyrium Term Loan B funds, and as a result, the Term Loan B funds are no longer available. The maturity date of the Athyrium Credit Facility is October 1, 2024, the six-year anniversary of the close. The Term Loan A bears interest at a rate of 9.875% per annum, with quarterly, interest-only payments until the fourth anniversary of the Term Loan A. The unpaid principal amount of the Term Loan A is due and payable in quarterly installments starting at the end of the fourth anniversary of the loan.

On October 5, 2018, we sold 7,500,000 shares of common stock in an underwritten offering pursuant to the 2018 Shelf Registration at a public offering price of $8.25 per share, before underwriting discounts and commissions. In addition, the underwriters were granted an overallotment option to purchase an additional 1,125,000 shares of the common stock at the same public offering price, less underwriting discounts and commissions. On October 11, 2018, the underwriters exercised in full their option to purchase the overallotment shares. The total number of shares sold by us in the offering was 8,625,000 shares, resulting in net proceeds to us, after underwriting discounts and offering expenses, of $66.1 million. In connection with the filing of the 2018 Shelf Registration, we entered into a sales agreement with Jefferies, pursuant to which we could issue and sell, from time to time, up to an aggregate of $50.0 million of our common stock in an ATM Offering, through Jefferies, as sales agent. As of December 31, 2019, we had issued an aggregate of 2,592,934 shares of our common stock under the ATM Offering, resulting in net proceeds to us of $13.1 million. During the first quarter of 2020, we issued an aggregate of 2,352,671 shares of our common stock under the ATM Offering, resulting in net proceeds to us of $12.5 million. On March 10, 2020, we suspended and terminated the prospectus related to the ATM Offering.

On March 11, 2020, we sold 16,000,000 shares of our common stock in an underwritten offering pursuant to the 2018 Shelf Registration at a public offering price of $7.89 per share, resulting in net proceeds of $118.2 million, after underwriting discounts, commissions, and offering expenses. In addition, the underwriters of the offering were granted the option for a period of 30 days to purchase up to an additional 2,400,000 shares of common stock offered in the public offering at the public offering price, less underwriting discounts, commissions, and offering expenses. On April 3, 2020, the underwriters exercised their option and purchased an additional 979,371 shares of common stock at $7.89 per share, resulting in net proceeds to us of $7.2 million, after underwriting discounts, commissions, and offering expenses. The total number of shares sold by us in the offering was 16,979,371, resulting in total net proceeds to us, after underwriting discounts and offering expenses, of $125.4 million.

Under the 2018 Shelf Registration, we have issued an aggregate of 30,549,976 shares of common stock, including under the ATM Offering, resulting in aggregate gross proceeds to us of $231.7 million. There was $18.3 million of securities available to be issued under the 2018 Shelf Registration as of December 31, 2020.

On May 7, 2020, we filed our 2020 Shelf Registration, under which we may offer and sell up to $350.0 million of a variety of securities including common stock, preferred stock, warrants, depositary shares, debt securities or units during the three-year period that commenced upon the 2020 Shelf Registration becoming effective. In connection with the filing of the 2020 Shelf Registration, we entered into an amended and restated sales agreement with Jefferies, pursuant to which we may issue and sell, from time to time, up to an aggregate of $75.0 million of our common stock under our ATM Offering. During the fourth quarter of 2020, we issued an aggregate of 2,821,059 shares of our common stock under the ATM Offering, resulting in net proceeds to us of $20.6 million. In January 2021, we issued and sold an additional 2,552,457 shares of our common stock under our ATM Offering, resulting in net proceeds to us of $18.2 million. As of the date of this Annual Report on Form 10-K, there was $35.0 million of shares of common stock remaining under the ATM Offering that we may issue and sell in the future and, excluding the funds designated to be

offered under our ATM Offering, there was approximately $275.0 million of securities available to be issued under the 2020 Shelf Registration.

Cash Flows

As of December 31, 2020 and 2019, we had $153.5 million and $85.4 million, respectively, in cash, cash equivalents and short-term investments and $75.0 million in indebtedness. The indebtedness in 2020 and 2019 represented the aggregate principal amount that was outstanding under the Athyrium Credit Facility.

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,	
	2020	2019
	(in thousands)	
Net cash used in operating activities	$ (90,694)	$ (92,720)
Net cash used in investing activities	(78,209)	(1,335)
Net cash provided by financing activities	160,628	8,982
Decrease in cash and restricted cash	$ (8,275)	$ (85,073)

Operating Activities

Net cash used in operating activities for the year ended December 31, 2020 was $90.7 million compared to $92.7 million for the year ended December 31, 2019, a decrease of $2.0 million, primarily due to the timing of working capital fluctuations which accounted for $8.3 million of the decrease and partially offset by a $6.3 million increase in the net loss adjusted for non-cash charges. Notable working capital fluctuations include a decrease to accounts receivable in the year ended December 31, 2020 by $2.0 million driven by improved days sales outstanding in the year ended December 31, 2020, whereas accounts receivable had increased by $11.6 million in the year ended December 31, 2019 driven by the launch of INVELTYS. Inventory increased by a greater amount during the year ended December 31, 2019 due to an increase in manufacturing activity for INVELTYS. Offsetting these increases was a decrease in accrued expenses and other current liabilities during the year ended December 31, 2020 by $1.8 million, as compared to an increase in accrued expenses and other current liabilities in the year ended December 31, 2019 of $9.6 million.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2020 was $78.2 million compared to $1.3 million for the year ended December 31, 2019, an increase of $76.9 million, largely due to purchases of short-term investments in 2020 of $113.6 million and partially offset by $37.3 million of sales or maturities of short-term investments, respectively. Additionally, we used an additional $0.6 million in cash for capital expenditures and other assets in the year ended December 31, 2020 compared to the year ended December 31, 2019.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2020 was $160.6 million, an increase of $151.6 million compared to $9.0 million in the year ended December 31, 2019. This increase is due to $125.4 million of net proceeds from the sale of shares of our common stock in an underwritten offering under the 2018 Shelf Registration, $33.1 million of net proceeds from the sale of shares of our common stock under the ATM Offering, and $2.1 million of proceeds from the exercise of stock options and the issuance of common stock under our employee stock purchase plan in 2020. Net cash provided by financing activities for the year ended December 31, 2019 consisted of $8.4 million of net proceeds from the sale of shares of our common stock under the ATM Offering and $0.6 million of proceeds from the exercise of stock options and the issuance of common stock under our employee stock purchase plan.

Funding Requirements

We anticipate that our expenses will increase substantially as compared to prior periods as we continue to commercialize INVELTYS in the United States and execute our commercial launch plans for EYSUVIS, as a result of increased headcount, including management personnel to support our clinical, manufacturing and commercialization activities, expanded infrastructure, increased legal, compliance, accounting and investor and public relations expenses associated with being a public company and increased insurance premiums, among other factors. The anticipated increase in expenses from an increase in headcount includes the expansion of our sales force from 56 TSMs to 91 TSMs, which occurred in the fourth quarter of 2020, and our plan to further increase our sales force from 91 TSMs to approximately 125 TSMs, pending the status of the COVID-19 pandemic, in 2021.

Our expenses will also increase if and as we:

- continue to grow our sales, marketing and distribution capabilities in connection with the commercialization of EYSUVIS, INVELTYS and any product candidates, for which we may submit for and obtain marketing approval;
- continue to scale-up our manufacturing processes and capabilities to support commercialization of EYSUVIS and INVELTYS;
- seek regulatory approval for EYSUVIS and INVELTYS outside of the United States;
- progress our current and any future preclinical development programs;
- in license or acquire the rights to other products, product candidates or technologies;
- conduct clinical trials and other development activities and/or seek marketing approval for future product candidates;
- leverage our proprietary AMPPLIFY technology to seek to advance additional therapeutics into preclinical and clinical development;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control, scientific, manufacturing, commercial and management personnel;
- expand our operational, financial and management systems; and
- increase our product liability insurance coverage as we expand our commercialization efforts for EYSUVIS and INVELTYS.

We expect to continue to incur significant expenses and operating losses. Net losses may fluctuate significantly from quarter-to-quarter and year-to-year. We anticipate that our cash, cash equivalents and short-term investments as of December 31, 2020, along with anticipated revenue from INVELTYS and the $18.2 million net proceeds raised under the ATM Offering program in January 2021, will enable us to fund our operations, lease and debt service obligations, and capital expenditure requirements into at least the fourth quarter of 2022. We expect anticipated revenue generated from sales of EYSUVIS to provide additional cash runway. We have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. As a result, we could deplete our available capital resources sooner or later than we currently expect.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses will increase from what we anticipate if:

- we elect or are required by the FDA or non-U.S. regulatory agencies to perform clinical trials or studies in addition to those expected;
- there are any delays in enrollment of patients in or completing our clinical trials or the development of our product candidates;
- we in-license or acquire rights to other products, product candidates or technologies; or
- there are any third-party challenges to our intellectual property portfolio, or the need arises to defend against intellectual property-related claims or enforce our intellectual property rights.

Our ability to become and remain profitable depends on our ability to generate revenue. While we began to generate revenue from the sales of EYSUVIS and INVELTYS in late December 2020 and January 2019, respectively, there can be no assurance as to the amount or timing of any future revenue from EYSUVIS and INVELTYS, and we may not achieve profitability. Achieving and maintaining profitability will require us to be successful in a range of challenging activities, including:

- successfully launching EYSUVIS and growing EYSUVIS revenues;
- successfully growing INVELTYS revenues;
- achieving an adequate level of market acceptance and obtaining and maintaining coverage and adequate reimbursement from third-party payors for EYSUVIS, INVELTYS and any other products we commercialize;
- manufacturing at commercial scale, marketing, selling and distributing EYSUVIS and INVELTYS;
- maintaining regulatory and marketing approvals for EYSUVIS and INVELTYS;
- discovering, developing and successfully seeking marketing approval and commercialization of additional product candidates;
- hiring and building a full commercial organization required for marketing, selling and distributing those products for which we obtain marketing approval;
- obtaining, maintaining and protecting our intellectual property rights; and
- adapting our business in response to the current pandemic health event resulting from COVID-19 and its collateral consequences.

EYSUVIS and INVELTYS are our only products that have been approved for sale, and they have only been approved in the United States. We plan to seek approval in other jurisdictions, but may not do so successfully, or at all. Further, the successful commercialization of EYSUVIS and INVELTYS in the United States is subject to many risks. As a company, we have limited experience commercializing products, and we may not be able to do so successfully. There are numerous examples of unsuccessful product launches and failures to meet expectations of market potential, including by pharmaceutical companies with more experience and resources than us. Our revenue from sales of EYSUVIS and INVELTYS alone may not be sufficient for us to become profitable in the near future, if at all.

In addition, our recent commercialization efforts have been hampered by the operational restrictions on our sales force from quarantines, travel restrictions and bans and other governmental restrictions related to COVID-19. As a result of these restrictions, we previously suspended our sales force from substantially all in-person interactions with physicians and customers and were limited to conducting educational and promotional activities virtually. However, our sales force has resumed substantially all in-person interactions in the field. To the extent we restrict, or are restricted from, in-person interactions with physicians and customers, we are limited to conducting educational and promotional activities virtually, which has hampered, and may continue to hamper, our ability to market INVELTYS and could adversely affect our ability to launch and market EYSUVIS. In addition, government restrictions have at times led to moratoria on elective ocular surgeries in many jurisdictions, which has significantly reduced, and may in the future continue to significantly reduce, the demand for INVELTYS, which is indicated for the treatment of inflammation and pain following ocular surgery. The extent of the impact of COVID-19 on our commercialization efforts will depend on the length and severity of this pandemic, including the extent any resurgence of the COVID-19 virus and any variant strains of the virus, the availability and effectiveness of vaccines, and the impact of the foregoing on our customers, employees, vendors, and government agencies, which is uncertain and cannot be predicted.

We may never succeed in these activities and may never generate revenue that is sufficient to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, royalty agreements, and marketing and distribution arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include pledging of assets as collateral, covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our pledge of our assets as collateral to secure our obligations under our Athyrium Credit Facility may limit our ability to obtain additional debt financing. Under our Athyrium Credit Facility, we are also restricted from paying dividends on our common stock and limited with respect to certain other uses of our cash without the lenders' consent.

We may need to raise additional capital in the future to advance our business. Additional private or public financings may not be available to us on acceptable terms, or at all. Additionally, the COVID-19 pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could impact our ability to raise additional funds. The COVID-19 pandemic has also impacted, and may continue to impact, the volatility of our stock price and trading in our stock. Even after the COVID-19 pandemic has subsided, we may continue to experience adverse impacts to our business as a result of any economic recession or depression that has occurred or may occur in the future.

Our failure to raise capital as and when needed would have a material adverse effect on our financial condition and our ability to pursue our business strategy. If we raise additional funds through collaborations, strategic alliances, licensing arrangements, royalty agreements, or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or current or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission.

Recently Issued Accounting Pronouncements

From time to time the Financial Accounting Standards Board, or FASB, or other standard-setting bodies, issue new accounting pronouncements. Where applicable, we adopt these new standards according to the specified effective dates. Unless otherwise disclosed in Note 2 to the financial statements appearing at the end of this Annual Report on Form 10-K, we believe that the impact of any recently issued standard(s) that are not yet effective will not have a material impact on our financial position or results of operation upon adoption.

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

Our financial instruments consist primarily of cash equivalents and short-term investments. Our short-term investments as of December 31, 2020 consist of U.S. Government Agency and Treasury Securities. Due to the short-term maturities of our cash equivalents and short-term investments, and the fixed income nature of these investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our cash equivalents and short-term investments.

As of December 31, 2020 and 2019, the aggregate principal outstanding under the Athyrium Credit Facility was $75.0 million, which bears interest at a fixed rate of 9.875% per annum.

Item 8. Financial Statements and Supplementary Data

Our financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-32 of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures.

Evaluation of disclosure controls and procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2020. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2020, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's annual report on internal control over financial reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for the company. Internal control over financial reporting is defined in Rule 13a-15(f) or 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.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2020. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control—Integrated Framework (2013). Based on that assessment, our management concluded that, as of December 31, 2020, our internal control over financial reporting was effective.

As an "emerging growth company", as defined in the JOBS Act, our independent registered public accounting firm is not required to issue an attestation report on the internal control over financial reporting.

Changes in internal control over financial reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fourth quarter ended December 31, 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

Part III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2021 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

Item 11. Executive Compensation

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2021 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

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

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2021 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

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

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2021 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

Item 14. Principal Accountant Fees and Services

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2021 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

Part IV

Item 15. Exhibits, Financial Statement Schedules

(1) **Financial Statements.**

The following documents are included beginning on page F-1 attached hereto and are filed as part of this Annual Report on Form 10-K.

KALA PHARMACEUTICALS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

(2) **Financial Statement Schedules.**

No financial statement schedules have been filed as part of this Annual Report on Form 10-K because they are not applicable, not required or because the information is otherwise included in our financial statements or notes thereto.

(3) **Exhibits**.

The following is a list of exhibits filed or furnished as part of this Annual Report on Form 10-K.

Exhibit Number	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's current report on Form 8-K (File No. 001-38150) filed on July 25, 2017)
3.2	Amended and Restated By-laws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's current report on Form 8-K (File No. 001-38150) filed on July 25, 2017)
4.1	Specimen Stock Certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's registration statement on Form S-1/A (File No. 333-218936) filed on July 10, 2017)
4.2*	Third Amended and Restated Registration Rights Agreement of the Registrant dated April 4, 2016, as amended by Amendment No. 1 dated December 13, 2017, of the Registrant
4.3	Description of the Registrant's Securities Registered under Section 12 of the Exchange Act (incorporated by reference to Exhibit 4.3 of the Registrant's annual report on Form 10-K (File No. 001-38150) filed on February 12, 2020)
10.1+	2009 Employee, Director and Consultant Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.2+	Form of Stock Option Agreement under the 2009 Employee, Director and Consultant Equity Incentive Plan (incorporated by reference to Exhibit 10.2 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.3+	Amended and Restated 2017 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.1 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on May 9, 2019)

Exhibit Number	Description of Exhibit
10.4+	2017 Equity Incentive Plan, as amended (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-38150) filed on June 26, 2020)
10.5+	Form of Incentive Stock Option Agreement under 2017 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's registration statement on Form S-1/A (File No. 333-218936) filed on July 10, 2017)
10.6+	Forms of Non-Qualified Option Agreement under 2017 Equity Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's registration statement on Form S-1/A (File No. 333-218936) filed on July 10, 2017)
10.7+	Form of Non-Employee Director Restricted Stock Unit Award under 2017 Equity Incentive Plan (incorporated by reference to Exhibit 10.2 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on May 7, 2020)
10.8+	Form of Non-Employee Director Deferred Restricted Stock Unit Award under 2017 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on May 7, 2020)
10.9+	Form of Employee Restricted Stock Unit Award under 2017 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on August 6, 2020)
10.10+	Form of Inducement Stock Option Agreement (incorporated by reference to Exhibit 10.1 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on November 8, 2018)
10.11†	Exclusive License Agreement, dated November 10, 2009, by and between the Registrant and The Johns Hopkins University, as amended by the First Amendment dated November 19, 2012, the Second Amendment dated May 23, 2014 and the Third Amendment dated August 26, 2014 (incorporated by reference to Exhibit 10.7 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.12†	Fourth Amendment to Exclusive License Agreement, dated June 22, 2018, by and between the Johns Hopkins University and the Registrant (incorporated by reference to Exhibit 10.1 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on August 9, 2018)
10.13#	Fifth Amendment to Exclusive License Agreement, date July 6, 2020, by and between the Johns Hopkins University and the Registrant (incorporated by reference to Exhibit 10.2 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on August 6, 2020)
10.14†	Exclusive License Agreement, effective as of May 1, 2017, by and between the Registrant and The Johns Hopkins University (incorporated by reference to Exhibit 10.15 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.15†	Assignment, dated April 26, 2017, by and between the Registrant and The Johns Hopkins University (incorporated by reference to Exhibit 10.16 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.16†	Assignment, dated April 26, 2017, by and between the Registrant and The Johns Hopkins University (incorporated by reference to Exhibit 10.17 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.17†	Settlement and License Agreement, dated October 24, 2014, by and between the Registrant and GrayBug, LLC (incorporated by reference to Exhibit 10.8 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.18+	Inducement Stock Option Agreement by and between the Registrant and Eric L. Trachtenberg (incorporated by reference to Exhibit 10.2 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on August 9, 2018)
10.19+	Letter Agreement, dated March 25, 2018, by and between the Registrant and Eric L. Trachtenberg (incorporated by reference to Exhibit 10.3 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on August 9, 2018)
10.20+	Amended and Restated Letter Agreement, dated September 10, 2015, by and between the Registrant and Mark Iwicki, as amended by the First Amendment, dated September 28, 2017 (incorporated by reference to Exhibit 10.1 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on November 7, 2017)

Exhibit Number	Description of Exhibit
10.21+	Letter Agreement, dated November 6, 2017, by and between the Registrant and Todd Bazemore (incorporated by reference to Exhibit 10.12 of the Registrant's annual report on Form 10-K (File No. 001-38150) filed on April 2, 2018)
10.22+	Amended and Restated Letter Agreement, dated May 10, 2016, by and between the Registrant and Kim Brazzell (incorporated by reference to Exhibit 10.13 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.23+	Form of Amendment to Offer Letters (incorporated by reference to Exhibit 10.30 to the Registrant's annual report on Form 10-K (File No. 001-38150) filed on March 12, 2019)
10.24+	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors (incorporated by reference to Exhibit 10.14 to the Registrant's registration statement on Form S-1/A (File No. 333-218936) filed on July 10, 2017)
10.25†	Amended and Restated Master Services Agreement, dated October 4, 2017, by and between the Registrant and Altasciences company (formerly Alliance Contract Pharma, LLC) (incorporated by reference to Exhibit 10.18 of the Registrant's annual report on Form 10-K (File No. 001-38150) filed on April 2, 2018)
10.26*#	Amendment No. 1 to Amended and Restated Master Services Agreement, dated August 25, 2020 by and between the Registrant and Altasciences company (formerly Alliance Contract Pharma, LLC)
10.27†	Manufacturing and Supply Agreement, dated January 10, 2017, by and between the Registrant and Chemo Iberica SA (incorporated by reference to Exhibit 10.20 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.28†	Commercial Supply Agreement, dated June 27, 2016, by and between the Registrant and Catalent Pharma Solutions, LLC (incorporated by reference to Exhibit 10.19 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.29†	Amendment No. 1 to Commercial Supply Agreement, dated February 16, 2018, by and between the Registrant and Catalent Pharma Solutions, LLC (incorporated by reference to Exhibit 10.21 of the Registrant's annual report on Form 10-K (File No. 001-38150) filed on April 2, 2018)
10.30#	Amendment No. 2 to Commercial Supply Agreement, dated March 27, 2020, by and between the Registrant and Catalent Pharma Solutions, LLC (incorporated by reference to Exhibit 10.1 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on May 7, 2020)
10.31*#	Amendment No. 3 to Commercial Supply Agreement, dated December 11, 2020, by and between the Registrant and Catalent Pharma Solutions, LLC
10.32	Lease, dated as of February 28, 2018, by and between the Registrant and 480 Arsenal Group LLC (incorporated by reference to Exhibit 10.1 to the Registrant's current report on Form 8-K filed on March 12, 2018)
10.33	Credit Agreement, dated as of October 1, 2018, among the Registrant, as the Borrower, certain subsidiaries of the Borrower, as the Guarantors, Athyrium Opportunities III Acquisition LP, as the Administrative Agent, and the lenders (incorporated by reference to Exhibit 10.1 to the Registrant's current report on Form 8-K (File No. 001-38150) filed on October 2, 2018)
10.34	Security Agreement, dated October 1, 2018, by and among the Registrant and Athyrium Opportunities III Acquisition LP (incorporated by reference to Exhibit 10.2 to the Registrant's current report on Form 8-K (File No. 001-38150) filed on October 2, 2018)
10.35	Pledge Agreement, dated October 1, 2018, by and among the Registrant and Athyrium Opportunities III Acquisition LP (incorporated by reference to Exhibit 10.3 to the Registrant's current report on Form 8-K (File No. 001-38150) filed on October 2, 2018)
10.36	Common Stock Purchase Warrant, dated October 1, 2018, by and among the Registrant and Athyrium Opportunities III Acquisition LP (incorporated by reference to Exhibit 10.4 to the Registrant's current report on Form 8-K (File No. 001-38150) filed on October 2, 2018)
10.37	Amended and Restated Sales Agreement, dated May 7, 2020, by and between the Registrant and Jefferies LLC (incorporated by reference to Exhibit 1.2 to the Registrant's Registration Statement on Form S-3 (File No. 333-238087) filed on May 7, 2020)
21.1*	Subsidiaries of the Registrant
23.1*	Consent of Deloitte & Touche LLP

Exhibit Number	Description of Exhibit
31.1*	Rule 13a-14(a) Certification of Principal Executive Officer
31.2*	Rule 13a-14(a) Certification of Principal Financial Officer
32.1*	Certification of Principal Executive Officer pursuant to 18 U.S.C. §1350
32.2*	Certification of Principal Financial Officer pursuant to 18 U.S.C. §1350
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 herewith.

† Confidential treatment granted as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

+ Management contract or compensatory plan or arrangement filed in response to Item 15(a)(3) of the Instructions to the Annual Report on Form 10-K.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

KALA PHARMACEUTICALS, INC.

Dated: February 25, 2021

By: /s/ Mark Iwicki
Mark Iwicki
Chief Executive Officer, President and Chairman of the Board of Directors

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

/s/ Mark Iwicki Mark Iwicki	President, Chief Executive Officer and Chairman of Board of Directors (Principal Executive Officer)	February 25, 2021
/s/ Mary Reumuth Mary Reumuth	Chief Financial Officer (Principal Financial and Accounting Officer)	February 25, 2021
/s/ Gregory Grunberg Gregory Grunberg, M.D.	Director	February 25, 2021
/s/ Andrew I. Koven Andrew I. Koven	Director	February 25, 2021
/s/ Robert Paull Robert Paull	Director	February 25, 2021
/s/ Gregory Perry Greg Perry	Director	February 25, 2021
/s/ Howard Rosen Howard Rosen	Director	February 25, 2021
/s/ Rajeev Shah Rajeev Shah	Director	February 25, 2021

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the shareholders and the Board of Directors of Kala Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Kala Pharmaceuticals, Inc. and subsidiary (the "Company") as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows, for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 25, 2021

We have served as the Company's auditor since 2013.

PART I – FINANCIAL INFORMATION

Item 1. Consolidated Financial Statements.

KALA PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share amounts)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 77,264	$ 85,449
Short-term investments	76,276	—
Accounts receivable, net	9,604	11,563
Inventory	5,229	4,648
Prepaid expenses and other current assets	3,006	3,824
Total current assets	171,379	105,484
Non-current assets:		
Property and equipment, net	3,166	2,698
Long-term inventory	6,219	3,778
Right-of-use assets	27,853	29,781
Restricted cash and other long-term assets	12,989	12,582
Total assets	$ 221,606	$ 154,323
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,724	$ 2,518
Accrued expenses and other current liabilities	18,971	20,929
Current portion of lease liabilities	1,530	1,327
Total current liabilities	22,225	24,774
Long-term liabilities:		
Long-term lease liabilities	27,143	28,673
Long-term debt	72,243	71,184
Total long-term liabilities	99,386	99,857
Total liabilities	121,611	124,631
Commitments and Contingencies (Note 15)		
Stockholders' equity:		
Common stock, $0.001 par value; 120,000,000 shares authorized as of December 31, 2020 and December 31, 2019; 58,915,375 and 36,086,254 shares issued and outstanding as of December 31, 2020 and December 31, 2019, respectively	59	36
Additional paid-in capital	499,715	325,112
Accumulated other comprehensive income	4	—
Accumulated deficit	(399,783)	(295,456)
Total stockholders' equity	99,995	29,692
Total liabilities and stockholders' equity	$ 221,606	$ 154,323

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

KALA PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share amounts)

	Year Ended December 31,	
	2020	2019
Product revenues, net	$ 6,362	$ 6,074
Costs and expenses:		
Cost of product revenues	3,173	2,008
Selling, general and administrative	81,068	65,015
Research and development	18,352	27,275
Total costs and expenses	102,593	94,298
Loss from operations	(96,231)	(88,224)
Other income (expense):		
Interest and other income	493	2,357
Interest and other expense	(8,589)	(8,480)
Total interest and other expense	(8,096)	(6,123)
Net loss	$ (104,327)	$ (94,347)
Net loss per share—basic and diluted	$ (1.99)	$ (2.76)
Weighted average shares outstanding—basic and diluted	52,377,526	34,209,756
Net loss	$ (104,327)	$ (94,347)
Other comprehensive income:		
Change in unrealized gains on investments	4	—
Total other comprehensive income	4	—
Total comprehensive loss	$ (104,323)	$ (94,347)

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

KALA PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(In thousands, except share amounts)

	Common Stock $0.001 Par Value		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance as of December 31, 2018	33,863,077	$ 34	$306,053	$ —	$ (201,109)	$ 104,978
At the market offering, net of offering costs of $262	2,074,799	2	8,423	—	—	8,425
Exercise of stock options	24,714	—	42	—	—	42
Issuance under employee stock purchase plan	123,664	—	545	—	—	545
Stock-based compensation expense	—	—	10,049	—	—	10,049
Net loss	—	—	—	—	(94,347)	(94,347)
Balance as of December 31, 2019	36,086,254	$ 36	$325,112	$ —	$ (295,456)	$ 29,692
At the market offering, net of offering costs $1,026	5,173,730	5	33,129	—	—	33,134
Exercise of stock options	345,479	1	1,086	—	—	1,087
Common stock offering, net of offering costs of $8,475	16,979,371	17	125,406	—	—	125,423
Issuance under employee stock purchase plan	314,397	—	1,016	—	—	1,016
Stock-based compensation expense	—	—	13,966	—	—	13,966
Warrant exercises	16,144	—	—	—	—	—
Change in fair value of investments	—	—	—	4	—	4
Net loss	—	—	—	—	(104,327)	(104,327)
Balance as of December 31, 2020	58,915,375	$ 59	$499,715	$ 4	$ (399,783)	$ 99,995

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

KALA PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (104,327)	$ (94,347)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation and amortization	912	843
Non-cash operating lease cost	1,928	1,773
Amortization of debt discount and other non-cash interest	1,059	958
Stock-based compensation	13,312	9,991
Amortization of discount on available-for-sale securities	(5)	—
Change in operating assets and liabilities:		
Accounts receivable	1,959	(11,563)
Prepaid expenses and other current assets	818	(1,789)
Inventory	(2,368)	(4,271)
Accounts payable	(924)	(2,770)
Accrued expenses and other current liabilities	(1,763)	9,630
Lease liabilities and other long-term liabilities	(1,295)	(1,175)
Net cash used in operating activities	(90,694)	(92,720)
Cash flows from investing activities:		
Purchases of property and equipment and other assets	(1,942)	(1,335)
Purchases of short-term investments	(113,592)	—
Proceeds from sales or maturities of short-term investments	37,325	—
Net cash used in investing activities	(78,209)	(1,335)
Cash flows from financing activities:		
Proceeds from common stock offerings, net of offering costs	158,557	8,425
Payment of principal on finance lease	(32)	(30)
Proceeds from exercise of stock options and issuance of common stock under employee stock purchase plan	2,103	587
Net cash provided by financing activities	160,628	8,982
Net decrease in cash, cash equivalents and restricted cash:	(8,275)	(85,073)
Cash, cash equivalents and restricted cash at beginning of period	98,031	183,104
Cash, cash equivalents and restricted cash at end of period	$ 89,756	$ 98,031
Reconciliation of cash, cash equivalents and restricted cash:		
Cash, cash equivalents, and restricted cash at end of period	$ 89,756	$ 98,031
Less restricted cash (Notes 9 and 10)	(12,492)	(12,582)
Cash and cash equivalents at end of period	$ 77,264	$ 85,449
Non-cash investing and financing activities:		
Right-of-use asset obtained in exchange for finance lease obligation	$ —	$ 136
Purchases of property and equipment in accounts payable	130	195
Supplemental disclosure:		
Cash paid for interest	$ 7,528	$ 7,522
Right-of-use assets obtained in exchange of operating lease obligations	—	1,852

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

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Note 1: Nature of business

Nature of Business— Kala Pharmaceuticals, Inc. (the "Company") was incorporated on July 7, 2009, and is a biopharmaceutical company focused on the discovery, development and commercialization of innovative therapies for diseases of the eye. The Company has applied its AMPPLIFY® mucus-penetrating particle ("MPP") Drug Delivery Technology to loteprednol etabonate ("LE"), a corticosteroid designed for ocular applications, resulting in the U.S. Food and Drug Administration's (the "FDA") approval of EYSUVIS™ (loteprednol etabonate ophthalmic suspension) 0.25%, for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease, and INVELTYS ® (loteprednol etabonate ophthalmic suspension) 1% as the first and only topical twice-daily ocular corticosteroid for treatment of post-operative inflammation and pain following ocular surgery.

In January 2019, the Company launched its first commercial product, INVELTYS, in the United States and began shipping its second commercial product, EYSUVIS, to wholesalers in the United States in late December 2020 with the full promotional launch commencing in early January 2021. The Company is engaged in the commercialization of EYSUVIS and INVELTYS, research and development activities, raising capital and recruiting skilled personnel. The Company is subject to a number of risks similar to those of other companies conducting high-risk, research and development of pharmaceutical product candidates and launching products for the first time. Principal among these risks are dependence on key individuals and intellectual property, competition from other products and companies and the technical risks associated with the successful research, development and marketing of its product candidates. The Company's success is dependent upon its ability to successfully commercialize its products, the success of its research and development efforts, its ability to obtain regulatory approval of its product candidates, its ability to raise additional capital when needed and, ultimately, attain profitable operations.

The Company is also progressing its pipeline of proprietary preclinical development programs targeted to address front and back of the eye diseases. These preclinical development programs, all of which are new chemical entities, include its receptor Tyrosine Kinase Inhibitor program, that is designed to inhibit the vascular endothelial growth factor pathway, for the treatment of retinal diseases, including wet age-related macular degeneration; its selective glucocorticoid receptor modulators, which are a novel class of therapies designed to modify the downstream activity of the receptors to exhibit the anti-inflammatory and immunomodulatory properties of the corticosteroid class of therapies without their associated side effects; and its novel surface targeting steroid designed to target the ocular surface and thus have the potential to have fewer side effects compared to traditional topical steroids. The Company owns all intellectual property and worldwide rights to these pipeline preclinical development programs.

Recent Financings— On August 9, 2018, the Company filed a shelf registration statement on Form S-3 with the SEC, which was declared effective on August 27, 2018 (the "2018 Shelf Registration"). Under the 2018 Shelf Registration, the Company could initially offer and sell up to $250,000 of a variety of securities including common stock, preferred stock, warrants, depositary shares, debt securities, purchase contracts, purchase units or any combination of such securities during the three-year period that commenced upon the 2018 Shelf Registration becoming effective. On October 5, 2018, the Company sold 7,500,000 shares of the Company's common stock (the "Shares") in an underwritten offering pursuant to the 2018 Shelf Registration at a public offering price of $8.25 per share, before underwriting discounts and commissions. In addition, the underwriters were granted an overallotment option to purchase an additional 1,125,000 shares of the common stock at the same public offering price, less underwriting discounts and commissions (the "Overallotment Shares"). On October 11, 2018, the underwriters exercised in full their option to purchase the Overallotment Shares. The total number of Shares and Overallotment Shares sold by the Company in the offering was 8,625,000 shares, resulting in net proceeds to the Company, after underwriting discounts and offering expenses, of approximately $66,132.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

In connection with the filing of the Shelf Registration, the Company entered into a sales agreement with Jefferies, LLC (the "2018 Sales Agreement") pursuant to which the Company may issue and sell, from time to time, up to an aggregate of $50,000 of its common stock in an at-the-market equity offering ("ATM Offering") through Jefferies, LLC, as sales agent. As of December 31, 2019, the Company issued 2,592,934 shares of its common stock under the ATM Offering, resulting in net proceeds to the Company of $13,059. During the first quarter of 2020, the Company issued an aggregate of 2,352,671 shares of its common stock under the ATM Offering, resulting in net proceeds to the Company of $12,546. On March 10, 2020, the Company notified Jefferies that it was suspending and terminating the prospectus related to the 2018 Sales Agreement.

On March 11, 2020, the Company sold 16,000,000 shares of its common stock in an underwritten offering (the "2020 Offering"), pursuant to the 2018 Shelf Registration, at a public offering price of $7.89 per share, resulting in net proceeds of $118,207, after underwriting discounts, commissions, and offering expenses. In addition, the underwriters of the 2020 Offering were granted the option for a period of 30 days to purchase up to an additional 2,400,000 shares of common stock offered in the public offering at the public offering price, less underwriting discounts, commissions and offering expenses. On April 3, 2020, the underwriters exercised their option and purchased an additional 979,371 shares of common stock at $7.89 per share, resulting in net proceeds to the Company of $7,216, after underwriting discounts, commissions, and offering expenses. The total number of shares sold by the Company in the 2020 Offering was 16,979,371, resulting in total net proceeds to the Company, after underwriting discounts, commissions, and offering expenses, of $125,423. Under the 2018 Shelf Registration, the Company has issued an aggregate of 30,549,976 shares of common stock, including under the ATM Offering, resulting in aggregate gross proceeds of $231,666. There was $18,334 of securities available to be issued under the 2018 Shelf Registration as of December 31, 2020.

On May 7, 2020, the Company filed a shelf registration statement on Form S-3 with the SEC, which was declared effective on May 19, 2020, (the "2020 Shelf Registration"). Under the 2020 Shelf Registration, the Company may offer and sell up to $350,000 of a variety of securities including common stock, preferred stock, warrants, depositary shares, debt securities or units during the three-year period that commenced upon the 2020 Shelf Registration becoming effective. In connection with the filing of the 2020 Shelf Registration, the Company entered into an amended and restated sales agreement with Jefferies pursuant to which it may issue and sell, from time to time, up to an aggregate of $75,000 of its common stock under its ATM Offering through Jefferies, as a sales agent. During the fourth quarter of 2020, the Company issued an aggregate of 2,821,059 shares of its common stock under the ATM Offering, resulting in net proceeds of $20,612. As of December 31, 2020, there was approximately $53,751 of shares of common stock remaining under the ATM Offering that the Company may issue and sell in the future and, excluding the funds designated to be offered under its ATM Offering, there was approximately $275,000 of securities available to be issued under the 2020 Shelf Registration. In January 2021, the Company issued and sold an additional 2,552,457 shares of its common stock under its ATM Offering, resulting in net proceeds of $18,226. As of the date of this Annual Report on Form 10-K, there was $35,000 of shares of common stock remaining under the ATM Offering that we may issue and sell in the future.

On October 1, 2018, the Company entered into a credit agreement (the "Athyrium Credit Facility"), with Athyrium Opportunities III Acquisition LP ("Athyrium"). The Athyrium Credit Facility provides for a Term Loan A in the aggregate principal amount of $75,000 (the "Athyrium Term Loan A"), and a Term Loan B in the aggregate principal amount of $35,000 (the "Athyrium Term Loan B"). On October 1, 2018, the Company borrowed the entire principal amount of the Athyrium Term A Loan. The Company did not satisfy the conditions to draw down any of the Term Loan B funds, and as a result, the Term Loan B funds are no longer available.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

COVID-19 – The ongoing novel coronavirus pandemic, commonly referred to as COVID-19, which began in December 2019 and was declared a global pandemic by the World Health Organization on March 11, 2020, has spread worldwide, causing federal, state and local governments to implement measures to slow the spread of the pandemic through quarantines, strict travel restrictions and bans, heightened border scrutiny and other measures. In order to safeguard the health of its employees, the Company is following, and will continue to follow, recommendations from the U.S. Centers for Disease Control and Prevention, as well as federal, state and local governments, regarding working-from-home practices for non-essential employees. As a result, all office-based personnel have been instructed to work from home, and the Company's laboratory facilities, that support its early-stage research activities, are being utilized as necessary. In addition, the Company previously suspended its sales force from substantially all in-person interactions with physicians and customers and was limited to conducting educational and promotional activities virtually. However, the Company's sales force has resumed substantially all in-person interactions in the field. If it suspends all or some in-person interactions with physicians and customers in the future, or to the extent physicians and customers limit in-person interactions, the Company is limited to conducting educational and promotional activities virtually, which has hampered, and may continue to hamper, its ability to market INVELTYS. The effects of COVID-19 may also disrupt the full promotional launch and commercialization of EYSUVIS.

In addition, government restrictions have at times led to moratoria on elective ocular surgeries in many jurisdictions, which has significantly reduced, and may in the future continue to significantly reduce, the demand for INVELTYS, which is indicated for the treatment of post-operative inflammation and pain following ocular surgery. The extent of the impact of COVID-19 on the Company's commercialization efforts of EYSUVIS and INVELTYS and its operational and financial performance will depend on certain developments, including the length and severity of this pandemic and the impact on its customers, employees, vendors, and government agencies, all of which are uncertain and cannot be predicted. The Company cannot reasonably estimate the extent to which the disruption may materially impact its consolidated results of operations or financial position.

Note 2: Summary of Significant Accounting Policies

Principles of Consolidation—The accompanying consolidated financial statements include the accounts of Kala Pharmaceuticals, Inc. and its wholly owned subsidiary, Kala Pharmaceuticals Security Corporation, which is a Massachusetts subsidiary created to buy, sell and hold securities. All intercompany transactions and balances have been eliminated.

Basis of Presentation—The accompanying consolidated financial statements have been prepared on a going concern basis which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The Company has generated only limited revenues to date from product sales and has incurred recurring losses and negative cash flows from operations, including a net loss of $104,327 and $94,347, for the years ended December 31, 2020 and 2019, respectively, and used cash in operations of $90,694 and $92,720, in the years ended December 31, 2020 and 2019, respectively. The Company has financed its operations to date primarily through proceeds from its initial public offering of common stock ("IPO"), follow-on public offerings of common stock and sales of its common stock under its ATM Offering facility, private placements of preferred stock, borrowings under credit facilities, convertible debt financings and warrants. The Company has devoted substantially all of its financial resources and efforts to research and development, including preclinical studies and clinical trials and engaging in activities to launch and commercialize EYSUVIS and INVELTYS. The Company expects to continue to incur significant expenses and operating losses. Net losses may fluctuate from quarter-to-quarter and year-to-year.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

The Company expects that its cash, cash equivalents and short-term investments as of December 31, 2020, together with anticipated net revenue from sales of INVELTYS, will enable it to fund its operating expenses, debt service obligations and capital expenditure requirements for at least 12 months from the date these consolidated financial statements were issued. This evaluation is based on relevant conditions and events that are known and reasonably knowable at the date that the consolidated financial statements are issued. As a result, the Company could deplete its available capital resources sooner than it currently expects.

Use of Estimates— The preparation of consolidated financial statements in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, expense, and related disclosures. The Company bases estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. The Company evaluates its estimates and assumptions on an ongoing basis. Estimates and assumptions relied upon in preparing these consolidated financial statements relate to, but are not limited to, revenue recognition, inventory, the present value of lease liabilities and the corresponding right-of-use assets, the fair value of warrants, stock-based compensation, accrued expenses and the recoverability of the Company's net deferred tax assets and related valuation allowance. Actual results may differ from these estimates under different assumptions or conditions.

Product Revenues, Net— The Company sells EYSUVIS for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease, and INVELTYS, its topical twice-a-day ocular steroid for the treatment of post-operative inflammation and pain following ocular surgery, primarily to wholesalers in the United States ("Customers"). These Customers subsequently resell the Company's products to specialty and other retail pharmacies. In addition to agreements with Customers, the Company enters into arrangements with third-party payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts for the purchase of its products.

The Company accounts for revenue in accordance with Accounting Standards Codification ("ASC") Topic 606, *Revenue from Contracts with Customers*. Under ASC Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to be entitled in exchange for those goods or services. The Company performs the following five steps to recognize revenue under ASC Topic 606: (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 recognizes revenue when it is probable that it will collect the consideration to which it is entitled in exchange for the goods or services that will be transferred to the customer.

Performance Obligations

The Company determined that performance obligations are satisfied and revenue is recognized when a customer takes control of the Company's products, which occurs at a point in time. This generally occurs upon delivery of the products to customers, at which point the Company recognizes revenue and records accounts receivable. Payment is typically received 70 to 90 days after satisfaction of the Company's performance obligations.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Transaction Price and Variable Consideration

Revenue is measured as the amount of consideration the Company expects to receive in exchange for transferring products to a customer ("transaction price"). The transaction price for product sales includes variable consideration related to chargebacks, rebates, sales incentives and allowances, distribution service fees, and returns. The Company will estimate the amount of variable consideration that should be included in the transaction price. These estimates take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as the Company's historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. These provisions reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained and is included in net sales only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. In general, performance obligations do not include any estimated amounts of variable consideration that are constrained. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

The following table summarizes activity in each of the Company's product revenue provision and allowance categories for the years ended December 31, 2020 and 2019:

	Trade Discounts, Allowances and Chargebacks (1)	Product Returns (2)	Rebates and Incentives (3)
Balance as of January 1, 2019	$ —	$ —	$ —
Provision related to current period sales	4,031	321	24,812
Credit/payments made	(2,248)	(141)	(14,768)
Balance as of December 31, 2019	$ 1,783	$ 180	$ 10,044
Provision related to current period sales	3,937	207	23,265
Changes in estimate related to prior period sales	21	213	74
Credit/payments made	(4,584)	—	(28,479)
Balance as of December 31, 2020	$ 1,157	$ 600	$ 4,904

(1) Trade discounts, allowances and chargebacks include fees for distribution service fees, prompt pay and other discounts, and chargebacks. Trade discounts, allowances and chargebacks are deducted from gross revenue at the time revenues are recognized and are recorded as a reduction to accounts receivable on the Company's consolidated balance sheets.
(2) Provisions for product returns are deducted from gross revenues at the time revenues are recognized and are included in accrued expenses and other current liabilities on the Company's consolidated balance sheets.
(3) Rebates and incentives include managed care rebates, government rebates, co-pay program incentives, and sales incentives and allowances. Provisions for rebates and discounts are deducted from gross revenues at the time revenues are recognized and are included in accrued expenses and other current liabilities on the Company's consolidated balance sheets.

As of December 31, 2020 and 2019, the Company did not have any transaction price allocated to remaining performance obligations and any costs to obtain contracts with customers, including pre-contract costs and set up costs, were immaterial.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Accounts Receivable, net—Accounts receivable are reported on the consolidated balance sheets at outstanding amounts due from Customers for product sales. The Company deducts sales discounts for prompt payments and other discounts, contractual fees for service arrangements, and chargebacks from accounts receivable. The Company evaluates the collectability of accounts receivable on a regular basis, by reviewing the financial condition and payment history of Customers, an overall review of collections experience on other accounts, and economic factors or events expected to affect future collections experience. An allowance for doubtful accounts is recorded when a receivable is deemed to be uncollectible.

The Company recorded no allowance for doubtful accounts as of December 31, 2020 or December 31, 2019. The Company recorded an allowance of $1,157 and $1,783 for expected sales discounts, related to prompt pay discounts and other discounts, contractual fee for service arrangements and chargebacks, to wholesalers and distributors as of December 31, 2020 and December 31, 2019, respectively.

Cost of Product Revenues—The cost of product revenues consists primarily of materials, third-party manufacturing costs, freight and distribution costs, royalty expense, allocation of labor, quality control and assurance, reserves for defective inventory as well as excess or obsolete inventory, and other manufacturing overhead costs. The Company expensed cost of product revenues related to INVELTYS as research and development expenses prior to regulatory approval and expensed cost of product revenues related to EYSUVIS as research and development expenses prior to the determination that FDA approval was probable and before the future economic benefit of the drug was expected to be realized.

Cash and Concentration of Credit Risk—Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents, short-term investments and accounts receivable. Periodically, the Company maintains cash, cash equivalents, short-term investments in accredited financial institutions in excess of federally insured limits. The Company deposits its cash, cash equivalents, short-term investments in financial institutions that it believes have high credit quality and has not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Three Customers comprised 10% or more of the Company's accounts receivable balance as of December 31, 2020 and 2019. These Customers comprised 39%, 33% and 25% of the accounts receivable balance, respectively, as of December 31, 2020 and 41%, 35% and 23% of the accounts receivable balance, respectively, as of December 31, 2019. To date, the Company has not experienced any losses with respect to the collection of its accounts receivable and believes that its entire accounts receivable balances is collectible as of December 31, 2020. The same three Customers comprised 10% or more of the Company's revenue during the years ended December 31, 2020 and 2019. These Customers comprised 40%, 29% and 28% of revenue, respectively, during the year ended December 31, 2020 and 39%, 33% and 26% of revenue, respectively, during the year ended December 31, 2019. The Company has no financial instruments with off-balance sheet risk of loss.

Cash Equivalents—The Company considers all short-term, highly liquid investments with original maturities of 90 days or less at acquisition date to be cash equivalents.

Restricted Cash—As of December 31, 2020 and 2019, the Company had restricted cash of $12,492 and $12,582, respectively, which represents cash held to satisfy its financial covenant (See Note 10) and serve as collateral for the Company's vehicle fleet lease, credit cards and its facility lease in Watertown, Massachusetts (See Note 9). This cash is classified as a non-current asset and included within Restricted cash and other long-term assets in the accompanying consolidated balance sheets.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Investments—The Company determines the appropriate classification of its investments at the time of purchase. The Company's investments are classified as available-for-sale in accordance with ASC Topic 320. The Company classifies investments available to fund current operations as current assets on its consolidated balance sheets. Investments are classified as long-term assets on the consolidated balance sheets if (i) the Company has the intent and ability to hold the investments for a period of at least one year and (ii) the contractual maturity date of the investments is greater than one year.

Available-for-sale investments are recorded at fair value, with unrealized gains or losses included in comprehensive loss on the consolidated statements of operations and comprehensive loss and in accumulated other comprehensive income or loss on the consolidated balance sheets. Realized gains and losses, interest income earned on the Company's cash, cash equivalents and investments, and amortization or accretion of discounts and premiums on investments are included within other income (expense).

The Company reviews investments for other-than-temporary impairment whenever the fair value of an investment is less than the amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. The Company did not record any such impairments during the year ended December 31, 2020.

Inventory—Inventory is stated at the lower of cost or net realizable value, on a first-in, first-out method. Costs include amounts related to third party manufacturing, transportation, internal labor and overhead. The Company capitalizes pre-launch inventory when it believes regulatory approval and subsequent commercialization of the product candidate is probable and expects the future economic benefit of the drug to be realized. In doing so, management must consider a number of factors in order to determine the amount of inventory to be capitalized, including the historical experience of achieving regulatory approvals for the Company's similar products, the amount of inventory that is likely to be used in commercial production, receipt and analysis of positive Phase 3 clinical trial results for the underlying product candidate, results from meetings with the relevant regulatory authorities prior to the filing of regulatory applications and the compilation of the regulatory application. The Company also monitors the status of the product within the regulatory review and approval process, including all relevant communication with regulatory authorities. For inventories capitalized in preparation for product launch, anticipated future sales, expected shelf life and expected approval date are taken into account when evaluating realizability. The shelf life of a product is determined as part of the regulatory approval process; however, in assessing whether to capitalize pre-launch inventory, the Company considers the product stability data of all of the pre-launch inventory procured or produced to date to determine whether there is adequate shelf life. If management is aware of any specific material risks or contingencies other than the normal regulatory review and approval process, or if the criteria for capitalizing inventory produced prior to regulatory approval are otherwise not met, the Company would not capitalize such inventory costs, choosing instead to recognize such costs as a research and development expense in the period incurred. For INVELTYS, capitalization of costs as inventory began when the Company believed regulatory approval and subsequent commercialization of the product candidate was probable and expected the future economic benefit of the drug to be realized, which was concluded to be upon U.S. regulatory approval. For EYSUVIS, capitalization of costs as inventory began in the third quarter of 2020 when the Company believed regulatory approval and subsequent commercialization of the product candidate was probable and expected the future economic benefit of the drug to be realized.

Inventory produced that will be used in a promotional sample program is expensed to selling, general and administrative expense when it is designated as a sample. Long-term inventory includes raw materials, work-in-progress and/or finished goods inventory with an anticipated consumption or sale beyond one year based on the Company's forecasted expectations.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Leases—At the inception of an arrangement the Company determines whether the arrangement is or contains a lease. Most leases with a term greater than one year are recognized on the balance sheet as right-of-use assets, lease liabilities and, if applicable, long-term lease liabilities. The Company has elected not to recognize on the balance sheet leases with terms of one-year or less. Lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable. As such, the Company utilizes the appropriate incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received.

The components of a lease should be split into three categories: lease components (e.g., land, building, etc.), non-lease components (e.g., common area maintenance, maintenance, consumables, etc.), and non-components (e.g., property taxes, insurance, etc.). Then the fixed and in-substance fixed contract consideration (including any related to non-components) must be allocated based on fair values to the lease components and non-lease components. Although separation of lease and non-lease components is required, certain practical expedients are available to entities. Entities electing the practical expedient would not separate lease and non-lease components. Rather, they would account for each lease component and the related non-lease component together as a single component. The Company's facilities operating leases have lease and non-lease components which the Company has elected to use the practical expedient and account for each lease component and related non-lease component as one single component. The lease component results in a right-of-use asset being recorded on the consolidated balance sheets and amortized as lease expense on a straight-line basis to the consolidated statements of operations and comprehensive loss.

Property and Equipment, net—Property and equipment are recorded at cost. Depreciation is provided using the straight-line method over the estimated useful lives of the related assets. Depreciation expense is included in loss from operations on the consolidated statements of operations and comprehensive loss. Laboratory equipment and office and computer equipment is depreciated over three to five years. Leasehold improvements are depreciated over the shorter of their useful life or the life of the lease. Major additions and upgrades are capitalized; maintenance and repairs, which do not improve or extend the life of the respective assets, are expensed as incurred. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in loss from operations on the consolidated statements of operations and comprehensive loss.

Patent Costs—Costs to secure and defend patents are expensed as incurred and are classified as selling, general and administrative expenses in the Company's consolidated statements of operations and comprehensive loss.

Impairment of Long-Lived Assets—Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to their undiscounted expected future cash flows. If the undiscounted cash flows are insufficient to recover the carrying value, the assets are recorded at the lesser of the carrying value or fair value. For the years ended December 31, 2020 and 2019, no impairment charges were recorded.

Segment Information—Operating segments are identified as components of an enterprise about which separate discrete financial information is made available for evaluation by the chief operating decision maker ("CODM") in making decisions regarding resource allocation and assessing performance. The CODM is the Company's Chief Executive Officer. The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular focus is on the development and commercialization of innovative therapies for diseases of the eye. All of the Company's tangible assets are held in the United States. To date, all of the Company's revenue has been generated in the United States.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Research and Development Costs—Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits for full-time research and development employees, an allocation of facilities expenses, overhead expenses and other outside expenses. Research and development costs are expensed as incurred. The Company expenses costs relating to the production of inventory for its product candidates as research and development expenses within its consolidated statements of operations and comprehensive loss in the period incurred, until the point the Company believes regulatory approval and subsequent commercialization of the product candidate is probable and it expects the future economic benefit from sales of the drug to be realized. Research and development costs that are paid in advance of performance, including nonrefundable prepayments for goods or services, are deferred and capitalized as a prepaid expense. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

Accrued Expenses— The Company accrues for variable consideration related to rebates, sales incentives and allowances, and returns. Such estimates are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of the accrued expense. The Company also accrues expenses related to development activities performed by third parties based on an evaluation of services received and efforts expended pursuant to the terms of the contractual arrangements. Payments under some of these contracts depend on clinical trial milestones. There may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of expenses. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual or prepaid expense accordingly.

Stock-Based Compensation—The Company accounts for all stock-based awards granted as compensation expense at fair value. The Company generally issues stock-based awards with the measurement date for awards as the date of grant. Stock-based compensation costs are recognized as expense over the employees' requisite service period, which is the vesting period, on a straight-line basis. For performance awards whose vesting is contingent upon a specified event, the Company recognizes stock-based compensation expense over the derived service period, based on the probability of achievement of the specified event. The Company recognizes compensation expense for the portion of awards that have vested. Forfeitures are recorded as they occur. Stock-based compensation is classified in the accompanying consolidated statements of operations and comprehensive loss based on the function to which the related services are provided, or capitalized with inventory until related expense is recognized.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. The assumptions used in calculating the fair value of stock-based payment awards represent management's best estimates. The Company lacks sufficient company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and will continue to do so until it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future. The fair value of restricted stock units ("RSUs") and performance stock units ("PSUs") are equal to the closing sale price of the Company's common stock on the date of grant.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Income Taxes—Deferred tax assets and liabilities are recognized for the expected future tax consequences of events that have been included in the Company's consolidated financial statements and tax returns. Deferred tax assets and liabilities are determined based upon the differences between the consolidated financial statement carrying amounts and the tax basis of existing assets and liabilities and for loss and credit carryforwards using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if it is more likely than not that some portion or all of the deferred tax asset will not be realized.

The Company provides reserves for potential payments of tax to various tax authorities related to uncertain tax positions and other issues. The Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not that the position will be sustained on examination by the taxing authorities based on the technical merits of the position. The tax benefits recognized in the consolidated financial statements from such a position is measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate settlement. As a result, reserves are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present.

Net Loss per Share—Basic net loss per share is computed using the weighted-average number of common shares outstanding during the period. Diluted net loss per share is computed using the weighted average number of common shares outstanding during the period and, if dilutive, the weighted average number of potential shares of common stock, including the assumed exercise of stock options and warrants and the issuance of unvested RSUs and PSUs.

The weighted average number of common shares included in the computation of diluted net loss gives effect to all potentially dilutive common equivalent shares, including outstanding stock options, warrants and unvested RSUs and PSUs. Common stock equivalent shares are excluded from the computation of diluted net loss per share if their effect is antidilutive. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2020 and 2019.

As of December 31, 2020 and 2019, potentially dilutive securities excluded from the calculation of diluted net loss per share because including such securities would have an anti-dilutive effect consisted of outstanding options to purchase 8,745,127 and 7,453,076 shares of the Company's common stock, respectively, an aggregate of 942,222 unvested RSUs and PSUs as of December 31, 2020 and an aggregate of 248,505 and 384,163 unexercised warrants as of December 31, 2020 and 2019, respectively.

Recent Accounting Pronouncements

In August 2018, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2018-13, *Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"). ASU 2018-13 is intended to improve the effectiveness of disclosures in the notes to financial statements related to fair value measurements in Topic 820. The ASU was effective on January 1, 2020 and the adoption of ASU 2018-13 did not have a material effect on the Company's consolidated financial statements.

In August 2018, the FASB issued ASU 2018-15*, Intangibles – Goodwill and Other – Internal-Use Software - Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract* ("ASU 2018-15"). ASU 2018-15 aligns the accounting for implementation costs incurred in a hosting arrangement that is a service contract with the guidance on capitalizing costs associated with developing or obtaining internal-use software. The ASU was effective on January 1, 2020 and the adoption of ASU 2018-15 did not have a material effect on the Company's consolidated financial statements.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). ASU 2016-13 significantly changes the impairment model for most financial assets and certain other instruments. ASU 2016-13 will require immediate recognition of estimated credit losses expected to occur over the remaining life of many financial assets, which will generally result in earlier recognition of allowances for credit losses on loans and other financial instruments. In November 2019, the FASB issued ASU 2019-10, *Financial Instruments – Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842)* ("ASU 2019-10"), which is effective for public business entities that meet the definition of an SEC filer, excluding entities eligible to be Smaller Reporting Companies ("SRCs") as defined by the SEC, for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years and for all other entities, including SRCs, for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Upon adoption, beginning January 1, 2023, the Company does not expect ASU 2019-10 to have a material effect on its consolidated financial statements.

Note 3: Fair Value of Financial Instruments

The Company has short-term investments which are considered financial instruments that are measured on a recurring basis. ASC 820, *Fair Value Measurements and Disclosures*, establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and its own assumptions (unobservable inputs). The hierarchy consists of three levels:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's financial instruments consist primarily of cash equivalents and short-term investments in money market funds and short-term securities. Cash equivalents and short-term investments are reported at their respective fair values on the Company's consolidated balance sheets. See Note 4, "Investments" for additional information.

The following table sets forth the fair value of the Company's financial assets by level within the fair value hierarchy as of December 31, 2020:

	December 31, 2020			
	Fair Value	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$ 63,811	$ 63,811	$ —	$ —
Short-term investments	76,276	76,276	—	—
Total Assets	$ 140,087	$ 140,087	$ —	$ —

During the year ended December 31, 2020 there were no transfers between Level 1, Level 2, and Level 3. There were no cash equivalents or short-term investments as of December 31, 2019.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

The carrying value reported on the accompanying consolidated balance sheets of cash, restricted cash, accounts receivable, accounts payable and accrued expenses approximate their fair value due to their short-term nature. Management believes that the Company's long-term debt (see Note 10) bears interest at the prevailing market rate for instruments with similar characteristics and, accordingly, the carrying value of long-term debt, also approximates its fair value. The fair value of the outstanding debt was estimated using a discounted cash flow analysis based on current market interest rates for debt issuances with similar remaining years to maturity, adjusted for credit risk, which represents a Level 3 measurement.

Note 4: Investments

Investments by security type consisted of the following as of December 31, 2020:

	December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	$ 26,744	$ 2	$ —	$ 26,746
U.S. government agencies securities	49,528	2	—	49,530
Total	$ 76,272	$ 4	$ —	$ 76,276

As of December 31, 2020, all of the Company's investments had a contractual maturity within one year. The fair value of all of the Company's investments are classified as short-term on its consolidated balance sheets. The Company did not have any investment securities as of December 31, 2019.

Note 5: Inventory

Inventory consists of the following:

	December 31, 2020	December 31, 2019
Raw materials	$ 801	$ 1,387
Work in progress	6,437	4,166
Finished goods	4,210	2,873
Total inventory	$ 11,448	$ 8,426

As of December 31, 2020, the Company had $5,229 of current inventory and $6,219 of long-term inventory. As of December 31, 2019, the Company had $4,648 of current inventory and $3,778 of long-term inventory.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Note 6: Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets, consists of the following:

	December 31, 2020	December 31, 2019
Insurance	$ 1,201	$ 906
Deposits	606	699
Non-trade receivables	250	1,535
Other	949	684
Prepaid expenses and other current assets	$ 3,006	$ 3,824

Note 7: Property and Equipment, Net

Property and equipment, net, consists of the following:

	December 31, 2020	December 31, 2019
Equipment	$ 2,652	$ 2,627
Furniture and office equipment	1,144	1,144
Computer hardware and software	1,108	892
Leasehold improvements	356	356
Construction in progress	1,330	195
Property and equipment—at cost	6,590	5,214
Less: Accumulated depreciation	(3,424)	(2,516)
Property and equipment—net	$ 3,166	$ 2,698

Depreciation expense for the years ended December 31, 2020 and 2019 was $908 and $843, respectively.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Note 8: Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2020	December 31, 2019
Compensation and benefits	$ 9,676	$ 6,502
Accrued revenue reserves (1)	5,224	9,482
Commercial costs	2,103	930
Professional services	926	760
Contract manufacturing	336	630
Development costs	154	1,600
Other	552	1,025
Accrued expenses	$ 18,971	$ 20,929

(1) As of December 31, 2020 and 2019, $280 and $742 of additional revenue reserves were in accounts payable, respectively.

Note 9: Lease

Operating leases

On February 28, 2018, the Company entered into a lease agreement with 480 Arsenal Group LLC (the "Arsenal Group") for the lease of a portion of the building located at 490 Arsenal Way Watertown, Massachusetts (the "Watertown Lease"). The initial term of the Watertown Lease is eight years with an option to extend for an additional five years, which are recognized as part of the Company's right of use asset and lease liability. The Company occupied the premises in Watertown in early 2019 as its corporate headquarters and for research and development. The lease commencement date was November 15, 2018 and the Company concluded that it controlled the space, as of the lease commencement date.

The Company identified and assessed the following significant assumptions in recognizing the right-of-use asset and corresponding liability for the Watertown Lease.

- *Expected lease term* – The expected lease term includes both contractual lease periods and, when applicable, cancelable option periods where failure to exercise such options would result in an economic penalty.

- *Incremental borrowing rate* - As the Company's lease does not provide an implicit rate, the Company estimated the incremental borrowing rate based on a yield curve analysis, utilizing the interest rate derived from the fair value analysis of the Company's Athyrium Credit Facility and adjusting it for factors that reflect the profile of secured borrowing over the expected term of the lease.

The Company recognized the right-of-use asset and corresponding lease liability by calculating the present value of lease payments, discounted at 9.9%, the Company's estimated incremental borrowing rate, over the 13 year expected term. As of December 31, 2020, the remaining lease term on the Watertown Lease was 10.8 years. Variable lease expense for the Watertown Lease, includes real estate taxes, common area maintenance, and management fees.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

In connection with the Watertown Lease, the Company issued a letter of credit to the Arsenal Group for $2,042. The Company secured the letter of credit for the full amount of the letter with cash on deposit, which is reported as restricted cash on the consolidated balance sheets as of December 31, 2020 and December 31, 2019.

Vehicle Fleet lease

During the year ended December 31, 2019, the Company entered into a master fleet lease agreement (the "Vehicle Fleet Lease"), pursuant to which it currently leases approximately 65 vehicles. In connection with the Vehicle Fleet Lease, the Company issued a letter of credit for $450, which is reported as restricted cash on the consolidated balance sheets as of December 31, 2020 and December 31, 2019. The Vehicle Fleet Lease has an expected term of three years, which commenced upon the delivery of the vehicles in March 2019. As of December 31, 2020, the remaining lease term was 1.2 years.

The components of lease expense and related cash flows were as follows:

	Year Ended December 31,	
	2020	2019
Lease cost		
Operating lease cost	$ 4,741	$ 4,614
Variable lease cost	1,848	1,766
Total lease cost	$ 6,589	$ 6,380
Operating cash outflows from operating leases	$ 5,981	$ 5,445

Maturities of lease liability due under these operating lease agreements as of December 31, 2020 are as follows:

Years Ending December 31,	
2021	$ 4,274
2022	4,062
2023	3,960
2024	4,079
2025	4,201
Thereafter	27,135
Total minimum lease payments	47,711
Less: amount representing interest	(19,038)
Present value of lease liabilities	$ 28,673

Note 10: Debt

On October 1, 2018, the Company entered into a credit agreement (the "Athyrium Credit Facility") with Athyrium Opportunities III Acquisition LP ("Athyrium") for up to $110,000. The Athyrium Credit Facility provided for a Term Loan A in the aggregate principal amount of $75,000 (the "Term Loan A"), and a Term Loan B in the aggregate principal amount of $35,000 (the "Term Loan B"). On October 1, 2018, the Company borrowed the entire principal amount of the Term Loan A. The Company did not satisfy the conditions to draw down any of the Term Loan B funds, and as a result, the Term Loan B funds are no longer available. The maturity date of the Athyrium Credit Facility is October 1, 2024, the six-year anniversary of the close.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

The Term Loan A bears interest at a rate of 9.875% per annum, with quarterly, interest-only payments until the fourth anniversary of the Term Loan A. The unpaid principal amount of the Term Loan A is due and payable in quarterly installments starting on October 1, 2022. The Company may make voluntary prepayments, in whole or in part, and subject to certain exceptions, is required to make mandatory prepayments upon the occurrence of certain events of default as defined in the agreement, including but not limited to, the occurrence of a change of control. In addition, upon payment or repayment of any outstanding balance under the Athyrium Credit Facility, the Company will have to pay a 1% exit fee of the total principal payments (whether mandatory, voluntary, or at maturity) made throughout the term. The exit fee of $750 based on the $75,000 principal amount outstanding, will be accreted to the carrying amount of the debt using the effective interest method over the term of the loan.

All mandatory and voluntary prepayments of the Athyrium Credit Facility are subject to the payment of prepayment premiums as follows: (i) if prepayment occurs prior to the second anniversary of the applicable date of issuance, an amount equal to the amount by which (a) the present value of 105% of the principal prepaid plus all interest that would have accrued on such principal through such second anniversary exceeds (b) the amount of principal prepaid, (ii) if prepayment occurs on or after the second anniversary of the applicable date of issuance but prior to the third anniversary of such issuance, an amount equal to 3% of the principal prepaid, and (iii) if prepayment occurs on or after the third anniversary of the applicable date of issuance but prior to the fourth anniversary of such issuance, an amount equal to 2% of the principal prepaid. No prepayment premium is due on any principal prepaid after the fourth anniversary of the applicable date of issuance.

The Athyrium Credit Facility includes features requiring (1) additional interest rate upon an event of default accrued at an additional 3%, or a total interest rate of 12.875%, and (2) the lender's right to declare all outstanding principal and interest immediately payable upon an event of default. These two features were analyzed and determined to be embedded derivatives to be valued as separate financial instruments. These embedded derivatives were bundled and valued as one compound derivative in accordance with the applicable accounting guidance for derivatives and hedging transactions. The Company determined that, due to the unlikely event of default, the embedded derivatives have a *de minimis* value as of December 31, 2020. The derivative liability will be remeasured at fair value at each reporting date, with changes in fair value being recorded as other income (expense) in the consolidated statements of operations and comprehensive loss.

The Athyrium Credit Facility is secured by a pledge of substantially all of the Company's assets and contains affirmative and negative covenants customary for financings of this type, including limitations on the Company's and its subsidiaries' ability to, among other things, incur and prepay additional debt, grant or permit additional liens, make investments and acquisitions, merge or consolidate with others, dispose of assets, change in the nature of business, enter into sale and leaseback transactions, make distributions, and enter into affiliate transactions, in each case, subject to certain exceptions. In addition, the Athyrium Credit Facility also contains a financial covenant requiring the Company to maintain at least $10,000 of cash and cash equivalents. As a result of this financial covenant, the Company has recorded $10,000 as restricted cash as of December 31, 2020 and December 31, 2019. As of December 31, 2020, the Company was in compliance with the covenants.

In connection with the Athyrium Credit Facility, the Company issued a warrant ("Warrant"), to purchase up to 270,835 shares of the Company's common stock, at an exercise price per share of $12.18456. The Warrant is immediately exercisable as to 184,660 shares. The remaining 86,175 shares under the Warrant were exercisable only upon the Company's draw of the Term Loan B and, as a result, the remaining 86,175 shares under the Warrant are no longer exercisable. The Warrant is exercisable through October 1, 2025 and is classified as an equity instrument. The Company allocated the proceeds from the Term Loan A to the Warrant using the relative fair value method. The fair value of the Warrant of $1,900 was recognized as equity with a corresponding debt discount of $1,980.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

In addition, the Company paid certain fees to Athyrium and other third-party service providers. These fees paid to Athyrium were recorded as a debt discount while the fees paid to other third-party service providers were recorded as debt issuance cost. These costs, along with the fair value of the Warrant of $1,900 are being amortized using the effective interest method over the term of the Athyrium Credit Facility. The amortization of debt discount and debt issuance cost is included in interest expense within the consolidated statements of operations and comprehensive loss. As of December 31, 2020, the effective interest rate was 11.63%, which takes into consideration the non-cash accretion of the exit fee and the amortization of the debt discount and issuance costs. During the year ended December 31, 2020, the Company recognized interest expense of $8,440 which consisted of amortization of the debt discount of $910, and the contractual coupon interest expense of $7,530. During the year ended December 31, 2019, the Company recognized interest expense of $8,316, which consisted of amortization of the debt discount of $807, and the contractual coupon interest expense of $7,509.

The components of the carrying value of the debt as of December 31, 2020 and December 31, 2019 are detailed below:

	December 31, 2020	December 31, 2019
Principal loan balance	$ 75,000	$ 75,000
Unamortized debt discount and issuance cost	(3,088)	(3,999)
Cumulative accretion of exit fee	331	183
Long-term debt, net	$ 72,243	$ 71,184

The annual principal payments due under the Athyrium Credit Facility as of December 31, 2020 were as follows:

Years Ending December 31,	
2021	$ —
2022	16,665
2023	33,330
2024	25,005
Total	$ 75,000

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Note 11: Warrants

The Company has issued warrants in connection with debt transactions that were completed prior to 2017.

In connection with and in consideration for the commitment of the Athyrium Credit Facility, on October 1, 2018, the Company issued to Athyrium the Warrant as described in Note 10.

The following table summarizes the common stock warrants outstanding as of December 31, 2020 and December 31, 2019, each exercisable into the number of shares of common stock set forth below as of the specified dates:

Issued	Exercise Price	Expiration Date	Exercisable From	Shares Exercisable at December 31, 2020	Shares Exercisable at December 31, 2019
2013	$ 7.50	April 2021	July 2017	33,333	82,816
2014	$ 7.50	November 2024	July 2017	16,000	16,000
2016	$ 8.27	October 2026	September 2017	14,512	14,512
2018	$ 12.18	October 2025	October 2018	184,660	184,660
				248,505	297,988

Note 12: Common and Preferred Stock

Preferred Stock

The Company was authorized to issue up to 5,000,000 shares of preferred stock as of December 31, 2020 and 2019. There was no preferred stock outstanding as of December 31, 2020 and 2019.

Common Stock

The Company was authorized to issue up to 120,000,000 shares of common stock with a $0.001 par value per share as of December 31, 2020 and 2019. The Company had 58,915,375 and 36,086,254 shares of common stock issued and outstanding as of December 31, 2020 and 2019, respectively.

Holders of the Company's common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Each election of directors by the Company's stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by the Company's Board of Directors (the "Board"), subject to any preferential dividend rights of outstanding preferred stock that it may issue in the future.

In the event of the Company's liquidation or dissolution, the holders of its common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any of its outstanding preferred stock. Holders of the Company's common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of the Company's common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of its preferred stock that it may designate and issue in the future.

Voting, dividend and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers and preferences of the holders of preferred stock that the Company may issue in the future.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Voting

Each holder of outstanding shares of common stock shall be entitled to one vote in respect of each share. The holders of outstanding shares of common stock, voting together as a single class, shall be entitled to elect one director. The number of authorized shares of common stock may be increased or decreased by the affirmative vote of a majority of the outstanding shares of common stock and preferred stock voting together as a single class.

Dividends

Subject to the payment in full of all preferential dividends to which the holders of preferred stock may be entitled, the holders of common stock shall be entitled to receive dividends out of funds legally available therefor at such times and in such amounts as the Board may determine in its sole discretion, with holders of preferred stock and common stock sharing pari passu in such dividends.

Liquidation Rights

Upon any liquidation, after the payment or provision for payment of all debts and liabilities of the Company and all preferential amounts to which the holders of preferred stock may be entitled with respect to the distribution of assets in liquidation, the holders of common stock shall be entitled to share ratably in the remaining assets of the Company available for distribution.

Reserved Shares

As of December 31, 2020 and 2019, the Company has reserved shares of common stock for issuance upon exercise of rights under warrants, under the Amended and Restated 2017 Employee Stock Purchase Plan (as amended, the "ESPP"), upon the exercise of stock options and upon the vesting of RSUs and PSUs as follows (see Note 13):

	December 31, 2020	December 31, 2019
Warrant rights to acquire common stock	248,505	384,163
ESPP	484,772	438,307
Outstanding inducement stock option awards	945,842	705,500
2009 Plan	2,251,570	2,530,586
2017 Plan	7,813,784	4,429,849
Total	11,744,473	8,488,405

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Note 13: Stock-based Compensation

Stock Incentive Plans

In December 2009, the Board adopted the 2009 Employee, Director and Consultant Equity Incentive Plan (the "2009 Plan") for the issuance of common stock and stock options to employees, officers, directors, consultants, and advisors. Upon the closing of the Company's IPO, no further awards will be made under the 2009 Plan.

In July 2017, the Company's 2017 Equity Incentive Plan (the "2017 Plan") became effective. The 2017 Plan was established to provide equity-based ownership opportunities for employees, officers, directors, consultants, and advisors. On June 25, 2020, the 2017 Plan was amended to increase the number of shares of common stock authorized for issuance thereunder by 2,000,000 shares. As of December 31, 2020, there were 1,323,847 shares of common stock available for grant under the 2017 Plan. In addition, any shares of common stock subject to awards under the 2009 Plan that expire, are forfeited, or are otherwise surrendered, without having been fully exercised or resulting in any common stock being issued will become available for issuance under the 2017 Plan, up to an additional 2,251,570 shares, which is the number of shares issuable pursuant to outstanding awards granted under the 2009 Plan.

Also approved under the 2017 Plan is an annual increase for each of the years through December 31, 2027, equal to the least of (i) 3,573,766 shares of common stock, (ii) 4% of the shares of common stock outstanding on December 31 of the prior year and (iii) an amount determined by the Board.

Under the plans, the Board determines the number of shares of common stock to be granted pursuant to the awards, as well as the exercise price and terms of such awards. The exercise price of incentive stock options cannot be less than the fair value of the common stock on the date of grant. Stock options awarded under the plans expire 10 years after the grant date, unless the Board sets a shorter term. Options granted under the plans generally vest over a four-year period. A portion of the unvested stock options will vest upon the sale of all or substantially all of the stock or assets of the Company.

Inducement Stock Option Awards

During the years ended December 31, 2020 and December 31, 2019, the Company granted non-statutory stock options to purchase an aggregate of 350,800 shares and 207,500 shares of the Company's common stock, respectively, to new employees. These stock options will vest over a four-year period, with 25% of the shares underlying each option award vesting on the one-year anniversary of the applicable employees' new hire date and the remaining 75% of the shares underlying each option award vesting monthly thereafter for three-years. Vesting of each option award is subject to such employee's continued service with the Company through the applicable vesting dates. These stock options were granted outside of the 2017 Plan as an inducement material to each employee's acceptance of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

A summary of option activity for employee awards under the 2009 Plan, the 2017 Plan and inducement grants for the year ended December 31, 2020 is as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of January 1, 2020	7,453,076	$ 7.46	7.7	$ 1,313
Granted	1,816,222	4.63		
Exercised	(345,479)	3.15		
Forfeited	(178,692)	8.30		
Outstanding as of December 31, 2020	8,745,127	$ 7.03	7.3	$ 16,275
Vested or expected to vest as of December 31, 2020	8,745,127	$ 7.03	7.3	$ 16,275
Options exercisable as of December 31, 2020	5,362,040	$ 7.45	6.5	$ 10,235

The Company records stock-based compensation related to stock options granted at fair value. The Company utilizes the Black-Scholes option-pricing model to estimate the fair value of stock option grants and to determine the related compensation expense. The assumptions used in calculating the fair value of stock-based payment awards represent management's best estimates. The assumptions used in determining fair value of the stock options granted during the years ended December 31, 2020 and 2019 are as follows:

	Year Ended December 31,	
	2020	2019
Expected volatility	79.6% – 82.5%	80.7% – 83.7%
Risk-free interest rate	0.37% – 1.73%	1.44% – 2.58%
Expected dividend yield	0%	0%
Expected term (in years)	5.91 – 6.08	5.27 – 6.63

The Company derived the risk-free interest rate assumption from the U.S. Treasury rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the awards being valued. The Company based the expected dividend yield on its expectation of not paying dividends in the foreseeable future. The Company calculated the expected term of options using the simplified method, as the Company lacks relevant historical data due to the Company's limited operating experience. The expected volatility is based upon the historical volatility of comparable companies with publicly available share prices. The impact of forfeitures on compensation expense is recorded as they occur.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

The weighted average grant-date fair value of options granted during the years ended December 31, 2020 and 2019, was $3.20 and $3.45, respectively. The fair value is being expensed over the vesting period of the options on a straight-line basis as the services are being provided. As of December 31, 2020 and 2019, there was $15,753 and $19,201, respectively, of unrecognized compensation cost related to the stock options granted, which is expected to be expensed over a weighted-average period of 2.35 years and 2.31 years, respectively. Stock-based compensation expense was classified in the consolidated statements of operations and comprehensive loss as follows:

	Year Ended December 31,	
	2020	2019
Cost of product revenues	$ 92	$ 268
Research and development	3,083	2,844
Selling, general and administrative	10,137	6,879
Total	$ 13,312	$ 9,991

Stock-based compensation costs capitalized into inventory totaled $888 and $59 for the years ended December 31, 2020 and 2019, respectively. Capitalized stock-based compensation is recognized as an expense in cost of product revenues when the related product is sold or in selling, general and administrative expense when the related product is designated as a sample.

The Company received cash proceeds from the exercise of stock options of $1,087 and $42 during the years ended December 31, 2020 and 2019, respectively. The total intrinsic value of options exercised for the year ended December 31, 2020 and 2019, was $2,124 and $98, respectively.

Restricted Stock Units and Performance-Based Restricted Stock Units—In June 2020, the Company issued RSUs to certain executives and Board members, as well as PSUs to certain executives and other employees. The Company granted 135,560 RSUs to certain executives which vest 50% on the first anniversary of the grant date, and 50% on the second anniversary of the grant date. Additionally, the Company issued 128,000 RSUs to members of the Board which will vest upon the earlier of the first anniversary of the 2020 Annual Meeting of Stockholders or the date of the 2021 Annual Meeting of Stockholders. The Company issued 693,537 PSUs to certain executives and other employees tied to certain performance criteria, which will vest, if at all, as to 50% on the first anniversary of satisfying the performance criteria and the remaining 50% vesting upon the second anniversary of satisfying the performance criteria. The Company has determined that the performance criteria for these awards has been achieved but the awards have not vested as of December 31, 2020. As of December 31, 2020, a total of 942,222 RSUs and PSUs were unvested and outstanding, which results in unrecognized stock-based compensation of $7,315 to be recognized as stock-based compensation expense over the remaining weighted-average vesting period of 1.16 years.

A summary of activity for RSUs and PSUs for the year ended December 31, 2020 is as follows:

	Shares	Weighted Average Grant Date Fair Value
Unvested and outstanding balance as of January 1, 2020	—	$ —
Changes during the period:		
RSUs granted	263,560	11.70
PSUs granted	693,537	11.70
PSUs forfeited	(14,875)	11.70
Unvested and outstanding balance as of December 31, 2020	942,222	$ 11.70

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Employee Stock Purchase Plan—In 2017, the Company approved the 2017 Employee Stock Purchase Plan, which was amended and restated in December 2018 (as amended, the "ESPP"). The ESPP reserved an aggregate of 223,341 shares of common stock and provides for an annual increase on the first day of each fiscal year, beginning on January 1, 2019 and ending on December 31, 2029, in an amount equal to the lowest of: (1) 893,441 shares of the Company's common stock; (2) 1% of the total number of shares of the Company's common stock outstanding on the first day of the applicable fiscal year; and (3) an amount determined by the Company's board of directors.

The ESPP provides for two six-month offering periods each year; the first offering period begins on the first trading day on or after each January 1; the second offering period begins on the first trading day on or after each July 1. Under the ESPP, participating employees can authorize the Company to withhold a portion of their base pay during consecutive six-month payment periods for the purchase of shares of the Company's common stock. At the conclusion of the period, participating employees can purchase shares of the Company's common stock at 85% of the lesser of the closing price of the common stock on (i) the first business day of the plan period or (ii) the exercise date. The fair value of the purchase rights granted under the ESPP was estimated on the date of grant, using the Black-Scholes option-pricing model. During the year ended December 31, 2020, employees of the Company purchased an aggregate of 314,397 shares under the ESPP. During the year ended December 31, 2019, employees of the Company purchased an aggregate of 123,664 shares under the ESPP.

Note 14: Income Taxes

The Company has had no income tax expense due to operating losses incurred for the years ended December 31, 2020 and 2019. The Company has also not recorded any income tax benefits for the net operating losses incurred in each period due to its uncertainty of realizing a benefit from those items. All of the Company's losses before income taxes were generated in the United States.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2020	2019
Federal statutory income tax rate	21.0 %	21.0 %
Effect of:		
Change in valuation allowance	(22.2)	(25.8)
Research and development tax credits	0.9	1.0
State income taxes, net of federal benefit	1.2	4.3
Other	(0.9)	(0.5)
Effective income tax rate	— %	— %

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Net deferred tax assets as of December 31, 2020 and 2019 consisted of the following:

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 67,368	$ 49,018
Lease liabilities	8,152	9,369
Stock-based compensation	7,413	5,414
Capitalized research and development and start-up expenditures	5,258	6,733
Research and development tax credit carryforwards	2,398	6,250
Rebates, incentives, trade discounts and allowances	2,177	—
Other	2,609	2,467
Total deferred tax assets	$ 95,375	$ 79,251
Deferred tax liabilities:		
Right-of-use assets	(7,810)	(9,178)
Total deferred tax liabilities	$ (7,810)	$ (9,178)
Valuation allowance	$ (87,565)	$ (70,073)
Net deferred tax assets	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2020 and 2019. The valuation allowance increased by $17,492 in 2020 due to an increase in the net operating loss carryforwards and research and development tax credits, partially offset by limitations caused by ownership changes under the provisions of Section 382 and Section 383 of the Internal Revenue Code of 1986. Management reevaluates the positive and negative evidence at each reporting period.

As of December 31, 2020 and 2019, the Company had federal net operating loss carryforwards of $243,155 and $168,801, respectively, which may be available to offset future federal tax liabilities and expire at various dates beginning in 2030. As of December 31, 2020 and 2019, the Company had state net operating loss carryforwards of $214,989 and $171,804, respectively, which may be available to offset future state income tax liabilities and expire at various dates beginning in 2030. As of December 31, 2020 and 2019, the Company also had federal and state research and development credit carryforwards of approximately $2,398 and $6,250, respectively, which begin to expire in 2039 (federal) and 2034 (state).

Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. Under the provisions of Section 382 of the Internal Revenue Code of 1986, certain substantial changes in the Company's ownership, including a sale of the Company, or significant changes in ownership due to sales of equity, may have limited, or may limit in the future, the amount of net operating loss carryforwards, which could be used annually to offset future taxable income. The Company previously completed an analysis and determined that an ownership change has materially limited the net operating loss carryforwards and research and development tax credits available to offset future tax liabilities.

The Company files its corporate income tax returns in the United States and various states. All tax years since the date of incorporation remain open to examination by the major taxing jurisdictions (state and federal) to which the Company is subject, as carryforward attributes generated in years past may still be adjusted upon examination by the Internal Revenue Service (''IRS'') or other authorities if they have or will be used in a future period. The Company is not currently under examination by the IRS or any other jurisdictions for any tax year.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

As of December 31, 2020 and 2019 the Company had no uncertain tax positions. The Company's policy is to recognize interest and penalties related to income tax matters as a component of income tax expense, of which no interest or penalties were recorded for the years ended December 31, 2020 and 2019.

Note 15: Commitments and Contingencies

License Agreement — In 2009, the Company entered into an exclusive license agreement with The Johns Hopkins University ("JHU"), as amended in November 2012, May 2014, August 2014, October 2014, June 2018, and July 2020, which licensed to the Company a portfolio of specified patent rights and remains in full force and effect. Pursuant to the terms of the agreement, as amended, the Company agreed to pay an initial license fee, minimum annual payments beginning in 2017, certain development and commercial milestone payments, royalties on product sales and reimburse all or a portion of the costs associated with the preparation, filing, prosecution and maintenance of the agreed-upon patents and patent applications to JHU.

After 2016 and until the first commercial sale of product, which occurred in January 2019, the minimum annual payment was $38. Upon the first commercial sale of INVELTYS, the annual minimum payment increased to $113. The Company is obligated to pay JHU low single-digit running royalties based upon a percentage of net sales of the licensed products, which is applied to the annual minimum payment. The Company also has an obligation to pay JHU certain one-time development and commercial milestone payments. During the year ended December 31, 2020, the Company paid JHU $113 in royalty payments associated with the sale of EYSUVIS and INVELTYS. During the year ended December 31, 2019, the Company paid JHU $413 related to the first commercial sale milestone and subsequent royalties. The Company is obligated to pay JHU a $150 milestone payment within 60 days of the first commercial sale of EYSUVIS in the United States which has been included within accrued expenses and other current liabilities on the consolidated balance sheet as of December 31, 2020.

The Company recorded other expenses related to the JHU agreement of $134 and $253 for each of the years ended December 31, 2020 and 2019, respectively.

The Company's minimum obligations due under its license agreements as of December 31, 2020, are as follows:

Years Ending December 31,		
2021	$	113
2022		113
2023		113
2024		113
2025		113
Thereafter		900
Total minimum license payments	$	1,465

Other Commitments — The Company entered into a commercial supply agreement with Catalent Pharma Solutions, LLC to manufacture commercial supplies of EYSUVIS and INVELTYS. The commercial supply agreement contains annual minimum purchase requirements, which increased upon FDA approval of EYSUVIS on October 26, 2020.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

The Company has the following minimum purchase obligations for EYSUVIS and INVELTYS:

Years Ending December 31,		
2021	$	2,295
2022		5,390
2023		6,285
2024		7,875
2025		8,199
Thereafter		17,925
Total minimum purchase commitments	$	47,969

Litigation—The Company is not currently subject to any material legal proceedings.

Guarantees and Indemnifications—The Company's Certificate of Incorporation authorizes the Company to indemnify and advance expenses to its officers and directors and agents to the fullest extent permitted by law. The Company leases office space under a non-cancelable operating lease, pursuant to which the Company is required to indemnify the landlord against claims, actions, or damages incurred in connection with, among other items, the Company's occupancy and use of the premises.

The Company's equity agreements and certain other arrangements include standard indemnifications against claims, actions, or other matters that may arise in connection with these arrangements.

As of December 31, 2020 and 2019, the Company had not experienced any losses related to these indemnification obligations, and no claims with respect thereto were outstanding. The Company does not expect significant claims related to these indemnification obligations and has no amount accrued related to these contingencies. The Company does not expect these indemnifications to have a material adverse effect on these consolidated financial statements.

Note 16: Defined Contribution Plan

The Company has a 401(k) defined contribution plan (the ''401(k) Plan'') for substantially all of its employees. Eligible employees may make pretax contributions to the 401(k) Plan up to statutory limits.

The Company made discretionary matching contributions of $446 and $454 to the 401(k) Plan during for the years ended December 31, 2020 and 2019, respectively.

KALA PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share amounts)

Note 17: Selected Quarterly Financial Data (Unaudited)

Selected quarterly financial data is as follows:

	Three months ended			
	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
Product revenues, net	$ 1,071	$ 833	$ 2,220	$ 2,238
Costs and expenses	21,196	22,113	28,062	31,222
Total other income (expense)	(1,830)	(2,032)	(2,106)	(2,128)
Net loss attributable to common stockholders	$ (21,955)	$ (23,312)	$ (27,948)	$ (31,112)
Net loss per share attributable to common stockholders —basic and diluted	$ (0.54)	$ (0.42)	$ (0.50)	$ (0.55)

	Three months ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
Product revenues, net	$ 1,386	$ 2,057	$ 1,451	$ 1,180
Costs and expenses	25,436	24,467	23,018	21,377
Total other income (expense)	(1,338)	(1,415)	(1,609)	(1,761)
Net loss attributable to common stockholders	$ (25,388)	$ (23,825)	$ (23,176)	$ (21,958)
Net loss per share attributable to common stockholders —basic and diluted	$ (0.75)	$ (0.70)	$ (0.68)	$ (0.63)

Exhibit 4.2

Execution Version

KALA PHARMACEUTICALS, INC.

THIRD AMENDED AND RESTATED REGISTRATION RIGHTS AGREEMENT

April 6, 2016

TABLE OF CONTENTS

THIRD AMENDED AND RESTATED
REGISTRATION RIGHTS AGREEMENT

This Third Amended and Restated Registration Rights Agreement, dated as of April 6, 2016 (this "Agreement"), is entered into by and among Kala Pharmaceuticals, Inc., a Delaware corporation (the "Company"), the individuals and entities listed on Schedule A attached hereto (collectively, the "Investors" and each individually, an "Investor") and the individual listed on Schedule B attached hereto (the "Key Holder," and together with the Investors, the "Stockholders").

RECITALS:

WHEREAS, the Company and certain of the Stockholders are parties to that certain Second Amended and Restated Registration Rights Agreement, dated as of April 16, 2014, as amended by Amendment No. 1 and Amendment No. 2 thereto (the "Existing Registration Rights Agreement");

WHEREAS, the Company and certain of the Investors (the "Series C Purchasers") have entered into a Series C Preferred Stock Purchase Agreement on or prior to the date hereof (as amended and/or restated from time to time, the "Series C Purchase Agreement") in connection with the issuance and sale by the Company to such Series C Purchasers of shares of the Company's Series C Preferred Stock, par value $0.001 per share (the "Series C Preferred Stock");

WHEREAS, as a condition precedent to the sale and purchase of the Series C Preferred Stock pursuant to the Series C Purchase Agreement, the Series C Purchasers have required that the Existing Registration Rights Agreement be amended and restated to, among other things, make the Series C Purchasers parties thereto;

WHEREAS, pursuant to Section 10 of the Existing Registration Rights Agreement, the amendment and restatement of the Existing Registration Rights Agreements requires the written consent of the holders of at least fifty percent (50%) of the Registrable Securities (as defined in the Existing Registration Rights Agreement);

WHEREAS, pursuant to Section 14 of the Existing Registration Rights Agreement, the Company shall not, without the written consent of the holders of at least fifty percent (50%) of the Registrable Securities, allow purchasers of the Company's securities to become a party to the Existing Registration Rights Agreement; and

WHEREAS, the signatories to this Agreement hold the requisite number of Registrable Securities to effect the amendment and restatement of the Existing Registration Rights Agreement and desire to amend and restate the Existing Registration Rights Agreement in its entirety in the manner set forth herein.

NOW, THEREFORE, in consideration of the foregoing and the mutual covenants and agreements hereinafter set forth, the parties hereto agree as follows:

1. Certain Definitions. As used in this Agreement, the following terms shall have the following respective meanings:

"Charter" shall mean the Company's Amended and Restated Certificate of Incorporation, as amended and/or restated from time to time.

"Commission" shall mean the United States Securities and Exchange Commission, or any other federal agency administering the Securities Act and the Exchange Act at the time.

"Common Stock" shall mean the Company's common stock, par value $0.001 per share.

"Damages" shall mean any loss, claim, damage, expense or liability, joint or several, to which a party hereto may become subject under the Securities Act, the Exchange Act or any other statute or at common law.

"Exchange Act" shall mean the Securities Exchange Act of 1934, as amended, or any similar successor federal statute, and the rules and regulations of the Commission thereunder, all as the same shall be in effect at the time.

"Indemnified Person" shall mean a Company Indemnified Person and/or a Stockholder Indemnified Person, as applicable.

"Joinder Agreement" shall mean a joinder agreement in substantially the form attached hereto as Exhibit I.

"Key Holder Registrable Securities" shall mean the shares of Common Stock held, or hereafter acquired, by the Key Holder from the Company, including without limitation any shares of Common Stock issued to the Key Holder upon the exercise of stock options."

"Person" shall mean an individual, a corporation, a partnership, a joint venture, a trust, an unincorporated organization, a limited liability company or partnership, a government and any agency or political subdivision thereof.

"Preferred Stock" shall mean, collectively, the Seed Preferred Stock, the Series A Preferred Stock, the Series B Preferred Stock, the Series B-1 Preferred Stock and the Series C Preferred Stock.

"Registrable Securities" shall mean (i) the shares of Common Stock issued or issuable upon conversion of the Preferred Stock held, or hereafter acquired, by the Investors (the "Investor Registrable Securities"), (ii) Key Holder Registrable Securities and (iii) any other shares of Common Stock issued or issuable in respect of such Investor Registrable Securities or Key Holder Registrable Securities (because of stock splits, stock dividends, reclassifications, recapitalizations or similar events).

"Securities Act" shall mean the Securities Act of 1933, as amended, or any similar successor federal statute, and the rules and regulations of the Commission thereunder, all as the same shall be in effect at the time.

"Seed Preferred Stock" shall mean the Company's Seed Preferred Stock, par value $0.001 per share.

"Series A Preferred Stock" shall mean the Company's Series A Preferred Stock, par value $0.001 per share.

"Series B Preferred Stock" shall mean the Company's Series B Preferred Stock, par value $0.001 per share.

"Series B-1 Preferred Stock" shall mean the Company's Series B-1 Preferred Stock, par value $0.001 per share."

2. Demand Registration

(a) At any time after the earlier of (i) five (5) years from the date of this Agreement and (ii) one hundred eighty (180) days after the initial public offering of the Company's Common Stock pursuant to an effective registration under the Securities Act, the holders (excluding the Key Holder) of at least fifty percent (50%) of the Registrable Securities then outstanding (excluding Key Holder Registrable Securities) may notify the Company that they intend to offer or cause to be offered for public sale at least fifty percent (50%) of the Registrable Securities then outstanding (excluding Key Holder Registrable Securities) or any lesser number of Registrable Securities (excluding Key Holder Registrable Securities) if the anticipated aggregate sale price, net of underwriting discounts and commissions, if any, would exceed $10,000,000. Upon receipt of such request, the Company shall promptly deliver notice of such request to all Stockholders holding Registrable Securities who shall then have thirty (30) days to notify the Company in writing of their desire to be included in such registration. If the request for registration contemplates an underwritten public offering, the Company shall state such in the written notice and in such event the right of any Person to participate in such registration shall be conditioned upon such Person's participation in such underwritten public offering and the inclusion of such Person's Registrable Securities in the underwritten public offering to the extent provided herein. The Company will use its reasonable best efforts to expeditiously effect (but in any event no later than thirty (30) days after such request) the registration of all Registrable Securities whose holders request participation in such registration under the Securities Act, but only to the extent provided for in this Agreement; provided, however, that the Company shall not be required to effect registration pursuant to a request under this Section 2(a) more than two (2) times for the holders of the Registrable Securities as a group. Notwithstanding anything to the contrary contained herein, no request may be made under this Section 2(a) within ninety (90) days after the effective date of a registration statement filed by the Company covering a firm commitment underwritten public offering in which the holders of Registrable Securities shall have been entitled to join pursuant to Section 4 and in which there shall have been effectively registered all Registrable Securities as to which registration shall have been requested. A registration will not count as a requested registration under this Section 2(a) unless and until the registration statement relating to such registration has been declared effective by the Commission; provided, however, that a majority in interest of the participating holders of Registrable Securities may request, in writing, that the Company withdraw a registration statement which has been filed under this Section 2(a) but has not yet been declared effective, and a majority in interest of such holders may thereafter request the Company to reinstate such registration statement, if permitted under the Securities Act, or to file another registration statement, in accordance with the procedures set forth herein and without reduction in the number of demand registrations permitted under this Section 2(a).

(b) If a requested registration involves an underwritten public offering and the managing underwriter of such offering determines in good faith that the number of securities sought to be offered should be limited due to market conditions, then the number of securities to be included in such underwritten public offering shall be reduced to a number deemed satisfactory by such managing underwriter; provided, that the securities to be excluded shall be determined in the following order of priority: (i) first, persons not having any contractual or other right to include such securities in the registration statement, (ii) second, securities held by any other Persons (other than the holders of Registrable Securities) having a contractual, incidental "piggy back" right to include such securities in the registration statement, (iii) third, securities to be registered by the Company pursuant to such registration statement, (iv) fourth, Registrable Securities of holders who did not make the original request for registration and, if necessary, (v) fifth, Registrable Securities of holders who requested such registration pursuant to Section 2(a). If there is a reduction of the number of Registrable Securities pursuant to clauses (iv) or (v), such reduction shall be made on a *pro rata* basis (based upon the aggregate number of Registrable Securities held by such holders).

(c) With respect to a request for registration pursuant to Section 2(a) which is for an underwritten public offering, the managing underwriter shall be chosen by the holders of a majority of the Registrable Securities to be sold in such offering, subject only to the consent of the Company, which consent shall not be unreasonably withheld. The Company may not cause any other registration of securities for sale for its own account (other than a registration effected solely to implement an employee benefit plan) to become effective within one hundred twenty (120) days following the effective date of any registration required pursuant to this Section 2.

3. Form S-3. An Investor or Investors holding Registrable Securities (excluding any Key Holder Registrable Securities) anticipated to have an aggregate sale price (net of underwriting discounts and commissions, if any) in excess of $1,000,000 shall have the right to request any number of registrations on Form S-3 (or any successor form) for the Registrable Securities held by such requesting holder or holders; provided, however, that the Company (i) is then eligible to use such Form S-3 (or successor form) and (ii) shall not be required to file more than two (2) such registration statements on Form S-3 (or any successor form) in any twelve (12) month period. Such requests shall be in writing and shall state the number of shares of Registrable Securities to be disposed of and the intended method of disposition of such shares by such holder or holders. The Company shall give notice to all other holders of the Registrable Securities of the receipt of a request for registration pursuant to this Section 3 and such holders of Registrable Securities shall then have thirty (30) days to notify the Company in writing of their desire to participate in the registration. The Company shall use its reasonable best efforts to effect promptly the registration of all shares on Form S-3 (or any successor form) to the extent requested by such holders. The Company shall use its reasonable best efforts to keep such registration statement effective until the earlier of ninety (90) days or until such holders have completed the distribution described in such registration statement.

4. Piggyback Registration. If the Company at any time proposes to register any of its securities under the Securities Act for sale to the public (except with respect to registration statements on Forms S-4, S-8 or another form not available for registering the Registrable Securities for sale to the public), each such time it will give written notice at the applicable address of record to each holder of Registrable Securities of its intention to do so. Upon the written request

of any of such holders of the Registrable Securities, given within twenty (20) days after receipt by such Person of such notice, the Company will, subject to the limits contained in this Section 4, use its reasonable best efforts to cause all such Registrable Securities of said requesting holders to be registered under the Securities Act and qualified for sale under any state blue sky law, all to the extent required to permit such sale or other disposition of said Registrable Securities; provided, however, that if the Company is advised in writing in good faith by any managing underwriter of the Company's securities being offered in a public offering pursuant to such registration statement that the amount to be sold by persons other than the Company (collectively, "Selling Stockholders") is greater than the amount which can be offered without adversely affecting the offering, the Company may reduce the amount offered for the accounts of Selling Stockholders (including such holders of shares of Registrable Securities) to a number deemed satisfactory by such managing underwriter; provided, further, that (a) in no event shall the amount of Registrable Securities of Selling Stockholders be reduced below twenty-five percent (25%) of the total amount of securities included in such offering, unless such offering is the initial public offering of the Company's securities; and (b) any shares to be excluded shall be determined in the following order of priority: (i) securities held by any Persons not having any such contractual, incidental registration rights, (ii) securities held by any Persons having contractual, incidental registration rights pursuant to an agreement which is not this Agreement, and (iii) the Registrable Securities sought to be included by the holders thereof as determined on a *pro rata* basis (based upon the aggregate number of Registrable Securities held by such holders).

5. Registration Procedures. If and whenever the Company is required by the provisions of this Agreement to use its reasonable best efforts to promptly effect the registration of any of its securities under the Securities Act, the Company will:

(a) use its reasonable best efforts to diligently prepare and file with the Commission a registration statement on the appropriate form under the Securities Act with respect to such securities, which form shall comply as to form in all material respects with the requirements of the applicable form and include all financial statements required by the Commission to be filed therewith, and use its reasonable best efforts to cause such registration statement to become and remain effective for, except as specified in Section 3 above, a period of up to one hundred eighty (180) days or, if earlier, until completion of the proposed offering;

(b) use its reasonable best efforts to diligently prepare and file with the Commission such amendments and supplements to such registration statement and the prospectus used in connection therewith as may be necessary to keep such registration statement effective until the selling Stockholder(s) have completed the distribution described in such registration statement, unless otherwise set forth herein, and to comply with the provisions of the Securities Act with respect to the sale or other disposition of all securities covered by such registration statement whenever the seller or sellers of such securities shall desire to sell or otherwise dispose of the same, but only to the extent provided in this Agreement;

(c) furnish to each selling Stockholder and the underwriters, if any, such number of copies of such registration statement, any amendments thereto, any documents incorporated by reference therein, the prospectus, including a preliminary prospectus, in conformity with the requirements of the Securities Act, and such other documents as such selling

Stockholder may reasonably request in order to facilitate the public sale or other disposition of the securities owned by such selling Stockholder;

(d) use its reasonable best efforts to register or qualify the securities covered by such registration statement under such other securities or state blue sky laws of such jurisdictions as each selling Stockholder shall reasonably request, and do any and all other acts and things which may be necessary under such securities or blue sky laws to enable such selling Stockholder to consummate the public sale or other disposition in such jurisdictions of the securities owned by such selling Stockholder, except that the Company shall not for any such purpose be required to qualify to do business as a foreign corporation or to file a general consent to service of process in any such states or jurisdictions wherein it is not already so qualified;

(e) within a reasonable time before each filing of the registration statement or prospectus or amendments or supplements thereto with the Commission, furnish to counsel selected by the selling Stockholders copies of such documents proposed to be filed, having considered in good faith any comments to such documents from such counsel;

(f) immediately notify each selling Stockholder, such selling Stockholder's counsel and any underwriter (and if requested by any such Person, confirm such notice in writing) of the happening of any event that makes any statement made in the registration statement or related prospectus untrue or which requires the making of any changes in such registration statement or prospectus so that they will not contain any untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein in the light of the circumstances under which they were made not misleading; and, as promptly as practicable thereafter, prepare and file with the Commission and furnish a supplement or amendment to such prospectus so that, as thereafter deliverable to the purchasers of such Registrable Securities, such prospectus will not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading;

(g) use its reasonable best efforts to prevent the issuance of any order suspending the effectiveness of a registration statement, and if one is issued, use its reasonable best efforts to obtain the withdrawal of any order suspending the effectiveness of a registration statement at the earliest possible moment;

(h) if requested by the managing underwriter or underwriters (if any), any selling Stockholder, or such selling Stockholder's counsel, promptly incorporate in a prospectus supplement or post-effective amendment such information as such Person reasonably and appropriately requests to be included therein and promptly make all required filings of such prospectus supplement or post-effective amendment;

(i) make available to each selling Stockholder, any underwriter participating in any disposition pursuant to a registration statement, and any attorney, accountant or other agent or representative retained by any such selling Stockholder or underwriter (collectively, the "Inspectors"), all financial and other records, pertinent corporate documents and properties of the Company (collectively, the "Records"), as shall be reasonably necessary to enable them to exercise their due diligence responsibility, and cause the Company's officers, directors and

employees to supply all information reasonably requested by any such Inspector in connection with such registration statement as necessary or advisable to verify the accuracy of the information in such registration statement and to conduct appropriate due diligence in connection therewith;

(j) in the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the underwriter(s) of such offering and use its reasonable best efforts to facilitate the public offering of the securities;

(k) furnish to each prospective selling Stockholder a signed counterpart, addressed to the prospective selling Stockholder, of (A) an opinion of counsel for the Company, dated the effective date of the registration statement, and (B) a "comfort" letter signed by the independent public accountants who have certified the Company's financial statements included in the registration statement, covering substantially the same matters with respect to the registration statement (and the prospectus included therein) and (in the case of the accountants' letter) with respect to events subsequent to the date of the financial statements, as are customarily covered (at the time of such registration) in opinions of the Company's counsel and in accountants' letters delivered to the underwriters in underwritten public offerings of securities;

(l) cause the securities covered by such registration statement to be listed on the securities exchange or quoted on the quotation system on which the Common Stock of the Company is then listed or quoted (or if the Common Stock is not yet listed or quoted, then on such exchange or quotation system as the Company shall determine);

(m) otherwise use its reasonable best efforts to comply with all applicable rules and regulations of the Commission and make generally available to its security holders, in each case as soon as practicable, but not later than thirty (30) days after the close of the period covered thereby, an earnings statement of the Company which will satisfy the provisions of Section 11(a) of the Securities Act and Rule 158 thereunder (or any comparable successor provisions);

(n) otherwise cooperate with the underwriter(s), the Commission and other regulatory agencies and take all actions and execute and deliver or cause to be executed and delivered all documents necessary to effect the registration of any securities under this Agreement; and

(o) during the period when the prospectus is required to be delivered under the Securities Act, promptly file all documents required to be filed with the Commission pursuant to Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act.

6. Expenses. All expenses incurred by the Company or the selling Stockholders in effecting the registrations provided for in Sections 2, 3 and 4 of this Agreement, including, without limitation, all registration and filing fees, printing expenses, fees and disbursements of counsel for the Company, the reasonable fees and disbursements of one counsel (the "Selling Stockholder Counsel") for the selling Stockholders (selected by at least fifty percent (50%) in interest of Registrable Securities being registered and held by the selling Stockholders participating in such registration), underwriting expenses (other than fees, commissions or discounts), expenses of any audits incident to or required by any such registration and expenses of complying with the

securities or blue sky laws of any jurisdictions (all of such expenses referred to as "Registration Expenses"), shall be paid by the Company; provided, however, that the Company shall not be required to pay for any Registration Expenses of any registration proceeding begun pursuant to Section 2 if the registration request is subsequently withdrawn at the request of the selling Stockholders holding at least fifty percent (50%) in interest of the Registrable Securities requested to be registered pursuant to Section 2 (in which case, all such selling Stockholders shall bear such Registration Expenses pro rata based upon the number of Registrable Securities held by each such selling Stockholder that were to be included in the withdrawn registration), unless the selling Stockholders holding at least fifty percent (50%) in interest of the Registrable Securities requested to be registered pursuant to Section 2 forfeit their right to one registration pursuant to Section 2; provided that if, at the time of such withdrawal, the selling Stockholders shall have learned of a material adverse change in the condition, business, or prospects of the Company from that known to the selling Stockholders at the time of their request and have withdrawn the request with reasonable promptness after learning of such information, then the selling Stockholders shall not be required to pay any of such Registration Expenses and shall not forfeit their right to one registration pursuant to Section 2. All Selling Expenses (as defined below) relating to Registrable Securities registered pursuant to this Agreement shall be borne and paid by the selling Stockholders pro rata on the basis of the number of Registrable Securities registered on their behalf. "Selling Expenses" means all underwriting discounts, selling commissions and stock transfer taxes applicable to the sale of Registrable Securities, and fees and disbursements of counsel for any selling Stockholder, except for the fees and disbursements of the Selling Stockholder Counsel borne and paid by the Company as provided in this Section 6.

7. Indemnification.

(a) The Company shall indemnify and hold harmless each selling Stockholder (including its partners (including partners of partners and shareholders of such partners)), the directors, officers, employees and agents of each such selling Stockholder, legal counsel, accountants and investment advisers for each such selling Stockholder, any underwriter (as defined in the Securities Act) of an offering of Registrable Securities of such Stockholder, and each Person, if any, who controls (within the meaning of the Securities Act) such selling Stockholder or underwriter (each, a "Company Indemnified Person") against any Damages, insofar as such Damages (or action in respect thereof) arise out of or are based upon (i) any untrue statement or alleged untrue statement of any material fact contained, on the effective date thereof, in any registration statement of the Company under which securities held by such party were registered under the Securities Act, including any preliminary prospectus or final prospectus contained therein, or any amendment or supplement thereto, (ii) any omission or alleged omission by the Company to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, or (iii) any violation by the Company of the Securities Act, the Exchange Act, any state securities or "blue sky" laws or any rule or regulation promulgated under the Securities Act, the Exchange Act or any state securities or "blue sky" laws. Except as otherwise provided in Section 7(d), the Company shall reimburse each such Company Indemnified Person in connection with investigating or defending any claim or proceeding from which Damages may result. Notwithstanding the foregoing, the Company shall not be liable to any Company Indemnified Person in any such case to the extent that any such Damages arise out of or are based upon any untrue statement or alleged untrue statement or omission or alleged omission made in such registration statement, preliminary or final prospectus, or amendment or supplement

thereto, in reliance upon and in conformity with information furnished in writing to the Company by such Company Indemnified Person specifically for use therein. The Company shall not be required to indemnify any Company Indemnified Person against any liability arising from any untrue or misleading statement or omission contained in any preliminary prospectus if such deficiency is corrected in the final prospectus or for any liability which arises out of the failure of any Company Indemnified Person to deliver a prospectus as required by the Securities Act regardless of any investigation made by or on behalf of such Company Indemnified Person; and the provisions of this sentence shall survive any transfer of such securities by such selling Stockholder.

(b) Each selling Stockholder shall indemnify and hold harmless each other selling Stockholder of any securities, the Company, its directors and officers, any underwriter (as defined in the Securities Act), legal counsel and accountants for the Company, and each other Person, if any, who controls (within the meaning of the Securities Act) the Company or such underwriter (each, a "Stockholder Indemnified Person"), against any Damages, insofar as such Damages (or action in respect thereof) arise out of or are based upon (i) any untrue statement or alleged untrue statement of any material fact contained, on the effective date thereof, in any registration statement of the Company under which securities held by such party were registered under the Securities Act, including any preliminary prospectus or final prospectus contained therein, or any amendment or supplement thereto or (ii) any omission or alleged omission by such selling Stockholder to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, in the case of clauses (i) and (ii) of this sentence to the extent, but only to the extent, that such untrue statement or alleged untrue statement or omission or alleged omission was made in such registration statement, preliminary or final prospectus, amendment or supplement thereto in reliance upon and in conformity with information furnished in writing to the Company by such selling Stockholder specifically for use therein. Such selling Stockholder shall reimburse any Stockholder Indemnified Person for any legal fees incurred in investigating or defending any claim or proceeding from which Damages may result. Notwithstanding the foregoing, except in the case of fraud or willful misconduct by a selling Stockholder, in no event shall the liability of any selling Stockholder for indemnification under this Section 7 exceed the lesser of (i) that proportion of the total of such Damages equal to the proportion of the total Registrable Securities sold under such registration statement by such selling Stockholder compared to the total Registrable Securities sold under such registration statement by the Selling Stockholders, or (ii) the amount equal to the net proceeds from the offering received by such selling Stockholder. No selling Stockholder shall be required to indemnify any Stockholder Indemnified Person against any Damages arising from any untrue or misleading statement or omission contained in any preliminary prospectus if such deficiency is corrected in the final prospectus or for any Damages which arise out of the failure of any Stockholder Indemnified Person to deliver a prospectus as required by the Securities Act.

(c) Indemnification similar to that specified in Sections 7(a) and (b) shall be given by the Company and each selling Stockholder (with such modifications as may be appropriate) with respect to any required registration or other qualification of their securities under any federal or state law or regulation of governmental authority other than the Securities Act.

(d) In the event the Company, any selling Stockholder or other Person receives a complaint, claim or other notice of any liability or action, giving rise to a claim for

indemnification under Section 7(a), (b) or (c) above, the Person claiming indemnification under such paragraphs shall promptly notify the Person against whom indemnification is sought of such complaint, notice, claim or action, and such indemnifying Person shall have the right to investigate and defend any such complaint, notice, claim or action.

(e) If the indemnification provided for in this Section 7 for any reason is held by a court of competent jurisdiction to be unavailable to an Indemnified Person in respect of any Damages, then each indemnifying party under this Section 7, in lieu of indemnifying such Indemnified Person under this Section 7, shall contribute to the amount paid or payable by such Indemnified Person as a result of such Damages (i) in such proportion as is appropriate to reflect the relative benefits received by the Company, the selling Stockholder(s) and the underwriters from the offering of Registrable Securities or (ii) if the allocation provided by clause (i) above is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) above but also the relative fault of the Company, the selling Stockholder(s) and the underwriters in connection with the statements or omissions which resulted in such Damages, as well as any other relevant equitable considerations. The relative benefits received by the Company, the selling Stockholder(s) and the underwriters shall be deemed to be in the same respective proportions that the net proceeds from the offering (before deducting expenses) received by the Company, the selling Stockholder(s), and the underwriting discount received by the underwriters, in each case, as set forth in the table on the cover page of the applicable prospectus, bear to the aggregate public offering price of the Registrable Securities. The relative fault of the Company, the selling Stockholder(s) and the underwriters shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company, the selling Stockholder(s), or the underwriters and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

The Company and the selling Stockholders agree that it would not be just and equitable if contribution pursuant to this Section 7 were determined by *pro rata* or per capita allocation or by any other method of allocation which does not take account the equitable considerations referred to in the immediately preceding paragraph. Except in the case of fraud or willful misconduct by a selling Stockholder, in no event shall a selling Stockholder be required to contribute under this Section 7(e), when combined with the amounts paid or payable by such Stockholder pursuant to Section 7(b), in excess of the lesser of (i) that proportion of the total of such Damages equal to the proportion of the total Registrable Securities sold under such registration statement by such selling Stockholder compared to the total Registrable Securities sold under such registration statement by the Selling Stockholders, or (ii) the amount equal to the net proceeds from the offering received by such selling Stockholder. No Person found guilty of fraudulent representation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not found guilty of such fraudulent misrepresentation.

(f) The amount paid by an indemnifying party or payable to an Indemnified Person as a result of any Damages referred to in this Section 7 shall be deemed to include, subject to limitations set forth above, any legal or other expenses reasonably incurred by such Indemnified Person in connection with investigating or defending any such action or claim, payable as the same are incurred. The indemnification and contribution provided for in this Section 7 will remain in

full force and effect regardless of any investigation made by or on behalf of the indemnified parties or any other officer, director, employee, agent or controlling person of the indemnified parties.

(g) No indemnifying party, in the defense of any complaint, notice, claim or action, shall enter into a consent or entry of any judgment or enter into a settlement without the consent of the Indemnified Person, which consent shall not be unreasonably withheld or delayed. Notwithstanding anything to the contrary set forth herein, (i) the indemnity agreement contained in Section 7(a) shall not apply to amounts paid in settlement of any complaint, notice, claim or action if such settlement is effected without the consent of the Company, which consent will not be unreasonably withheld or delayed, and (ii) the indemnity agreement contained in Section 7(b) shall not apply to amounts paid in settlement of any complaint, notice, claim or action if such settlement is effected without the consent of the selling Stockholders, which consent will not be unreasonably withheld or delayed.

8. Compliance with Rule 144. In the event that the Company (i) registers a class of securities under Section 12 of the Exchange Act or (ii) shall commence to file reports under Section 13 or 15(d) of the Exchange Act, the Company will use its reasonable best efforts thereafter to file with the Commission such information as is required under the Exchange Act for so long as there are holders of Registrable Securities; and in such event, the Company shall use its reasonable best efforts to take all action as may be required as a condition to the availability of Rule 144 under the Securities Act (or any comparable successor rules). After the occurrence of the first underwritten public offering of Common Stock pursuant to an offering registered under the Securities Act on Form S-l (or any comparable successor forms), subject to the limitations on transfers imposed by this Agreement, the Company shall use its reasonable best efforts to facilitate and expedite transfers of Registrable Securities pursuant to Rule 144 under the Securities Act, which efforts shall include timely notice to its transfer agent to expedite such transfers of Registrable Securities.

9. Rule 144A Information. The Company shall, upon written request of any Investor, provide to such Investor and to any prospective institutional transferee of the Common Stock designated by such Investor, such financial and other information as is available to the Company or can be obtained by the Company without material expense and as such Investor may reasonably determine is required to permit such transfer to comply with the requirements of Rule 144A promulgated under the Securities Act.

10. Amendments and Waivers. Subject to the last sentence of Section 12, any term of this Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance, and either retroactively or prospectively) only with the written consent of the Company and the holders of at least sixty-seven percent (67%) of the Registrable Securities issued or issuable upon conversion of Preferred Stock then outstanding, provided that any amendment that would materially and adversely affect any Stockholder in a disproportionate manner than any other Stockholder shall not be effective against such Stockholder without such Stockholder's written consent with respect thereto. For the purposes of this Agreement, no course of dealing between or among any of the parties hereto and no delay on the part of any party hereto in exercising any rights hereunder shall operate as a waiver of the rights hereof.

11. Postponement. The Company may postpone the filing of any registration statement required hereunder for a reasonable period of time, not to exceed ninety (90) days in the aggregate during any twelve-month period, if the Company has been advised by legal counsel that such filing would require a special audit or the disclosure of a material impending transaction or other matter and the Company's Board of Directors determines reasonably and in good faith that such disclosure would have a material adverse effect on the Company (a "Black-Out Period"). Upon notice of the existence of a Black-Out Period from the Company to any Stockholder or Stockholders with respect to any registration statement already effective, such Stockholder or Stockholders shall refrain from selling their Registrable Securities under such registration statement until such Black-Out Period has ended; provided, however, that the Company shall not have the right to impose a Black-Out Period with respect to any registration statement that is already effective more than once during any period of twelve (12) consecutive months and in no event shall such Black-Out Period exceed sixty (60) days.

12. Market Stand-Off. Each Stockholder agrees, that if requested by the Company and an underwriter in connection with the initial public offering of the Company of Common Stock under the Securities Act on a registration statement on Form S-1(the "IPO"), not to directly or indirectly offer, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant for the sale of or otherwise dispose of or transfer any securities of the Company held by it immediately prior to the effectiveness of the registration statement relating to the IPO for such period, not to exceed one hundred eighty (180) days (plus any additional period of time as may be requested by the Company or such underwriter for the purpose of complying with FINRA Rule 2711(f)(4) or NYSE Rule 472(f)(4), or any successor provisions or amendments thereto) following the effective date of the registration statement for the IPO, as such underwriter shall specify reasonably and in good faith; provided, however, that all officers and directors of the Company and all 1% or greater stockholders of the Company enter into similar agreements; provided, further, however, that in the event the Company or such underwriter, as applicable, releases any securities of the Company from the restrictions set forth in this Section 12 or similar restrictions (in any such case, the "Released Securities"), the foregoing provisions shall be waived or terminated, as applicable, to the same extent and with respect to the same percentage of securities of each Stockholder as the percentage of Released Securities represent with respect to the securities held by the holder of such Released Securities. For purposes of clarity, the restrictions set forth herein shall not apply to shares acquired in the IPO or in the open market following the IPO. Notwithstanding anything to the contrary contained herein, any amendment to this Section 12 that would adversely affect the holders of the Series B Preferred Stock or the Series B-1 Preferred Stock or the Series C Preferred Stock, as the case may be, shall require the written consent of (i) the holders of at least a majority of the Series B Preferred Stock and Series B-1 Preferred Stock then outstanding, in the case of an amendment that adversely affects the holders of the Series B Preferred Stock or the Series B-1 Preferred Stock and (ii) the holders of at least a majority of the Series C Preferred Stock then outstanding in the case of an amendment that adversely affects the holders of the Series C Preferred Stock.

13. Transferability of Registration Rights. The registration rights set forth in this Agreement are transferable to each transferee of Registrable Securities. Each subsequent holder of Registrable Securities must consent in writing to be bound by the terms and conditions of this Agreement in order to acquire the rights granted pursuant to this Agreement.

14. Rights Which May Be Granted to Subsequent Stockholders. Other than permitted transferees of Registrable Securities under Section 13, the Company shall not, without the prior written consent of holders of at least fifty percent (50%) in interest of the Registrable Securities then outstanding, (a) allow purchasers of the Company's securities to become a party to this Agreement (except as permitted by Section 17(e) of this Agreement) or (b) grant any other registration rights, other than any incidental or so called piggyback registration rights to any third parties that are not inconsistent with the terms of this Agreement.

15. Termination of Registration Rights. The right of any Stockholder to request registration or inclusion of Registrable Securities in any registration pursuant to Sections 2, 3, or 4 of this Agreement shall terminate on the seventh (7th) anniversary of the Company's initial public offering.

16. Damages. The Company recognizes and agrees that each holder of Registrable Securities may not have an adequate remedy if the Company fails to comply with the terms and provisions of this Agreement and that damages may not be readily ascertainable, and the Company expressly agrees that, in the event of such failure, the holder of Registrable Securities or any other Person entitled to the benefits of this Agreement shall be entitled to seek specific performance of any and all provisions hereof or to seek injunctive relief against the Company from continuing to commit any such breach of this Agreement.

17. Miscellaneous.

(a) Notices. All notices, requests, demands and other communications provided for herein shall be in writing and shall be deemed to have been duly given, delivered and received upon the earlier of actual receipt or: (a) personal delivery to the party to be notified, (b) when sent, if sent by electronic mail or facsimile during normal business hours of the recipient, and if not sent during normal business hours, then on the recipient's next business day, (c) one (1) business day after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) deposit with a nationally recognized overnight courier, freight prepaid, specifying next business day delivery. All notices, requests, demands and other communications provided for herein shall be given to the applicable party at the addresses indicated below:

To the Company:

Kala Pharmaceuticals, Inc.
100 Beaver Street
Suite 201
Waltham, MA 02453
Attention: Chief Executive Officer
Facsimile: 781-642-0399
Email: mark.iwicki@kalarx.com

With a copy to:

Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109

Attention: Lia Der Marderosian, Esq.
Facsimile: 617-526-5000
Email: Lia.DerMarderosian@wilmerhale.com

If to the Investors, only at their respective addresses as set forth on the signature pages or Schedule A attached hereto, with a copy to Proskauer Rose LLP, One International Place, Boston, Massachusetts 02110-2600, Attn: Ori Solomon, Esq., osolomon@proskauer.com, Facsimile: 617-526-9899, a copy to Greenberg Traurig, LLP, One International Place, Boston, Massachusetts 02110, Attn: Bradley A. Jacobson, Esq., jacobsonb@gtlaw.com, Facsimile: 617-279-8402, a copy to Morrison, Foerster LLP, 755 Page Mill Road, Palo Alto, CA 94304, Attn: Paul "Chip" Lion III, PLion@mofo.com.

If to the Key Holder, at his address as set forth on Schedule B attached hereto.

If to any other holder of Registrable Securities:

At such Person's address for notice as set forth in the books and records of the Company or, as to each of the foregoing, at such other address as shall be designated by such Person in a written notice to other parties complying as to delivery with the terms of this Section 17(a).

(b) Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the state of Delaware, without giving effect to conflict of laws principles thereof.

(c) Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered via facsimile, electronic mail or other transmission method, and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

(d) Severability. If any provision of this Agreement shall be held to be illegal, invalid or unenforceable, such illegality, invalidity or unenforceability shall attach only to such provision and shall not in any manner affect or render illegal, invalid or unenforceable any other provision of this Agreement, and this Agreement shall be carried out as if any such illegal, invalid or unenforceable provision were not contained herein.

(e) Additional Investors. Notwithstanding anything to the contrary contained herein, if the Company issues additional shares of the Company's Preferred Stock after the date hereof, any purchaser of such shares of Preferred Stock may become a party to this Agreement by executing and delivering to the Company a Joinder Agreement, and thereafter shall be deemed an "Investor" for all purposes hereunder. No action or consent by the Stockholders shall be required for such joinder to this Agreement by such additional Investor, so long as such additional Investor has agreed in writing to be bound by all of the obligations as an "Investor" hereunder.

(f) Entire Agreement. This Agreement, including any schedules and exhibits hereto, constitutes the entire agreement among the parties with respect to the subject matter hereof, and any other written or oral agreement relating to the subject matter hereof existing between the parties is expressly canceled. For the avoidance of doubt, upon the effectiveness of this

Agreement, the Existing Registration Rights Agreement shall be deemed amended and restated and superseded and replaced in its entirety by this Agreement, and shall be of no further force or effect.

[Signature pages follow.]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first set forth above.

COMPANY:

KALA PHARMACEUTICALS, INC.

By: /s/ Mark Iwicki
Name: Mark Iwicki
Title: Chief Executive Officer

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS:

LUX VENTURES II, L.P.
By: Lux Venture Partners II, L.P., its General Partner
By: Lux Venture Associates II, LLC, its General Partner
By: Lux Capital Management, LLC, its Sole Member

By: /s/ Peter Hébert
Name: Peter Hébert
Title: Managing Partner

LUX VENTURES II SIDECAR, L.P.
By: Lux Venture Partners II, L.P., its General Partner
By: Lux Venture Associates II, LLC, its General Partner
By: Lux Capital Management, LLC, its Sole Member

By: /s/ Peter Hébert
Name: Peter Hébert
Title: Managing Partner

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

HOLLY SMITH-NORMAN 2007 TRUST, DATED NOVEMBER 24, 2007, AS AMENDED

By: /s/ Burr R. Smith
Name: Burr R. Smith
Title: Trustee

2012 TRUST AGREEMENT OF VICTORIA SMITH TRAUSCHT, DATED SEPTEMBER 18, 2012

By: /s/ Victoria Smith Trauscht
Name: Victoria Smith Trauscht
Title: Trustee

BRISCO-DAVIS GROUP, LLC

By: /s/ Burr R. Smith
Name: Burr R. Smith
Title: Manager

DAVIS CLEARING HOUSE, LLC

By: /s/ Burr R. Smith
Name: Burr R. Smith
Title: Manager

INVESTORS (cont.):

2011 TRUST AGREEMENT OF KAREN CHASE SMITH, DATED FEBRUARY 22, 2012

By: /s/ Karen Chase Smith
Name: Karen Chase Smith
Title: Trustee

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

THIRD ROCK VENTURES, L.P.
By: Third Rock Ventures GP, L.P., its General Partner
By: TRV GP, LLC, its General Partner

By: /s/ Kevin Gillis
Name: Kevin Gillis
Title: CFO

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

POLARIS VENTURE PARTNERS V, L.P.
By: Polaris Venture Management Co. V, L.L.C., its General Partner

By: /s/ William E. Bilodeau
Name: William E. Bilodeau
Title: Attorney-in-fact

POLARIS VENTURE PARTNERS ENTREPRENEURS' FUND V, L.P.
By: Polaris Venture Management Co. V, L.L.C., its General Partner

By: /s/ William E. Bilodeau
Name: William E. Bilodeau
Title: Attorney-in-fact

POLARIS VENTURE PARTNERS FOUNDERS' FUND V, L.P.
By: Polaris Venture Management Co. V, L.L.C., its General Partner

By: /s/ William E. Bilodeau
Name: William E. Bilodeau
Title: Attorney-in-fact

INVESTORS (cont.):

POLARIS VENTURE PARTNERS SPECIAL FOUNDERS' FUND V, L.P.
By: Polaris Venture Management Co. V, L.L.C., its General Partner

By: /s/ William E. Bilodeau
Name: William E. Bilodeau
Title: Attorney-in-fact

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

LIGHTHOUSE CAPITAL PARTNERS VI, L.P.
By: Lighthouse Management Partners VI, L.L.C., its General Partner

By: /s/ Christy Barnes
Name: Christy Barnes
Title: Managing Director

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

CVF, LLC

By: /s/ Richard H. Robb
Name: Richard H. Robb
Title: Manager

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

BENON GROUP LTD.

By: /s/ Pierre Valla
Name: Pierre Valla
Title: Director

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

RA CAPITAL HEALTHCARE FUND, L.P.

BY: RA CAPITAL MANAGEMENT, LLC
ITS: GENERAL PARTNER

By: /s/ Rajeev Shah
Name: Rajeev Shah
Title: Authorized Signatory

BLACKWELL PARTNERS LLC—SERIES A

By: /s/ Justin B. Nixon
Name: Justin B. Nixon
Title: DUMAC, Inc.
Authorized Agent

By: /s/ Jannine M. Lall
Name: Jannine M. Lail
Title: Controller
DUMAC, Inc.
Authorized Agent

INVESTORS (cont.):

YSIOS BIOFUND I FCR
By: Ysios Capital Partners SGEIC, SA, its General Partner

By: /s/ Karen Wagner
Name: Karen Wagner
Title: General Partner

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

HADLEY HARBOR MASTER INVESTORS (CAYMAN) L.P.

By: Wellington Management Company LLP, as investment adviser

By: /s/ Emily Babalas
Name: Emily Babalas
Title: Managing Director and Counsel

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

LONGITUDE VENTURE PARTNERS II, L.P.

By: Longitude Capital Partners II, LLC

Its: General Partner

By: /s/ Juliet Tammenoms Bakker
Name: Juliet Tammenoms Bakker
Title: Managing Director

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

CDK ASSOCIATES, L.L.C.

By: /s/ Karen Cross
Name: Karen Cross
Title: Treasurer

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

SCOTT MORENSTEIN

By: /s/ Scott Morenstein
Name: Scott Morenstein

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

ORBIMED PRIVATE INVESTMENTS VI, LP

By: OrbiMed Capital GP VI LLC
Its: General Partner

By: OrbiMed Advisors LLC
Its: Managing Member

By: /s/ Jonathan Silverstein
Name: Jonathan Silverstein
Title: Member

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

VIVO CAPITAL FUND VIII, L.P.

By: Vivo Capital VIII, LLC
Its: General Partner

By: /s/ Chen Yu
Name: Chen Yu
Title: Managing Member

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

VIVO CAPITAL SURPLUS FUND VIII, L.P.

By: Vivo Capital VIII, LLC
Its: General Partner

By: /s/ Chen Yu
Name: Chen Yu
Title: Managing Member

[Signature Page to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

ALEXANDRIA EQUITIES, LLC,
a Delaware limited liability company

By: Alexandria Real Estate Equities, Inc., a Maryland corporation, its managing member

By: /s/ Jennifer Banks
Name: Jennifer Banks
Title: EVP, General Counsel

[Signature Page to Third Amended and Restated Registration Rights Agreement]

KEY HOLDER:

/s/ Mark Iwicki
Mark Iwicki

[Signature Page to Third Amended and Restated Registration Rights Agreement]

Schedule A

Investors

Lux Ventures II, L.P.
Lux Ventures II Sidecar, L.P.
c/o Lux Capital Management, LLC
295 Madison Avenue, 24th floor
New York, NY 10017
Attn: Robert Paull

Brisco-Davis Group, LLC
Davis Clearing House, LLC
2012 Trust Agreement of Victoria Smith Trauscht, dated September 18, 2012
Holly Smith-Norman 2007 Trust, dated November 24, 2007, as amended
2011 Trust Agreement of Karen Chase Smith, dated February 22, 2012
453 N. Lindbergh Blvd., 2nd Floor
St. Louis, MO 63141
Attn: Kate Smith

CVF, LLC
222 N. La Salle St.
Suite 2000
Chicago, IL 60601
Attn: Richard H. Robb

Polaris Venture Partners V, L.P.
Polaris Venture Partners Entrepreneurs' Fund V, L.P.
Polaris Venture Partners Founders' Fund V, L.P.
Polaris Venture Partners Special Founders' Fund V, L.P.
Polaris Venture Partners
One Marina Park Drive, 10th Floor
Boston, MA 02210
Attn: Kevin Bitterman

Schedule A

Investors

Third Rock Ventures, L.P.
Third Rock Ventures
29 Newbury Street #301
Boston, MA 02116
Attn: Robert I. Tepper, M.D.

William Wachtel
c/o Wachtel Missry LLP
One Dag Hammarskjold Plaza
885 Second Avenue
New York, NY 10017
Attn: William Wachtel

Larry Fritz
P.O. Box 676150
Rancho Santa Fe, CA 92067

Adam Kalish
Lux Capital Management
295 Madison Avenue, 24th Floor
New York, NY 10017
Attn: Adam Kalish

Lighthouse Capital Partners VI, L.P.
3555 Alameda de las Pulgas, Suite 200
Menlo Park, California 94025
Attn: Contracts Administration

Schedule A

Investors

Benon Group Ltd.
Address For Notice:
Benon Group Ltd.
c/o Nathaniel de Rothschild Holdings, Ltd.
152 West 57th Street
37th Floor
New York, NY 10019

With a copy to:

Ellen S. Brody
Roberts & Holland LLP
825 8th Avenue, 37th Fl
New York, NY 10019

Ysios BioFund I FCR
c/o Ysios Capital Partners SGEIC, SA
Travessera de Gracia 11, 8th Floor
08021 Barcelona, Spain
Attn: Karen Wagner, General Partner

Alexandria Equities, LLC
385 E. Colorado Blvd., Suite 299
Pasadena, California 91101
Attn: Chief Financial Officer

RA Capital Healthcare Fund, L.P.
Blackwell Partners LLC — Series A
20 Park Plaza
Suite 1200
Boston, Massachusetts 02116
Attn: Nicholas McGrath

Schedule A

Investors

Hadley Harbor Master Investors (Cayman) L.P.
c/o Wellington Management Company LLP
Attention: Legal and Compliance Department
280 Congress Street
Boston, Massachusetts 02210
Facsimile Number: 617-289-5699

Longitude Venture Partners II, L.P.
800 El Camino Real, Suite 220
Menlo Park, CA 94025
Attention: Greg Grunberg

Vivo Capital Fund VIII, L.P.
575 High Street, Suite 201
Palo Alto, CA 94301
Attention: Chen Yu, Managing Partner

Vivo Capital Surplus Fund VIII, L.P.
575 High Street, Suite 201
Palo Alto, CA 94301
Attention: Chen Yu, Managing Partner

OrbiMed Private Investments VI, LP
c/o OrbiMed Advisors LLC
601 Lexington Avenue, 45th Floor
New York, NY 10022
Attn: Jonathan Silverstein

CDK Associates, L.L.C.
Attn: Heath Weisberg
CAM Capital
731 Alexander Road, Building 2
Princeton, NJ 08540

Scott Morenstein
635 West 42nd Street, Apt 45E
NY, NY 10036

Schedule B
Key Holder

Mark Iwicki
120 Dover Rd.
Wellesley, MA 02482

Exhibit I

Form of Joinder Agreement

The undersigned hereby agrees, effective as of the date hereof, to become a party to that certain Third Amended and Restated Registration Rights Agreement, dated as of April 6, 2016 (as amended and/or restated from time to time, the "Agreement"), by and among Kala Pharmaceuticals, Inc., a Delaware corporation, and the parties named therein, and for all purposes of the Agreement, the undersigned shall be included within the term "Investor" (as defined in the Agreement).

INVESTOR:
[·]

By: _____
Name:
Title:

Date: _____

Address For Notice:

[Address]
[Address]
Tel: [ ]
Email: [ ]

AMENDMENT NO. 1 TO
THIRD AMENDED AND RESTATED REGISTRATION RIGHTS AGREEMENT

This Amendment No. 1 (this **"Amendment"**) to the Third Amended and Restated Registration Rights Agreement, dated April 6, 2016 (the **"Registration Rights Agreement"**), by and among the Company and the Stockholders (as defined therein) is entered into as of the 13th day of December, 2017 by and among Kala Pharmaceuticals, Inc., a Delaware corporation (the **"Company"**), and each of the signatories hereto. Capitalized terms not defined herein shall have the meanings given to such terms in the Registration Rights Agreement.

RECITALS

WHEREAS, the Company and the Requisite Holders (as defined below) desire to amend the Registration Rights Agreement as set forth herein; and

WHEREAS, the Registration Rights Agreement may be amended pursuant to Section 10 thereof only with the written consent of the (a) Company and (b) the holders of at least sixty-seven percent (67%) of the Registrable Securities issued or issuable upon conversion of Preferred Stock then outstanding (together, the **"Requisite Holders"**).

NOW, THEREFORE, in consideration of the mutual covenants contained herein and for other valuable consideration, the receipt of which is hereby acknowledged, the parties agree as follows:

1. Amendment of Section 1. Section 1 of the Registration Rights Agreement is hereby amended by deleting the definition of "Registrable Securities" in its entirety and substituting in lieu thereof the following:

> ""Registrable Securities" shall mean (i) the shares of Common Stock issued or issuable upon conversion of the Preferred Stock held, or hereafter acquired, by the Investors (the "Investor Registrable Securities"), (ii) Key Holder Registrable Securities and (iii) any other shares of Common Stock issued or issuable in respect of such Investor Registrable Securities or Key Holder Registrable Securities (because of stock splits, stock dividends, reclassifications, recapitalizations or similar events); *provided, however,* that any shares for which registration rights have terminated pursuant to Section 15 of this Agreement shall not be "Registrable Securities"."

2. Amendment of Section 15. Section 15 of the Registration Rights Agreement is hereby amended by deleting Section 15 in its entirety and substituting in lieu thereof the following:

> ""Termination of Registration Rights." The right of any Stockholder to request registration or inclusion of Registrable Securities in any registration pursuant to Sections 2, 3 or 4 of this Agreement shall terminate upon the earlier to occur of (a) the seventh (7^{th}) anniversary of the Company's IPO and (b) following the Company's IPO, at such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of all of such Stockholder's shares without

limitation during a three-month period without registration and without regard to the requirement for the Company to be in compliance with the current public information required under Rule 144(c)(1)."

3. Effectiveness of Amendment. Except as expressly amended hereby, all terms, conditions and provisions of the Registration Rights Agreement shall remain in full force and effect in accordance with the Registration Rights Agreement.

4. Counterparts. This Amendment may be executed in one or more counterparts, each of which shall for all purposes be deemed to be an original and all of which shall constitute the same instrument.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date first written above.

COMPANY:

KALA PHARMACEUTICALS, INC.

By: /s/ Mark Iwicki
Name: Mark Iwicki
Title: Chief Executive Officer

[Signature Page to Amendment No. 1 to
Third Amended and Restated Registration Rights Agreement]

INVESTORS:

LUX VENTURES II, L.P.
By: Lux Venture Partners II, L.P., its General Partner
By: Lux Venture Associates II, LLC, its General Partner
By: Lux Capital Management, LLC, its Sole Member

By: /s/ Peter Hébert
Name: Peter Hébert
Title: Managing Partner

LUX VENTURES II SIDECAR, L.P.
By: Lux Venture Partners II, L.P., its General Partner
By: Lux Venture Associates II, LLC, its General Partner
By: Lux Capital Management, LLC, its Sole Member

By: /s/ Peter Hébert
Name: Peter Hébert
Title: Managing Partner

[Signature Page to Amendment No. 1 to
Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

THIRD ROCK VENTURES, L.P.
By: Third Rock Ventures GP, L.P., its General Partner
By: TRV GP, LLC, its General Partner

By: /s/ Kevin Gillis
Name: Kevin Gillis
Title: CFO

[Signature Page to Amendment No. 1 to
Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

POLARIS VENTURE PARTNERS V, L.P.
By: Polaris Venture Management Co. V, L.L.C., its General Partner

By: /s/ Max Eisenberg
Name: Max Eisenberg
Title: Attorney-in-fact

POLARIS VENTURE PARTNERS ENTREPRENEURS' FUND V, L.P.
By: Polaris Venture Management Co. V, L.L.C., its General Partner

By: /s/ Max Eisenberg
Name: Max Eisenberg
Title: Attorney-in-fact

POLARIS VENTURE PARTNERS FOUNDERS' FUND V, L.P.
By: Polaris Venture Management Co. V, L.L.C., its General Partner

By: /s/ Max Eisenberg
Name: Max Eisenberg
Title: Attorney-in-fact

INVESTORS (cont.):

POLARIS VENTURE PARTNERS SPECIAL FOUNDERS' FUND V, L.P.
By: Polaris Venture Management Co. V, L.L.C., its General Partner

By: /s/ Max Eisenberg
Name: Max Eisenberg
Title: Attorney-in-fact

[Signature Page to Amendment No. 1 to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

CVF, LLC

By: /s/ Richard H. Robb
Name: Richard H. Robb
Title: Manager

[Signature Page to Amendment No. 1 to
Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

RA CAPITAL HEALTHCARE FUND, L.P.

BY: RA CAPITAL MANAGEMENT, LLC
ITS: GENERAL PARTNER

By: /s/ Rajeev Shah
Name: Rajeev Shah
Title: Authorized Signatory

BLACKWELL PARTNERS LLC—SERIES A

By: /s/Abayomi A. Adigun
Name: Abayomi A. Adigun
Title: Investment Manager
DUMAC, Inc.
Authorized Agent

By: /s/ Jannine M. Lall
Name: Jannine M. Lall
Title: Controller
DUMAC, Inc.
Authorized Agent

[Signature Page to Amendment No. 1 to
Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

HADLEY HARBOR MASTER INVESTORS (CAYMAN) L.P.

By: Wellington Management Company LLP, as investment adviser

By: /s/ Emily Babalas
Name: Emily Babalas
Title: Managing Director and Counsel

[Signature Page to Amendment No. 1 to Third Amended and Restated Registration Rights Agreement]

INVESTORS (cont.):

LONGITUDE VENTURE PARTNERS II, L.P.

By: Longitude Capital Partners II, LLC

Its: General Partner

By: /s/ Greg Grunberg
Name: Greg Grunberg
Title: Member

[Signature Page to Amendment No. 1 to
Third Amended and Restated Registration Rights Agreement]

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

AMENDMENT NO. 1
TO
AMENDED AND RESTATED MASTER SERVICES AGREEMENT

THIS AMENDMENT NO. 1 ("**Amendment No. 1**"), effective as of the date signed by the last party to sign below (the "**Amendment No. 1 Effective Date"**), is by and between Kala Pharmaceuticals, Inc. ("**SPONSOR**") and Alliance Contract Pharma, an Altasciences company (as successor in interest to Alliance Contract Pharma, LLC, "**SUPPLIER**") and amends the Amended and Restated Master Services Agreement dated October 4, 2017 between SPONSOR and Alliance Contract Pharma, LLC (the "**Agreement**"). Any capitalized term used but not defined herein shall have the meaning ascribed to such term in the Agreement.

WHEREAS, SPONSOR and Alliance Contract Pharma, LLC entered into the Agreement; and

WHEREAS, on February 27, 2020, Altasciences acquired Alliance Contract Pharma, LLC; and

WHEREAS, SPONSOR and SUPPLIER desire to amend the Agreement in order to assign the Agreement to SUPPLIER following the above referenced acquisition, to update contact information regarding the Parties, and to update the pricing schedule set forth therein.

NOW THEREFORE, the parties hereto agree as follows:

1. As of February 27, 2020, (a) the Agreement is assigned to SUPPLIER, (b) SPONSOR consents to such assignment, and (c) SUPPLIER assumes all rights and responsibilities of Alliance Contract Pharma, LLC set forth in the Agreement.

2. SPONSOR's address is hereby updated to 490 Arsenal Way, Suite 120, Watertown, MA 02472.

3. **ARTICLE 4, Section B** of the Agreement, entitled "**Purchase Orders**," is hereby deleted in its entirety and replaced with the following:

   "B. Purchase Orders. All Product ordered by SPONSOR shall be in the form of a firm written Purchase Order not less than [**] days prior to expected delivery. The Lead Time for the Product shall not exceed the number of days set forth in the applicable Proposal/SOW. Each Purchase Order shall contain at a minimum, the following information: description of the Product and quantity ordered, price, delivery terms, delivery date, and Purchase Order number for billing purposes. Each Purchase Order issued pursuant to this Agreement shall be binding, except that delivery dates may be moved ahead or back by mutual written agreement of SUPPLIER and SPONSOR. To the extent there are any conflicts between the terms of any Purchase Order and

the terms of this Agreement, the terms of this Agreement shall prevail and control. There shall be no minimum purchase requirements except for binding forecasts. Batches will be invoiced upon the completion of manufacturing and release testing. As noted in the table below, the cost per batch is based on the following four-tier pricing schedule: (i) upon the completion of manufacturing the first [**] batches in each calendar year, batches [**] will be invoiced at Tier 1 pricing; (ii) upon the completion of manufacturing the [**] batches in each calendar year, batches [**] will be invoiced at Tier 2 pricing; (iii) upon the completion of manufacturing batches [**] in each calendar year, batches [**] will be invoiced at Tier 3 pricing; and (iv) all remaining batches manufactured from batch [**] on will be invoiced at Tier 4 pricing.

Pricing Schedule	**Product Manufactured in each Calendar Year (number of batches)**	**Cost per Batch**
Tier 1	[**]	[**]
Tier 2	[**]	[**]
Tier 3	[**]	[**]
Tier 4	[**]	[**]

SUPPLIER shall have the right, but not the obligation, to increase prices in January of each calendar year. Price increases shall not exceed the percentage change in the Producer Price Index for Pharmaceutical Preparation Manufacturing [PCU325412325412] for the twelve (12) month period ending in December of the previous year. Price increases shall not apply to any Purchase orders that have already been placed by SPONSOR and accepted by SUPPLIER."

4. SPONSOR's contact for notices in ARTICLE 16, Section A, is hereby deleted in its entirety and replaced with the following:

"SPONSOR: [**]
Kala Pharmaceuticals, Inc.
490 Arsenal Way, Suite 120
[**]
E-mail: [**]

With a copy to: General Counsel
Kala Pharmaceuticals, Inc.
490 Arsenal Way, Suite 120
Watertown, MA 02472
Email not permitted; Notice to be sent pursuant to (i) or (ii) above"

5. Except as expressly provided in this Amendment No. 1, the remaining terms and conditions of the Agreement shall remain in full force and effect. This Amendment No. 1 may be executed in one or more counterparts, each of which will be deemed an original, and all of which together will be deemed to be one and the same instrument. Signature pages of this Amendment No. 1 may be exchanged by facsimile or electronically as a portable document format (PDF) file and such signature pages will be deemed originals.

IN WITNESS WHEREOF, the undersigned have executed this Amendment No. 1 effective as of the Amendment No. 1 Effective Date.

KALA PHARMACEUTICALS, INC.	**ALLIANCE CONTRACT PHARMA, AN ALTASCIENCES COMPANY**
By: /s/ Vincent Kosewski	By: /s/ Steve Schweibenz
Name: Vincent Kosewski	Name: Steve Schweibenz
Title: Sr. VP Mfg. & Supply	Title: President
Date: August 24, 2020	Date: August 25, 2020

Exhibit 10.31

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed.
Double asterisks denote omissions.

AMENDMENT THREE TO
COMMERCIAL SUPPLY AGREEMENT

This Amendment Three ("**Amendment 3**") to the Commercial Supply Agreement dated June 27, 2016, as amended by Amendment 1, dated February 16, 2008 and, Amendment 2, dated March 27, 2020 (collectively the "**Agreement**") is made as of this 11th day of December, 2020 ("**Amendment 3 Effective Date**"), by and between **Kala Pharmaceuticals, Inc.** having a place a business at 490 Arsenal Way, Suite 120
Watertown, MA 02472 ("**Client**") and **Catalent Pharma Solutions, LLC,** with a place of business at 14 Schoolhouse Road, Somerset NJ 08873 ("**Catalent**").

RECITALS

A. Client and Catalent entered into the Agreement, pursuant to which Catalent performs Services as requested by Client from time to time;

C. Client and Catalent mutually desire to amend the Agreement as set forth below;

THEREFORE, in consideration of the mutual covenants, terms and conditions set forth below, the Parties agree as follows:

1. Recitals. The definition of Catalent set out in the Recital shall be reworded to now refer to Catalent Pharma Solutions, its subsidiaries and affiliates. For the purposes of this Agreement, as amended, the term "**Affiliates**" shall mean, with respect to Client, any corporation, firm, partnership or other entity that controls, is controlled by or is under common control with Client; and with respect to Catalent, Catalent Pharma Solutions, Inc. ("**CPS, Inc.**") and any corporation, firm, partnership or other entity controlled by CPS, Inc. For purposes of this definition, "**control**" shall mean the ownership of at least fifty percent (50%) of the voting share capital of an entity or any other comparable equity or ownership interest.

2. Definitions. Capitalized terms used and not otherwise defined in this Amendment 3 shall have the meanings assigned to them in the Agreement. For clarity, the term "Agreement" as used in the Agreement and herein shall mean the Agreement as amended hereby.

3. Pursuant to Section 2.3 of the Agreement, the Agreement is hereby amended to add the following:

- "Attachment D (the "Product Maintenance Services and Other Related Services"), – Fees table hereby defines Payable [**]. For avoidance of doubt, Product maintenance Services Fees of $[**] shall be payable [**] for the period covering [**].

4. No Other Variation. Except as expressly provided in this Amendment, all the terms, conditions and provisions of the Agreement (including the rights, duties, liabilities and obligations of the Parties thereunder) remain in full force and effect, and shall apply to the construction of this Amendment.

5. Entire Agreement. This Amendment 3 and the Agreement, including its attachments, constitute the entire agreement between the Parties relating to the subject matter hereof and thereof, and may not be varied except in writing signed by a duly authorized representative of each Party.

6. Counterparts. This Amendment 3 may be executed in one or more counterparts, each of which shall be deemed an original but all of which together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the Parties have caused their respective duly authorized representatives to execute this Amendment 3 effective as of the Amendment 3 Effective Date.

Catalent Pharma Solutions, LLC	**Kala Pharmaceuticals, Inc**
By: /s/ Bill Hartzel	By: /s/ Vin Kosewski
Name: Bill Hartzel	Name: Vin Kosewski
Title: 13-Dec-2020	Title: 15-Dec-2020

Exhibit 21.1

Subsidiaries of the Registrant

Name	Jurisdiction of Organization
Kala Pharmaceuticals Security Corporation	Massachusetts

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-226748 and 333-238087 on Form S-3 and Nos. 333-219403, 333-224083, 333-230206, 333-236402, and 333-239426 on Form S-8 of our report dated February 25, 2021, relating to the consolidated financial statements of Kala Pharmaceuticals, Inc. and its subsidiary appearing in the Annual Report on Form 10-K of Kala Pharmaceuticals, Inc. for the year ended December 31, 2020.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 25, 2021

Exhibit 31.1

CERTIFICATIONS

I, Mark Iwicki, certify that:

1. I have reviewed this Annual Report on Form 10-K of Kala 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 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 change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

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

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

Date: February 25, 2021

/s/ Mark Iwicki
Mark Iwicki
President and Chief Executive Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATIONS

I, Mary Reumuth, certify that:

1. I have reviewed this Annual Report on Form 10-K of Kala 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 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 change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

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

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

Date: February 25, 2021

/s/ Mary Reumuth
Mary Reumuth
Chief Financial Officer
(principal financial and accounting officer)

Exhibit 32.1

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

In connection with the Annual Report on Form 10-K of Kala Pharmaceuticals, Inc. (the "Company") for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Mark Iwicki, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge on the date hereof:

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

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

Date: February 25, 2021

/s/ Mark Iwicki
Mark Iwicki
President and Chief Executive Officer
(principal executive officer)

Exhibit 32.2

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

In connection with the Annual Report on Form 10-K of Kala Pharmaceuticals, Inc. (the "Company") for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Mary Reumuth, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of her knowledge on the date hereof:

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

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

Date: February 25, 2021

/s/ Mary Reumuth
Mary Reumuth
Chief Financial Officer
(principal financial and accounting officer)