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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31, 2021
OR

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

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.)
1167 Massachusetts Avenue **Arlington, MA** (Address of principal executive offices)	**02476** (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, 2021, 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 $254.3 million, based on the closing price of the registrant's common stock on June 30, 2021.

There were 72,594,005 shares of Common Stock ($0.001 par value) outstanding as of March 28, 2022.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2022 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, 2021.

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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 subsidiaries, 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 expectations with respect to the potential financial impact, synergies, growth prospects and benefits of our acquisition of Combangio, Inc., or Combangio, which was completed on November 15, 2021, or the Acquisition, pursuant to the Agreement and Plan of Merger dated November 15, 2021, by and among Ceres Merger Sub, Inc., Combangio and the Combangio equityholder representative, or the Merger Agreement, including the estimated costs and potential realization of the expected benefits from the Acquisition;
- our expectations with respect to, and the amount of, future milestone payments pursuant to the Merger Agreement;
- our expectations with respect to potential advantages of KPI-012, our lead product candidate, for the treatment of persistent corneal epithelial defects, or PCED;
- the anticipated and unanticipated costs, fees, expenses and liabilities related to the Acquisition, including the estimated costs for development of KPI-012;
- our ability to successfully integrate Combangio's business into our business;
- 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, including KPI-012, and our ability to discover and develop new programs and product candidates, including those from our receptor Tyrosine Kinase Inhibitor program and our novel selective glucocorticoid receptor modulators program;
- the timing, progress and results of clinical trials for KPI-012 and other product candidates, including statements regarding the timing of initiation and completion of clinical trials, dosing of subjects and the period during which the results of the trials will become available;
- the timing, scope and likelihood of regulatory filings, including the filing of an investigational new drug application and biologics license application for KPI-012 and any other product candidate we develop;
- our estimates regarding potential future revenue from sales of EYSUVIS and INVELTYS and, if approved, KPI-012;

- 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, INVELTYS and, if approved, KPI-012;
- our ability to maintain regulatory approvals for EYSUVIS and INVELTYS and our ability to obtain regulatory approvals for KPI-012;
- 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, including KPI-012;
- the rate and degree of market acceptance and clinical utility of our products and KPI-012;
- our estimates regarding the potential market opportunity for EYSUVIS, INVELTYS and our product candidates, including KPI-012;
- plans to pursue the development of KPI-012 for indications in addition to PCED;
- our commercialization, marketing and manufacturing capabilities and strategy for EYSUVIS, INVELTYS and, if approved, KPI-012;
- our intellectual property position, including intellectual property acquired in the Acquisition;
- 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;
- our business and business relationships, including with employees and suppliers;
- 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, including KPI-012, 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, 2021, we had an accumulated deficit of $542.4 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.
- We may fail to realize the anticipated benefits of our acquisition of Combangio, those benefits may take longer to realize than expected, and we may encounter significant integration difficulties.
- 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, is believed to have impacted the commercialization of EYSUVIS and could impact the development of KPI-012 or any other product candidate we develop and may continue to adversely affect our business, results of operations and financial condition.
- EYSUVIS, INVELTYS, KPI-012 or any other product candidate that receives 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, KPI-012 or any other 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, KPI-012 or any other product candidate 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 competitors include major pharmaceutical companies

with significantly greater financial resources. EYSUVIS, INVELTYS, KPI-012 and our product candidates will also compete with existing branded, generic and off-label products.

- If we are unable to successfully complete the clinical development of, and obtain marketing approval for, KPI-012 or any other product candidate, or experience significant delays in doing so, or if, after obtaining marketing approvals, we fail to commercialize our products and product candidates, our business will be materially harmed.

- We contract with third parties for the manufacture of EYSUVIS, INVELTYS and KPI-012 and plan to contract with third parties for preclinical, clinical and commercial supply of any other product candidates we develop. 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 are committed to purchasing a minimum amount of EYSUVIS and INVELTYS for commercial use which may result in us paying for product in excess of our needs if we are not able to successfully commercialize our products and/or successfully estimate our supply needs.

- 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 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, KPI-012 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.

- Existing and future legislation may increase the difficulty and cost for us to obtain reimbursement for our products and product candidates.

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 products 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. Our product candidates and programs include a proprietary regenerative biotherapy for severe ocular diseases and a pipeline of preclinical 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, and we commenced a full promotional launch of EYSUVIS in January 2021. 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 offer 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 are 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.

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. The FDA approved INVELTYS in August 2018, and we commercially launched the product in January 2019. INVELTYS 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.

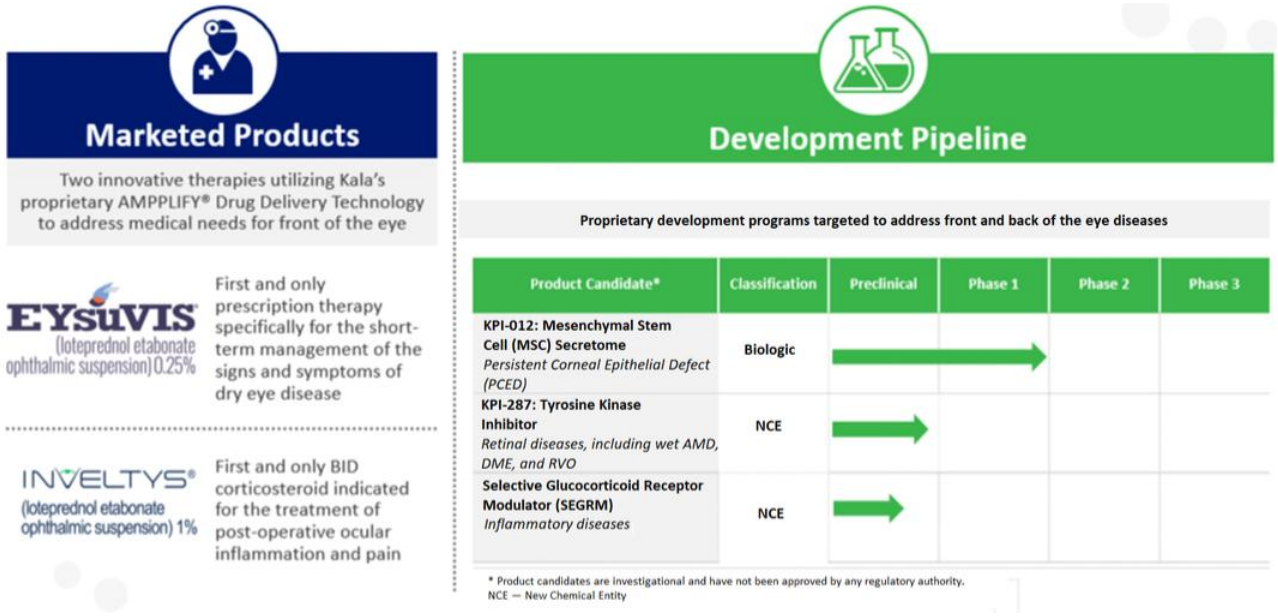
Upon the consummation of our acquisition of Combangio, Inc., or Combangio, on November 15, 2021, we acquired Combangio's product candidate, CMB-012, which we now refer to as KPI-012. KPI-012 is our lead product candidate and is currently in clinical development for the treatment of persistent corneal epithelial defects, or PCED, a rare disease of impaired corneal healing. We believe the multifactorial mechanism of action of KPI-012 also makes it a platform technology, and we are evaluating KPI-012 for potential expansion to indications for rare front of the eye diseases, such as limbal stem cell deficiency, chemical burns and Sjogren's Syndrome, as well as select rare back of the eye diseases, such as retinitis pigmentosa and optic neuritis. For a description of the financial terms of the acquisition of Combangio, see "Item 7., Management's Discussion and Analysis of Financial Condition and Results of Operations".

We are also progressing our pipeline of proprietary NCE preclinical development programs targeted to address both front and back of the eye diseases. These preclinical development programs include KPI-287, our receptor Tyrosine Kinase Inhibitor, or TKI, and our selective glucocorticoid receptor modulators, or SEGRMs.

KPI-287 is designed to inhibit the vascular endothelial growth factor, or VEGF, and platelet derived growth factor, or PDGF, pathways, and is administered by suprachoroidal injection for the treatment of retinal diseases, including wet age-related macular degeneration, or wet AMD, diabetic macular edema, or DME, and retinal vein occlusion, or RVO. SEGRMs are a novel class of therapies designed to modify the downstream activity of the

glucocorticoid receptors to exhibit the anti-inflammatory and immunomodulatory properties of the corticosteroid class of therapies while markedly reducing their associated side effects, which we are developing for the treatment of inflammatory diseases.

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



We have retained worldwide commercial rights for EYSUVIS, INVELTYS, KPI-012 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 approximately 100 field-based commercial sales personnel. Our sales representatives promote both EYSUVIS and INVELTYS.

We own and/or exclusively license patents relating to EYSUVIS, INVELTYS, KPI-012, 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 the issued U.S. patents that we control covering KPI-012 are in 2040, and a portfolio of additional U.S. and ex-U.S. patent applications covering KPI-012 is currently in prosecution. The expiration dates of issued U.S. and ex-U.S. patents relating to our AMPPLIFY technology are in 2025 through 2036.

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:

- ***Maximize the commercial potential of EYSUVIS and INVELTYS.*** 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 also expect to explore commercialization of EYSUVIS for the treatment of dry eye disease in certain markets outside of the United States, utilizing a variety of collaboration, distribution and other marketing arrangements with one or more third parties.

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.

- ***Advance the clinical development of, and seek and obtain regulatory approval for, KPI-012 for the treatment of PCED and other indications.*** KPI-012 is a novel, human bone-marrow derived mesenchymal stem cells, or MSC, secretome currently in clinical development for the treatment of PCED. A PCED is a persistent non-healing corneal defect or wound that is refractory to conventional treatments. Based on the positive results of a Phase 1b clinical efficacy trial of KPI-012 in patients with PCED, we plan to submit an investigational new drug, or IND, application to the FDA for KPI-012 and, subject to regulatory clearance, commence a Phase 2/3 clinical trial of KPI-012 for PCED in the United States in the fourth quarter of 2022. If the results of our planned Phase 2/3 clinical trial of KPI-012 are positive, and subject to discussions with regulatory authorities, we believe this trial can serve as the first of two required pivotal trials. If so, we plan to conduct an additional Phase 3 pivotal trial in PCED patients to support the potential submission of a biologics license application, or BLA, to the FDA. If approved, we intend to commercialize KPI-012 with a small, targeted, internal sales force in the United States. We also expect to explore commercialization of KPI-012 for the treatment of PCED in certain markets outside the United States utilizing a variety of collaboration, distribution and other marketing arrangements with one or more third parties. We further believe that the multifactorial nature of KPI-012 also makes it a platform technology, and we are evaluating KPI-012 for potential expansion to indications for rare front of the eye diseases, such as limbal stem cell deficiency, chemical burns and Sjogren's Syndrome, as well as select rare back of the eye diseases, such as retinitis pigmentosa and optic neuritis.

- ***Advance our pipeline of preclinical development programs.*** We are also progressing our pipeline of proprietary NCE preclinical development programs targeting both front and back of the eye diseases. These programs include KPI-287, our TKI product candidate that inhibits the VEGF and PDGF pathways, for the treatment of retinal diseases, including wet AMD, and 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 while markedly reducing side effects associated with corticosteroids. 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.

- ***Business development through selective transactions.*** We plan to pursue value-driven business development opportunities as they arise in order to enhance our business and product pipeline, which may include strategically acquiring preclinical or clinical product candidates, particularly in the ophthalmic area. We also plan to explore a variety of transactions to maximize the value of our assets, including out-licensings, collaborations, divestitures, distributions and other development and marketing arrangements with one or more third parties for our products and product candidates.

Our Products

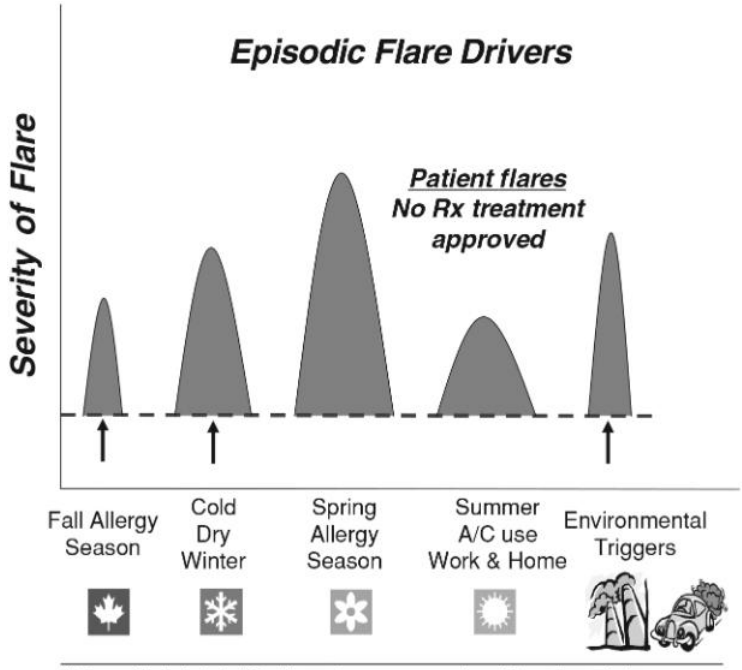
EYSUVIS for Dry Eye Disease

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 are commonly referred 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 hormonal changes, 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 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 independent studies conducted in 2020 and 2021 of 774 and 756 dry eye sufferers, respectively, 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.

Limitations of Existing Treatments for 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" or lubricating eye drops, and four prescription pharmaceutical products, Restasis®, Xiidra®, Cequa™ and Tyrvaya™.

Most over-the-counter artificial tears are palliative in nature and are intended to supplement insufficient tear production or improve tear film instability. Artificial tears typically provide only short term or temporary relief by lubricating the eyes and helping to maintain moisture on the outer surface of the eye. Artificial tears do not treat the underlying inflammatory components of dry eye disease.

In addition to over-the-counter artificial tears, Restasis, Xiidra, Cequa and Tyrvaya are sometimes prescribed as a chronic therapy for the treatment of dry eye disease. We believe that less than 10% of patients diagnosed with dry eye disease in the United States use a chronic therapy to treat their disease. Restasis and Cequa are each topically applied, ophthalmic formulations of the immunosuppressant 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. In clinical trials, the most common adverse reactions (incidence rate of approximately 5% to 25%) following the use of Xiidra were instillation-site irritation, dysgeusia, and decreased visual acuity. Tyrvaya (varenicline solution) nasal spray is a cholinergic agonist that was approved by the FDA in October 2021 to increase tear production and treat the signs and symptoms of dry eye disease. According to the Tyrvaya package insert, 82% of patients reported sneezing upon instillation. Tyrvaya, like Xiidra, Restasis and Cequa, is typically used chronically for dry eye patients who have continuous symptoms. As each of these medications 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 for whom EYSUVIS, an FDA-approved therapy for short-term use, can address a significant unmet need. For example, our patient surveys and the independent study of 774 dry eye sufferers 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 the 2021 independent, multi-sponsor survey of 756 dry eye sufferers indicating that they suffer a median of 5.25 flares per year lasting on average 4.9 days. In our 2021 survey of 201 eye care professionals, or ECPs, all reported that their patients have dry eye flares, but many underestimated the actual number of patients with flares. 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.

EYSUVIS Opportunity in Dry Eye Disease

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.

We believe that EYSUVIS has a favorable profile for the management of dry eye disease flares and other dry eye associated conditions, 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, Xiidra, Cequa and Tyrvaya. Therefore, we expect EYSUVIS 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, 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.

Our current estimates of potential future revenue from sales of EYSUVIS 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 the COVID-19 pandemic 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.

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 intraocular 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 in 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.

EYSUVIS Customer Concentration

Three customers comprised 10% or more of our revenue attributable to EYSUVIS during the year ended December 31, 2021 and 2020. These customers comprised 48%, 26% and 23% of our revenue, respectively, during the year ended December 31, 2021 and 35%, 32% and 29% of our revenue, respectively, during the year ended December 31, 2020.

INVELTYS for Post-Operative Inflammation and Pain

Post-Operative Inflammation and Pain Overview

Ocular inflammation and pain are common complications following ocular surgery. In 2019, Marketscope, a third-party provider of market data, projected that the number of ocular surgeries in the United States would grow to approximately 10.1 million by 2024. The COVID-19 pandemic impacted the ocular surgery market, and in 2020, there were only 7.0 million ocular surgeries reported by Marketscope, representing a decline of approximately 1.4 million from approximately 8.4 million ocular surgeries reported in 2019. In November 2021, Marketscope reported that ocular surgeries were projected to reach pre-COVID levels by the end of 2021. Commonly performed ocular surgeries include cataract, cornea, refractive, oculoplastic and glaucoma procedures. Tissue damage caused by ocular surgery leads to the production of prostaglandins, lipids that aid in recovery at the site of an injury, and increases in blood flow to the affected area, which contribute to inflammation. The standard of care for postoperative inflammation and pain includes anti-inflammatory drugs such as corticosteroids, which improve patient comfort and accelerate recovery through disruption of the inflammatory cascade.

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

Limitations of Existing Treatments for Post-Operative Inflammation and Pain

Loteprednol etabonate, or 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 first generic formulations of loteprednol suspension 0.5% (Lotemax suspension) and loteprednol ophthalmic gel 0.5% (Lotemax Gel) were launched in May 2019 and February 2021, respectively, and the first generic version of Durezol was launched in September 2021.

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 a three or four times-a-day dosing regimen 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 postoperative inflammation and pain are approved for dosing three or four times-a-day. INVELTYS 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. 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 was well tolerated with similar increases in IOP, a common side effect of steroids, compared to placebo and 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 Clinical Development Program

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.

INVELTYS Customer Concentration

Three customers comprised 10% or more of our revenue attributable to INVELTYS during the years ended December 31, 2021 and 2020. These customers comprised 47%, 30% and 21% of our revenue, respectively, during the year ended December 31, 2021 and 40%, 28% and 28% of our revenue, respectively, during the year ended December 31, 2020.

Our Clinical-Stage Product Candidate

KPI-012 for Persistent Corneal Epithelial Defects

Persistent Corneal Epithelial Defects Overview

Persistent corneal epithelial defects, or PCED, is a persistent non-healing corneal defect or wound that is refractory to conventional treatments. PCED is a disease of impaired corneal healing and can be the result of numerous etiologies, including (but not limited to) neurotrophic keratitis, or NK, microbial/viral keratitis, surgical epithelial debridement, corneal transplant surgery, limbal stem cell deficiency, mechanical/thermal trauma and exposure

keratopathy. Normal healing is a highly regulated multifactorial process that involves numerous biologic pathways and molecules, including growth factors, cell signaling, proliferation, migration and extracellular matrix remodeling. In PCED, the normal healing process is impaired due to an imbalance of the key biomolecules that orchestrate the normal wound healing process. We believe that effective treatment of PCED across the various etiologies requires a multifactorial mechanism of action to address the impaired healing that is responsible for the defects.

PCED is a rare disease with an estimated incidence of 100,000 cases per year in the United States and 238,000 cases per year in the United States, European Union and Japan combined. Clinical symptoms of PCED include pain, foreign body sensation, redness, photophobia and tearing. Clinical signs include non-healing epithelial defects, stromal scarring and stomal thinning. A PCED may lead to infection, corneal ulceration, corneal perforation, scarring, opacification and significant vision loss.

Limitations of Existing Treatments for Persistent Corneal Epithelial Defects

There is currently a significant unmet need for therapies to effectively treat PCED. Conventional therapies, which include bandage contact lenses, autologous serum and surgery, are usually ineffective in overcoming the dysregulation present in multiple cellular pathways that may need to be addressed to heal a PCED. Surgical procedures used in the treatment of PCED include tarsorrhaphy, corneal epithelial stem cell transplants and corneal transplants which are used to aid in restoration and maintenance of vision capabilities.

The only currently approved prescription product in the PCED space is OxervateÔ, indicated for the treatment of NK, which we believe to be the primary etiology for approximately one-third of PCED cases. Oxervate contains a single growth factor – nerve growth factor (NGF) – and has been demonstrated to be effective in only the subgroup of PCED cases whose underlying etiology is neurotrophic disease. Oxervate is a topical eye drop that is administered six times per day at two-hour intervals for eight weeks. Each administration of Oxervate requires the use of a vial containing the drug product, a vial adapter, a single-use pipette and disinfectant wipes.

KPI-012 Opportunity in Persistent Corneal Epithelial Defects

KPI-012 is a novel, human bone-marrow derived MSC secretome composed of biologically active components secreted from the MSCs, such as growth factors, protease inhibitors, matrix proteins and neurotropic factors, that have been shown in preclinical studies by Combangio and others to facilitate corneal healing. KPI-012 is cell-free and produced from a proprietary cell bank. The drug substance for KPI-012 is produced as a chemically-defined cell-free solution followed by formulation and filling of the drug product in non-preserved single dose units. We believe that KPI-012's multi-factorial mechanism of action has the potential to normalize the impaired healing in PCED and other severe ocular surface diseases driven by impaired healing. As such, KPI-012 offers a potentially promising approach for the treatment of PCED and other ocular surface diseases across multiple etiologies. Key biological factors contained in KPI-012 and their potential wound healing functions are shown below:

Key KPI-012 Components	**Ocular Surface Wound-Healing Function**
Protease Inhibitors (TIMP-1, TIMP-2, Serpin E)	Inhibit destructive proteases that degrade matrix in the wound bed
Matrix Proteins (Collagen)	Build a molecular scaffold in the wound bed for cells to migrate and adhere to
Growth Factors (HGF)	Suppress inflammation and promote corneal epithelium repair
Neurotrophic Factors (PEDF)	Promote maintenance of neurons to support corneal health

The multifactorial mechanism of action of KPI-012 is thought to be responsible for the significant wound healing activity observed in Combangio's preclinical animal models and in the Phase 1b clinical trials. KPI-012 has received orphan drug designation from the FDA, for the treatment of PCED, and we believe KPI-012 should meet the criteria for fast-track and breakthrough designations.

Preliminary Clinical Development Plan for KPI-012

We are initially developing KPI-012 for the treatment of PCED. Combangio completed a Phase 1b clinical efficacy trial in nine patients with PCED in Mexico City. Based on the results of this Phase 1b clinical trial, we plan to submit an IND application to the FDA for KPI-012 and, subject to regulatory clearance, commence a Phase 2/3 clinical trial of KPI-012 for PCED in the United States in the fourth quarter of 2022. Our planned Phase 2/3 randomized, placebo-controlled clinical trial of KPI-012 will evaluate the safety and efficacy of various dosing regimens of KPI-012 in patients diagnosed with PCED. If the results of our planned Phase 2/3 clinical trial of KPI-012 are positive, and subject to discussions with regulatory authorities, we believe this trial can serve as the first of two required pivotal trials. If so, we plan to conduct an additional Phase 3 pivotal trial in PCED patients to support the potential submission of a BLA to the FDA.

Phase 1b Clinical Trial Results of KPI-012

Combangio conducted two Phase 1b clinical trials with KPI-012 in Mexico City, Mexico during 2020 and 2021, one in 3 subjects without active corneal disease who were dosed twice a day (25 ng/mL FNE) for one week and another in nine patients with PCED, or the PCED cohort, who were dosed twice a day (25 ng/ml FNE) for up to 8 weeks. Key inclusion criteria for the PCED cohort included:

- Subjects with PCED of at least 10 days without improvement from one or more conventional non-surgical treatments in study eye due to any of the following:
  - NK, provided there was no active herpetic infection of the eye in the prior three months
  - Corneal Burns (alkali, acid and thermal)
  - Post-photorefractive Keratectomy
  - Post-corneal Transplant Surgery
  - Corneal epithelial debridement resulting from Diabetic Vitrectomy Surgery
  - Trauma
  - Keratoconjunctivtis sicca
  - Sjogren's Syndrome
  - Corneal cross-linking
- Subjects with bilateral corneal burns could only have one eye entered into the clinical trial
- Any previous treatment was stopped except for the study medication

The subjects were treated with KPI-012 topically twice a day, with the subjects in the safety cohort without active corneal disease treated for one week and patients in the PCED cohort treated between one to eight weeks. KPI-012 was generally well tolerated during both trials, with only one subject experiencing treatment-related TEAEs (mild and transient itching, red eye, and blurred vision after study drug administration). There were no deaths or treatment-related serious adverse events during either trial. One subject in the PCED cohort had to withdraw from the trial due to a protocol screening violation.

As depicted in Figure 1 below, six of the eight patients in the PCED cohort (75%) who completed the trial achieved complete healing of the lesion after four weeks of treatment, with one additional patient experiencing some clinical improvement but not complete healing. Four of eight patients in the PCED cohort (50%) achieved complete healing of the lesion after one week of treatment and the other two patients achieved complete healing within two to four weeks of initiation of treatment with KPI-012. All six of the patients who achieved complete healing remained healed through the follow-up period of the trial, which ranged between eight to 19 weeks. Of the two patients who did not show complete healing in the trial, clinical investigators noted some clinical improvement in one of the patients (Patient 2-05), but the corneal staining images did not show complete healing of the defect. Patient 2-04 had a PCED in a blind eye which was perhaps too severe to respond to a pharmaceutical intervention. Patient 2-05 had a PCED that had existed for 871 days before treatment; corneal specialists have advised that it is rare for a PCED to have persisted for this duration and that it could be indicative of systemic disease.

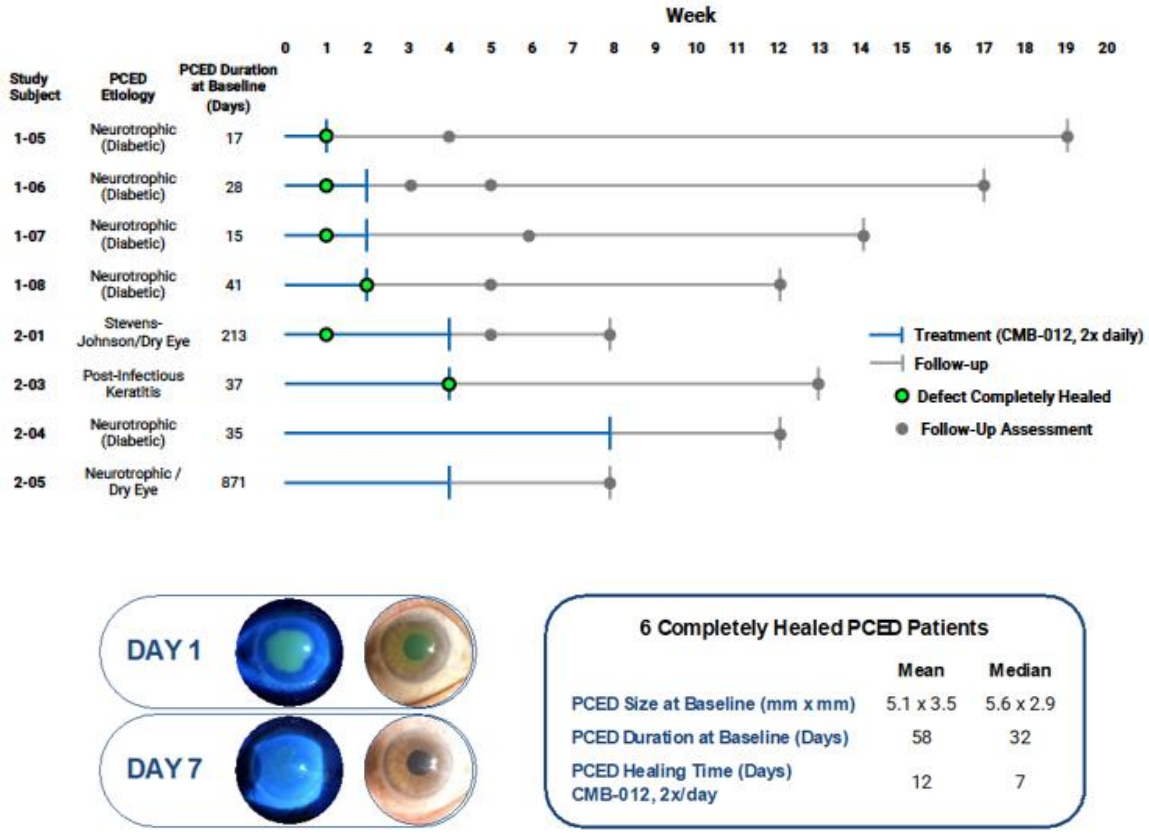


Figure 1. Summary of Phase 1b clinical trial of KPI-012 for PCED, including representative images for a healed patient study eye. The Day 1 images were taken on the first day of treatment, prior to first KPI-012 administration, with the fluorescein (green) stain demarking the corneal wound boundary of the study eye image. The Day 7 images were taken on the last day of KPI-012 treatment showing the PCED completely healed. The images on the left depict the study eye viewed under blue light to visualize the PCED with fluorescein stain.

Significant pain relief was reported by patients in the PCED cohort within one week of treatment with KPI-012, as shown in Figure 2 below. Of the six patients who reported pain at the baseline, all six patients reported a reduction in pain after one week of treatment, four patients reported a pain score of zero after one week of treatment and all six patients reported a pain score of zero after three weeks of treatment.

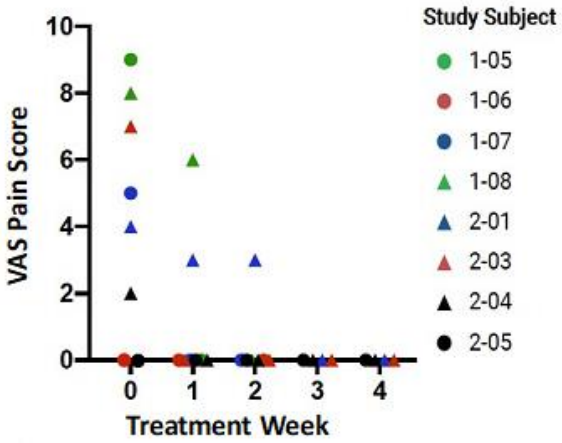


Figure 2. PCED cohort patient-reported score of pain level due to defect using a visual analogue scale, or VAS, which is a subjective rating of pain levels on a scale of 0 to 10 where a score of 0 represents no pain at all and a score of 10 represents the worst possible pain.

KPI-012 Preclinical Studies and Results

KPI-012 has been evaluated by Combangio in a number of preclinical studies. In these studies, KPI-012 promoted rapid ocular re-epithelialization and mitigated scarring and neovascularization in a number of well-established animal models.

In vitro Human Corneal Epithelial Wound Closure Assay

The therapeutic mechanism of action of KPI-012 involves stimulating corneal re-epithelialization and ocular surface healing. Combangio evaluated KPI-012 in an *in vitro* wound gap assay developed using human corneal epithelial cells. In this assay, a mechanical defect (cell-free region) was introduced into a two-dimensional monolayer of epithelial cells to create a wound. The 'injured' monolayer was then treated with KPI-012 and the cell free region was monitored for wound closure as show in Figure 3 below. In this assay, KPI-012 exhibited a dose-dependent and potent wound closure response.

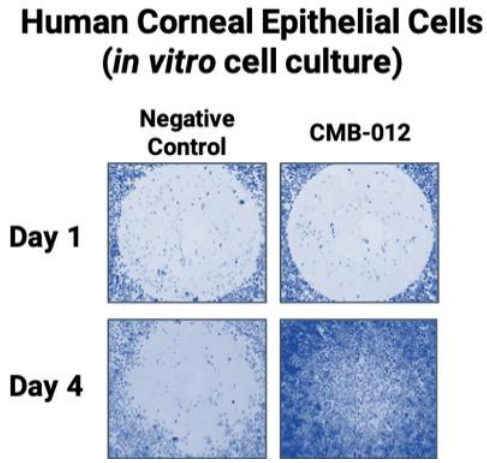


Figure 3. Representative images from an in vitro human corneal epithelial wound closure assay. A mechanical wound instilled to a corneal epithelial cell monolayer on Day 1 healed after treatment with KPI-012 (Day 4 of treatment), but not negative control (vehicle). Depicted images are wounded cell monolayers stained with Gentian Violet.

In vivo Mechanical Wound Studies of Activity

Combangio also evaluated the activity of KPI-012 in a mechanical corneal injury mouse model. In this model, a circular area on the surface of the cornea was debrided (mechanically scraped) to remove the epithelial layer and create a circular wound.

Topical formulations of vehicle or KPI-012 were administered twice daily to the wounded eyes. As shown in Figure 4 below, mice treated with KPI-012 exhibited prominent wound healing at day four of the treatment period, while the vehicle-treated wounded eyes remained largely unhealed. Further, treatment with KPI-012 resulted in reduced corneal haze and scarring relative to treatment with vehicle. Results of this mouse model suggested that at Day 4 of treatment KPI-012 promoted *in vivo* closure of cornea mechanical wounds relative to vehicle control.

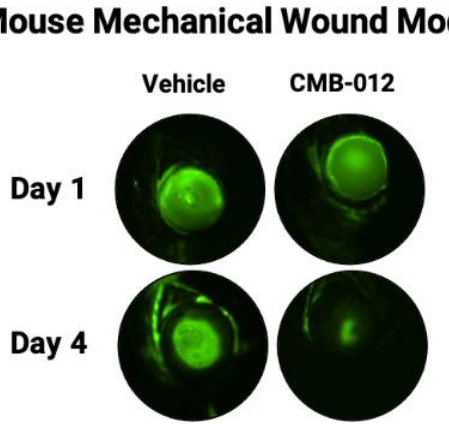


Figure 4. Representative images of wounded mouse corneas after mechanical injury (Day 1). Depicted is the fluorescein (green) stain, which demarks the corneal wound boundary. Treatment with KPI-012 rapidly healed the wound size (as indicated by the disappearance of the green stain by Day 4) relative to vehicle control-treated eyes.

A second confirmatory mechanical corneal injury mouse model study was performed according to the method described above using a different lot of KPI-012. The study yielded similar results, with KPI-012 promoting wound healing relative to vehicle as well as exhibiting dose-dependent potency dynamics. After four days of treatment, KPI-012 treated eyes exhibited more pronounced reduction in wound staining relative to vehicle-treated eyes, as shown in Figure 5A below, and after five days most KPI-012 treated eyes completely healed, as shown in Figure 5B below. Further, a KPI-012 formulation lacking key biologic factors known to mediate wound healing exhibited reduced healing capacity in the study, supporting the selection of KPI-012's critical quality attributes.

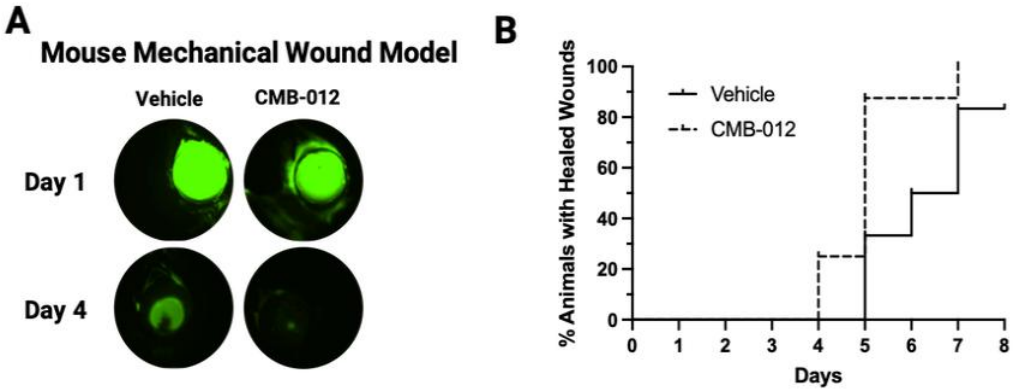


Figure 5. Summary of second mouse corneal mechanical study. (A) Representative images of wounded mouse corneas after mechanical injury (Day 1) and after four days of treatment with KPI-012 or vehicle (Day 4). Depicted is the fluorescein (green) stain, which demarks the corneal wound boundary. Treatment with KPI-012 rapidly healed the wound size (as indicated by the disappearance of the green stain by Day 4) relative to vehicle control-treated eyes; (B) Treatment with KPI-012 resulted in more rapid complete healing and a greater percentage of completely healed eyes (dashed line), relative to vehicle-treated eyes (solid line).

Rabbit Tolerability Study

To evaluate tolerability of KPI-012, Combangio conducted a 15-day good laboratory practice toxicology study following ocular instillation of KPI-012 in rabbits. The purpose of the study was to determine the ocular and systemic toxicity of KPI-012 following repeated topical ocular instillation for 15 days. One group of rabbits was administered KPI-012 three times a day via topical ocular instillation to the right eye (the low dose) and another group was administered KPI-012 six times a day via topical ocular instillation to the right eye (the high dose), in each case with a one-week recovery period. The left eye served as a contralateral control and received vehicle at the same frequency as the KPI-012-treated right eye. All rabbits survived to the end of the study, and no gross lesions and abnormalities were recorded. There were no observed test article-related findings on body weight, intraocular pressure, clinical pathology, gross pathology, organ weights, ophthalmologic examination or ocular histopathology. The data of the toxicology study supported that repeated daily topical administration of KPI-012, at both three times a day and six times a day for 15 days, was well-tolerated and resulted in no overt toxicities in rabbits.

Other Potential Indications for KPI-012

We believe the multifactorial mechanism of action of KPI-012 also makes it a platform technology, and we are evaluating KPI-012 for potential expansion to indications for rare front of the eye diseases, such as limbal stem cell deficiency, chemical burns and Sjogren's Syndrome, as well as select rare back of the eye diseases, such as retinitis pigmentosa and optic neuritis.

The wound-healing mechanism of action of KPI-012 also potentially enables partnering opportunities in chronic and/or severe indications outside of the eye such as diabetic foot ulcer.

Our Preclinical Development Programs

We are progressing a pipeline of proprietary NCE preclinical development programs, targeted to address both front and back of the eye diseases, including our TKI program for retinal diseases, and our SEGRM program.

TKI Program for Retinal Disease

Retinal Disease Overview

There are a range of retinal diseases and conditions that adversely affect vision, including age-related macular degeneration, or 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.

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 the leakage of existing blood vessels often accompanied by the growth of abnormal and leaky 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 biologic agents 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 signaling 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 TKIs 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 TKIs 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 receptor TKIs to treat various retinal diseases, such as AMD, DR, DME, RVO and related neovascular diseases.

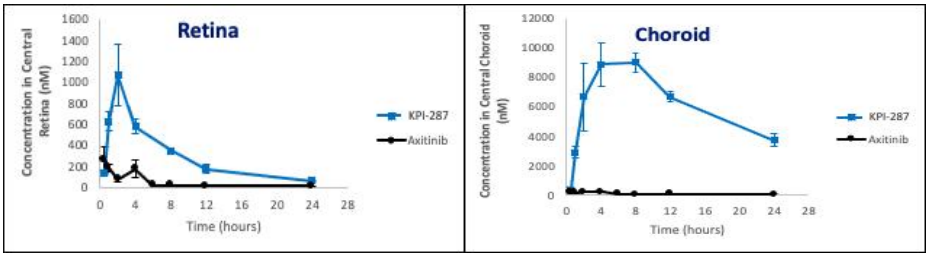
The PDGF family of signaling proteins function through the PDGF receptor, a receptor tyrosine kinase, or RTK, that plays a critical role in the formation of new blood vessels and fibrotic scar, two pathological processes that contribute to the vision loss associated with ocular disease. The combined inhibition of both VEGF and PDGF signaling pathways through their respective RTK are believed to be beneficial in treating certain retinal 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 intravitreal injections, or 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 $1.9 billion and $4.9 billion, respectively, in the United States in 20208. A new biologic form of Novartis' Beovu® was approved in October 2019 and had approximately $200 million in worldwide sales in 2020. An effective therapeutic to treat retinal diseases with improved dosing regimen would bring significant benefits to patients.

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

Through our TKI program we have developed several novel, potent, and selective TKIs, including KPI-287, which can inhibit the VEGF pathway and the platelet derived growth factor, or PDGF, pathway. In vitro assays show that KPI-287 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 developing KPI-287 via suprachoroidal injection for the treatment of various retinal diseases.

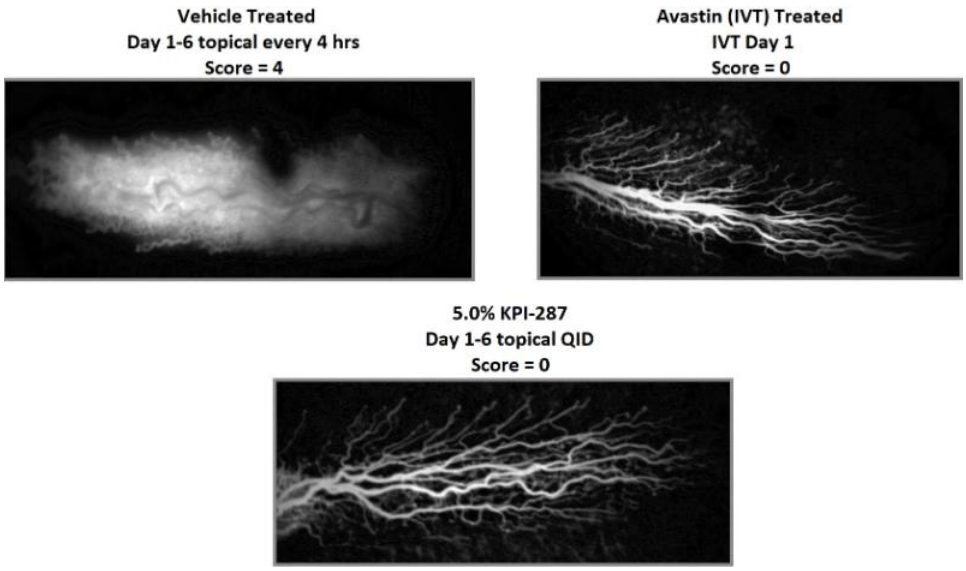
In preclinical rabbit studies, topical administration of KPI-287 achieved concentrations in tissues in the retina and the choroid well above the concentrations required for *in vitro* inhibition of 50% of the VEGF receptor 2 kinase activity. As shown in the figures below, the concentrations observed in these rabbit studies were higher than the concentrations observed in similar rabbit studies with topical administration of axitinib, which is the most common TKI currently being developed for retinal disease.



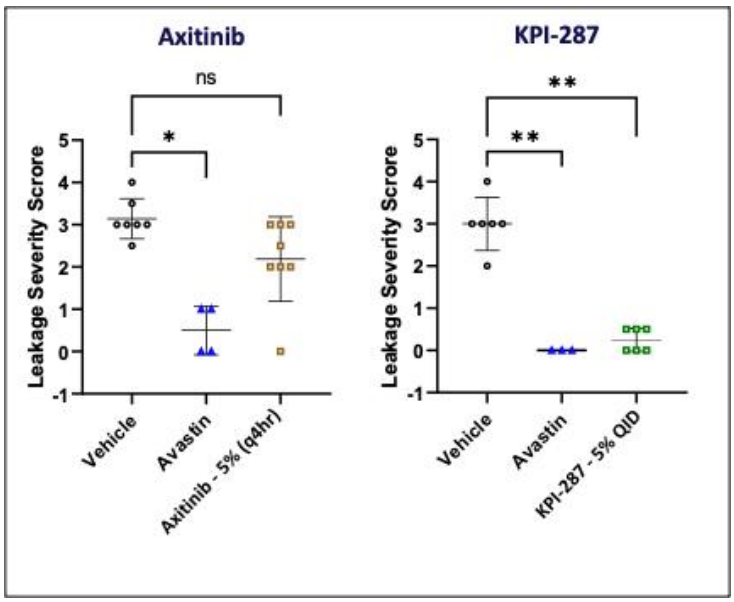
Tissues collected after a single topical dose 5% KPI-287 suspension *vs* 5% axitinib suspension in Dutch Belted rabbits

In addition, in a rabbit model of VEGF induced vascular leakage, topically applied KPI-287 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. Avastin is approved as an anticancer agent, but is widely used off-label in ophthalmic diseases. 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-287 5.0% was similar to that observed with IVT injection of Avastin.



In addition, the magnitude of effect observed with KPI-287 was greater than the magnitude of effect observed with topical administration of axitinib in studies similar to those we have conducted.



Axitinib (5% q4 hr) or KPI-287 (5% QID) dosed topically days 1 through 6, with VEGF challenge on day 3, and efficacy evaluation (fluorescein angiography) on day 6 (72 hrs post VEGF challenge). IVT Avastin used as positive control.

We are currently conducting additional preclinical studies with KPI-287 administered via suprachoroidal administration to evaluate both the pharmacokinetics and efficacy over six months following a suprachoroidal injections.

These studies are designed to evaluate the potential of KPI-287 for sustained durable delivery inhibiting VEGF induced ocular disease associated with vision loss.

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 for Inflammatory Diseases

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 or minimizing the TA pathway. As a result, we believe our SEGRM program has the potential for anti-inflammatory and immunomodulatory activity comparable to corticosteroids while markedly reducing their associated side effects. We plan to study our SEGRMs for the potential treatment of inflammatory diseases. Our SEGRM program is currently in the lead optimization stage, and we are aiming to identify a development candidate for the program.

Our AMPPLIFY Technology

Opportunities in Drug Delivery across Eye and other Mucosal Barriers

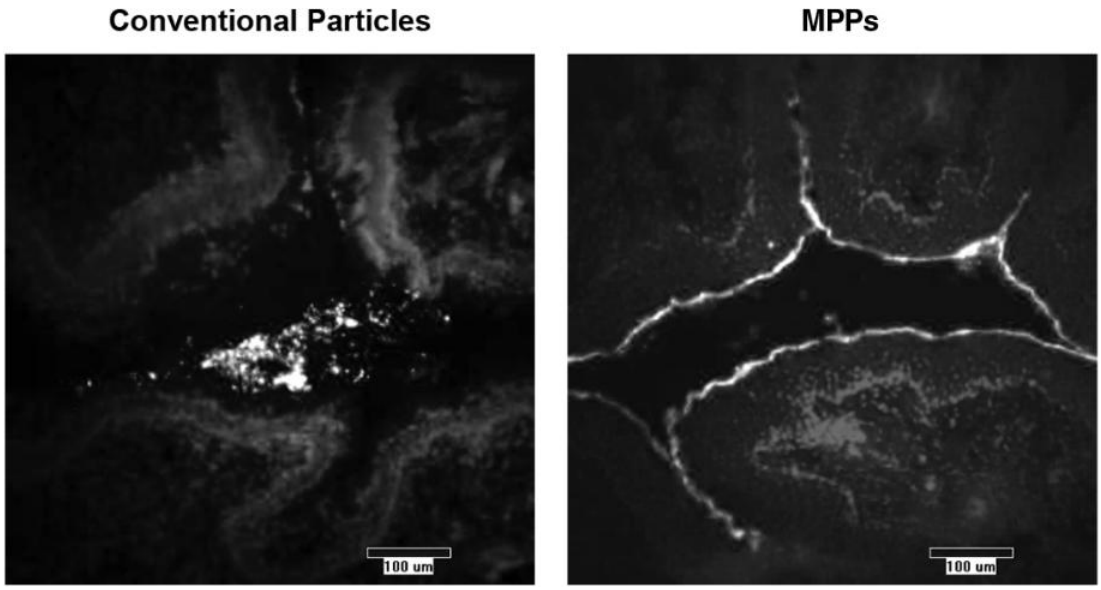
The body is surrounded by boundary tissues that play the important physiological role of preventing foreign bodies from penetrating into the body. The mucus that coats these tissues, the eyes, lung, cervical/vaginal tract and gastrointestinal tract, for example, serves as a protective barrier to trap 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 noncovalent 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.

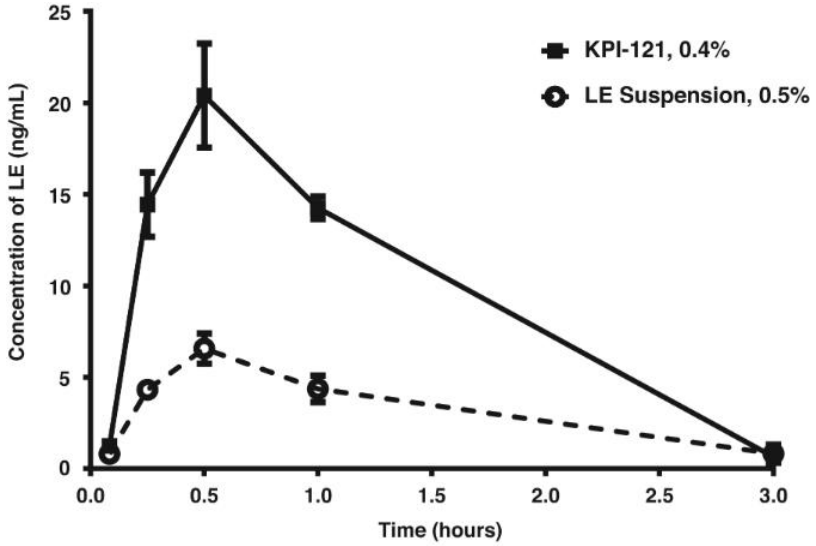


Source: Laura M. Ensign et al., Mucus-Penetrating Nanoparticles for Vaginal Drug Delivery Protect Against Herpes Simplex Virus, Science Translational Medicine, June 14, 2012.

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.

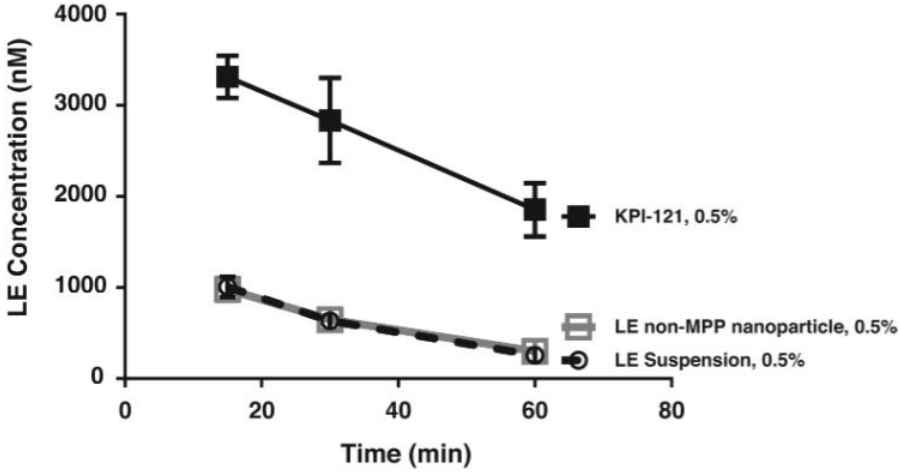
We aim to leverage our MPP technology, to enhance delivery of drugs into the eye. In preclinical studies, KPI-121 demonstrated favorable pharmacokinetic characteristics and increased drug penetration into ocular tissues as compared to a branded form of LE. In a preclinical study of ocular inflammation 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.

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, KPI-012 and any other 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®, Cequa™ and Tyrvaya™ 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 have been available in the United States since February 2022. 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 inflammation associated with dry eye disease. Xiidra is a topical anti-inflammatory therapy approved for treatment of the signs and symptoms of dry eye disease. Tyrvaya (varenicline solution) nasal spray is a cholinergic agonist that was approved by the FDA in October 2021 to increase tear production and treat 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 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 formulations of loteprednol suspension 0.5% (Lotemax suspension) and loteprednol ophthalmic gel 0.5% (Lotemax Gel) were launched in May 2019 and February 2021, respectively, and the first generic version of Durezol was launched in September 2021.

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 PCED

There is currently a significant unmet need for therapies to effectively treat PCED. Conventional therapies, which include bandage contact lenses, autologous serum and surgery, are usually ineffective in overcoming the dysregulation present in multiple cellular pathways that may need to be addressed to heal a PCED. Surgical procedures used in the treatment of PCED include tarsorrhaphy, corneal epithelial stem cell transplants and corneal transplants which are used to aid in restoration and maintenance of vision capabilities.

There is one approved prescription pharmaceutical product in the PCED space. Oxervate (cenegermin-bkbj), which was approved in August 2018 for the treatment of NK, a degenerative disease characterized by decreased corneal sensitivity and poor corneal healing, which we believe to be the primary underlying etiology of approximately one-third of all PCED cases. Oxervate is a topical eye drop that is administered six times per day at two-hour intervals for eight weeks. Each administration of Oxervate requires the use of a vial containing the drug product, a vial adapter, a single-use pipette and disinfectant wipes.

To our knowledge, there is currently only one product candidate in active clinical development for the treatment of a broad PCED population. ST266, an eye drop, is currently being studied in a Phase 2b clinical trial in patients with PCED and is being developed by Noveome Biotherapeutics Inc. ST266 is a secretome produced from amnion-derived epithelial cells from donated full-term placentas.

A number of companies are pursuing development of product candidates for the treatment of NK.

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 Novartis' Beovu.

Avastin is approved as an anticancer 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, Clearside Biomedical, Eyepoint Pharmaceuticals, and Ocular Therapeutix. There are also a number of preclinical research 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. 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 corticosteroids for the treatment of a variety of inflammatory diseases.

Sales and Marketing

In January 2019, we began commercializing INVELTYS in the United States with our own focused, specialty sales force. During late 2020 and in 2021, we expanded our sales force, which now includes approximately 100 field-based commercial sales personnel. Our sales force promotes EYSUVIS and INVELTYS.

We have not yet established our own commercial organization or distribution capabilities specific to KPI-012. We believe that we will be able to commercialize KPI-012, if approved, for the treatment of PCED with a small, targeted, internal sales force in the United States and potentially other major markets.

We expect to explore commercialization of EYSUVIS and potentially other product candidates, including KPI-012, if approved, in certain markets outside the United States utilizing a variety of collaboration, co-promotion distribution and other marketing arrangements with one or more third parties.

Manufacturing and Supply

We do not own or operate manufacturing facilities for the production of commercial quantities or preclinical or clinical supply of EYSUVIS, INVELTYS or any product candidates, including KPI-012. We utilize our substantial inhouse 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, INVELTYS and KPI-012 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 Manufacturing

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.

Woodstock Commercial Supply Agreement. In June 2016, we entered into a Commercial Supply Agreement, or the Woodstock Agreement, which we amended in February 2018, March 2020 and December 2020, with Woodstock Sterile Solutions, Inc. (formerly known as Catalent Pharma Solutions, LLC), or Woodstock, pursuant to which Woodstock has agreed to manufacture and supply to us, and we have agreed to purchase from Woodstock, a combined minimum amount of EYSUVIS and INVELTYS for commercial use. The Woodstock 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 Woodstock 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 Woodstock Agreement. The Woodstock 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 Woodstock Agreement, subject to our minimum purchase obligations. Each party has the right to terminate the Woodstock Agreement for customary reasons such as material breach and bankruptcy. The Woodstock Agreement contains provisions relating to compliance by Woodstock 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 LE, with pricing structured on a per-kilogram basis. Under the Chemo Agreement, we will provide a forecast of orders for the quantities of LE 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 nonrenewal 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.

KPI-012 Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities for KPI-012. We rely, and expect to continue to rely, on third parties for the manufacture of both drug substance and finished drug product for KPI-012 for preclinical and clinical testing, as well as for commercial manufacture of KPI-012 if it receives marketing approval. We also rely, and expect to continue to rely, on third parties for packaging, labeling, sterilization, storage, distribution and other production logistics. We have only limited agreements in place with respect to the manufacturing of KPI-012, and these arrangements do not extend to commercial supply. We obtain supplies of drug substance and finished drug product for KPI-012 on a purchase order basis and do not have long term committed supply arrangements with respect to KPI-012.

Manufacturing biologics is complex, especially in large quantities. Biologic products must be made consistently and in compliance with a clearly defined manufacturing process. KPI-012 is a bone-marrow derived mesenchymal stem cell secretome therapeutic composed of biologically active components, including protease inhibitors and growth factors, and is produced from a proprietary cell bank. The manufacturing process for KPI-012 is comprised of three stages: (1) cultivation of mesenchymal stem cells from a working cell bank and production of unprocessed conditioned media (cell-free secretome), (2) production of drug substance as a chemically defined solution and (3) formulation and filling of drug product. While the drug product for Combangio's early research and Phase 1b clinical trials was cultivated using a planar culture model, we plan to implement a bioreactor cultivation model for our planned clinical trials and for commercial supply of KPI-012. We are continuing the process of scaling up our manufacturing processes and capabilities with our third-party manufacturers to support longer term clinical development. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance.

KPI-012 drug product is manufactured from a vial of a working cell bank, which in turn was produced from a vial of master cell bank. KPI-012 master cell bank and working cell bank is stored in two separate locations. It is possible that we could lose the cell bank in both locations and have our manufacturing severely impacted by the need to replace the cell bank.

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 March 1, 2022, we owned 47 U.S. issued patents and 18 U.S. patent applications, as well as 90 foreign issued patents and 91 foreign patent applications (including Patent Cooperation Treaty, or PCT, applications). We exclusively licensed a total of 38 U.S. issued patents and 14 U.S. patent applications, as well as 54 foreign issued patents and 26 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:

- 18 U.S. patents and three 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, six related foreign patents jointly owned by us and JHU, four related foreign patent applications jointly owned by us and JHU, 20 related foreign patents owned by us and 27 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 nine related foreign patents and five 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;

- three U.S. patents and two U.S. patent applications relating to pharmaceutical compositions including KPI-012 for treating ocular conditions, and 13 related foreign patent applications including a pending PCT application, 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 beginning in 2040;

- One U.S. patent application, related to secreted stem cell factors for tissue repairment and regeneration, and two related foreign patent applications, which are exclusively in-licensed from Stanford University, 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 2038;

- 39 U.S. patents and 10 U.S. patent applications, relating to TKI compounds, including KPI-287, and their uses, and 45 related foreign patents, and 41 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;

- three U.S. patents relating to antibiotic compounds and their uses, and five related foreign patents and one related foreign patent application, 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;

- 10 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 18 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

- 10 U.S. patents and five U.S. patent applications, related to our AMPPLIFY technology, and 34 related foreign patents and four 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 2021. 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 LE, 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.

Stanford University

As part of our acquisition of Combangio, we acquired Combangio's exclusively in-licensed patent portfolio from Stanford University. In October 2019, Combangio entered into a license agreement with The Board of Trustees of The Leland Stanford Junior University, or Stanford, which was amended in February 2020. Pursuant to the license agreement with Stanford, or the Stanford Agreement, we hold a worldwide, exclusive, sublicensable license under certain patent rights, or licensed patents, directed to methods to promote eye wound healing, to make, have made, use, import, offer to sell and sell products that are covered by the licensed patents, or licensed products, for use in all fields.

Financial Terms

In consideration for that license, Combangio paid Stanford an upfront fee of $15,000. Under the Stanford Agreement, we are obligated to pay Stanford annual license maintenance fees in the low-to-mid five figures which are creditable against earned royalties owed to Stanford for the same year, an aggregate of up to $1.075 million for the achievement of specified development and regulatory milestones, and an aggregate of up to $1.1 million for the achievement of specified sales milestones. Stanford is also entitled to receive tiered royalties from us in a low single digit percentage range of our, our affiliates' and our sublicensees' net sales of licensed products that are covered by a valid claim of a licensed patent. Our obligation to pay royalties will continue, on a country-by-country and licensed product-by-licensed product basis, until the last-to-expire valid claim of a licensed patent covering such licensed product in the country of manufacture and sale. Additionally, we are obligated to pay Stanford a low double-digit percentage of certain consideration we receive as a result of granting sublicenses to the licensed patents and, in connection with our acquisition of Combangio, Stanford became eligible to receive a one-time change of control fee of $100,000. Stanford retains the right, on behalf of itself, Stanford Health Care, Lucile Packard Children's Hospital at Stanford, and all other non-profit research institutions, to practice the licensed patents for any non-profit purpose. In addition, the United States government retains nonexclusive rights under the licensed patents to practice or have practiced the licensed patents by or on behalf of the United States government or on behalf of any foreign government or international organization pursuant to treaty or agreement.

Diligence Obligations

Under the Stanford Agreement, we are obligated to diligently develop, manufacture and sell licensed product, diligently develop markets for licensed product, and use commercially reasonable efforts to achieve certain funding and development milestones by specified dates.

Term and Termination

Unless earlier terminated, our exclusive license under the Stanford Agreement will continue until the expiration of the licensed patents. We may terminate the Stanford Agreement at any time for any reason by providing at least 30 days' written notice to Stanford. Stanford may terminate the agreement if we breach certain provisions of the agreement and fail to remedy such breach within 60 days after written notice of such breach by Stanford.

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.

U.S. Government Regulation of Drugs and Biological Products

In the United States, the FDA approves and regulates human drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA. Biological products, or biologics, are licensed for marketing under the Public Health Service Act, or the PHSA, and regulated under the FDCA. The failure of an applicant to comply with applicable U.S. requirements may result in FDA delays or refusal to approve pending NDAs or BLAs, and may subject an applicant to administrative or judicial sanctions, such as issuance of warning letters, or the imposition of fines, civil penalties, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or civil or criminal prosecution brought by the FDA and the U.S. Department of Justice or other governmental entities. The FDA must approve our product candidates for therapeutic indications before they may be marketed in the United States. For drug products, the FDA must approve an NDA. For biologic products, the FDA must approve a BLA. An applicant seeking approval to market and distribute a new drug or biologic in the United States must satisfactorily complete each of the following steps:

- completion of preclinical laboratory tests, animal studies and formulation studies according to good laboratory practices, or GLP, regulations or other applicable regulations;
- design of a clinical protocol and submission to the FDA of an IND, which must become effective before human clinical trials may begin and must be updated when certain changes are made;
- approval by an independent institutional review board, or IRB, or ethics committee representing each clinical trial site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practices, or GCPs, and other clinical-trial related regulations to evaluate the safety and efficacy of the investigational product for each proposed indication;
- preparation and submission to the FDA of an NDA or BLA requesting marketing approval for one or more proposed indications, including payment of application user fees;
- review of the NDA or BLA by an FDA advisory committee, where applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the drug or biologic is produced to assess compliance with cGMP requirements 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 clinical trial sites to assure compliance with GCPs and the integrity of the clinical data submitted in support of the NDA or BLA; and

- FDA review and approval of the NDA or BLA, which may be subject to additional post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and 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 and the United States Department of Agriculture's Animal Welfare Act, if applicable. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. 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.

Reporting Clinical Trial Results

Under the PHSA, sponsors of clinical trials of certain FDA-regulated products, including prescription drugs and biologics, are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. The NIH's final rule on registration and reporting requirements for clinical trials became effective in 2017, and both NIH and the FDA have recently signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors.

Specifically, the PHSA grants the Secretary of Health and Human Services the authority to issue a notice of noncompliance to a responsible party for failure to submit clinical trial information as required. The responsible party, however, is allowed 30 days to correct the noncompliance and submit the required information. The failure to submit clinical trial information to clinicaltrials.gov, as required, is also a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. In addition to civil monetary penalties, violations may also result in other regulatory action, such as injunction and/or criminal prosecution or disqualification from federal grants. Although the FDA has historically not enforced these reporting requirements due to the Department of Health and Human Services, or HHS's, long delay in issuing final implementing regulations, those regulations have now been issued and the FDA did issue its first Notice of Noncompliance to a manufacturer in April 2021.

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.

There is no obligation for a sponsor to make its investigational products available for expanded access. Sponsors are required, however, to make their expanded access 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 or BLA

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 or biologic: such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve an NDA or BLA 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 products 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.

In response to the COVID-19 pandemic, FDA issued guidance on March 18, 2020, and has updated it periodically since that time to address the conduct of clinical trials during the pandemic. The guidance sets out a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical study report (or as a separate document) contingency measures implemented to manage the study, and any disruption of the study as a result of COVID-19; a list of all study participants affected by COVID-19-related study disruptions by a unique subject identifier and by investigational site, and a description of how the individual's participation was altered; and analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the study, among other

things. The FDA has indicated that it will continue to provide any necessary guidance to sponsors, clinical investigators, and research institutions as the public health emergency evolves.

Interactions with FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. Progress reports detailing the results of 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.

In addition, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Specifically, sponsors may meet with the FDA prior to the submission of an IND (Pre-IND meeting), at the end of Phase 2 clinical trial (EOP2 meeting) and before an NDA or BLA is submitted (Pre-NDA or Pre-BLA meeting). Meetings at other times may also be requested. There are three types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-NDA/pre-BLA meetings, as well as end of phase meetings such as EOP2 meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product, including for example meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use.

These meetings provide an opportunity for the sponsor to share information about the data gathered to date with the FDA and for the FDA to provide advice on the next phase of development. For example, at an EOP2, a sponsor may discuss its Phase 2 clinical results and present its plans for the pivotal Phase 3 clinical trial(s) that it believes will support the approval of the new product. Such meetings may be conducted in person, via teleconference/videoconference or written response only with minutes reflecting the questions that the sponsor posed to the FDA and the FDA's responses. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Manufacturing and Other Regulatory Requirements

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

Specifically, the FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Manufacturers and other entities involved in the manufacture and distribution of approved pharmaceuticals are required to register their establishments with the FDA and some state agencies, and they are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other requirements. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to

be adulterated. Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product.

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. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has recently taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population.

Expedited Review Programs

The FDA is authorized to expedite the review of applications in several ways. Under the Fast Track program, the sponsor of a product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Candidate products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.

Any product candidate submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as breakthrough therapy designation, priority review and accelerated approval.

- *Breakthrough therapy designation.* To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.
- *Priority review.* A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.
- *Accelerated approval.* Drug or biologic products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may

be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials.

- *Regenerative advanced therapy.* 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 candidate 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 the 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.

None of these expedited programs change the standards for approval but they may help expedite the development or approval process of product candidates.

Acceptance and Review of NDAs and BLAs

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, along with information relating to the product's chemistry, manufacturing, controls, safety updates, patent information, abuse information and proposed labeling, are submitted to the FDA as part of an application requesting approval to market the product candidate for one or more indications. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of a drug product and the safety, potency and purity of the biological product to the satisfaction of the FDA. The fee required for the submission and review of an application under the Prescription Drug User Fee Act, or PDUFA, is substantial (for example, for fiscal year 2022 this application fee is approximately $3.1 million), and the sponsor of an approved application is also subject to an annual program fee, currently more than $369,000 per eligible prescription product. These fees are typically adjusted annually, and exemptions and waivers may be available under certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the applicant is a small business submitting its first human therapeutic application for review.

The FDA conducts a preliminary review of all applications within 60 calendar days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In pertinent part, FDA's regulations state that an application "shall not be considered as filed until all pertinent information and data have been received" by the FDA. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the applicant. Typically, an RTF will be based on administrative incompleteness, such as clear omission of information or sections of required information; scientific incompleteness, such as omission of critical data, information or analyses needed to evaluate safety and efficacy or provide adequate directions for use; or inadequate content, presentation, or organization of information such that substantive and meaningful review is precluded. The FDA may request additional information rather than accept an 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. After the submission is accepted for filing, the FDA begins an in-depth substantive review of the application. The FDA reviews the application to determine, among other things, whether the proposed product is safe and effective for its intended use, whether it has an acceptable purity profile and whether the product is being manufactured in accordance with cGMP. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months from the filing date in which to complete its initial review of a standard application that is a new molecular entity, and six months from the filing date for an application with "priority review". The review process may be extended by the FDA for three additional months to consider new information or in

the case of a clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission. Despite these review goals, it is not uncommon for FDA review of an application to extend beyond the PDUFA goal date.

In connection with its review of an application, the FDA will typically submit information requests to the applicant and set deadlines for responses thereto. The FDA will also conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the manufacturing processes and facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. The FDA also may inspect the sponsor and one or more clinical trial sites to assure compliance with IND and GCP requirements and the integrity of the clinical data submitted to the FDA. To ensure cGMP and GCP compliance by its employees and third-party contractors, an applicant may incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

Additionally, the FDA may refer an application, including applications for novel product candidates which present difficult questions of safety or efficacy, to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. 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 when making final decisions on approval. Data from clinical trials are not always conclusive, and the FDA or its advisory committee may interpret data differently than the sponsor interprets the same data. The FDA may also re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process.

The FDA also may require submission of a REMS, if it determines that a REMS is necessary to ensure that the benefits of the product outweigh its risks and to assure the safe use of the product. The REMS could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS and the FDA will not approve the application without a REMS.

Decisions on NDAs and BLAs

The FDA reviews an applicant to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The term "substantial evidence" is defined under the FDCA as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."

The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. This approach was subsequently endorsed by Congress in 1998 with legislation providing, in pertinent part, that "If [FDA] determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, FDA may consider such data and evidence to constitute substantial evidence." This modification to the law recognized the potential for FDA to find that one adequate and well controlled clinical investigation with confirmatory evidence, including supportive data outside of a controlled trial, is sufficient to establish effectiveness. In December 2019, FDA issued draft guidance further explaining the studies that are needed to establish substantial evidence of effectiveness. It has not yet finalized that guidance.

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue

either a Complete Response Letter, or CRL, or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA or BLA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks. In connection with this assessment, the FDA review team will assemble all individual reviews and other documents into an "action package," which becomes the record for FDA review. The review team then issues a recommendation, and a senior FDA official makes a decision.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. 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. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the applicant will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the applicant an additional six month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Under the Ensuring Innovation Act, which was signed into law in April 2021, the FDA must publish action packages summarizing its decisions to approve new drugs and biologics within 30 days of approval of such products. To date, CRLs are not publicly available documents.

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 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 product's safety or effectiveness are prohibited before the product is approved. After approval, a product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In September 2021, the FDA published final regulations which describe the types of evidence that the FDA will consider in determining the intended use of a drug or biologic.

In the United States, health care professionals are generally permitted to prescribe products for such uses not described in the 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 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."

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.

Generic Drugs and Regulatory Exclusivity

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 and it also enacted Section 505(b)(2). To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the FDA. 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.

Under the Hatch-Waxman Act, the FDA may not approve an ANDA or 505(b)(2) application until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity, or NCE. For the purposes of this provision, FDA has consistently taken the position that an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. 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, a generic or follow-on drug application may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the

applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as new indications, dosage forms, route of administration or combination of ingredients. 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 or 505(b)(2) NDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; rather, this three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving follow-on applications for drugs containing the original active ingredient.

Five-year and three-year exclusivity also will not delay the submission or approval of a traditional NDA filed under Section 505(b)(1) of the FDCA; however, an applicant submitting a traditional NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

As part of the submission of an NDA or certain supplemental applications, 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. Upon approval of a new product, each of the patents listed in the application for the product is then published in the Orange Book. The FDA's regulations governing patient listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021. 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. Specifically, the ANDA applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. Moreover, to the extent that the Section 505(b)(2) NDA 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.

If the generic drug or follow-on drug applicant does not challenge the innovator's listed patents, FDA will not approve the ANDA or 505(b)(2) application until all the listed patents claiming the referenced product have expired. A certification that the new generic 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 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 owner and patent holders once the ANDA has been accepted for filing by the FDA. The NDA owner and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earliest of 30 months after the receipt of the Paragraph IV notice, expiration of the patent and a decision in the infringement case that is favorable to the ANDA or 505(b)(2) NDA applicant.

Regulatory Exclusivity Governing Biologics

When a biological product is licensed for marketing by FDA with approval of a BLA, the product may be entitled to certain types of market and data exclusivity barring FDA from approving competing products for certain periods of time. In March 2010, the Patient Protection and Affordable Care Act was enacted in the United States and included the Biologics Price Competition and Innovation Act of 2009, or the BPCIA. The BPCIA amended the PHSA to create an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. To date, the FDA has approved a number of biosimilars and the first interchangeable biosimilar product was approved on July 30, 2021 and a second product previously approved as a biosimilar was designated as interchangeable in October 2021. The FDA has also issued numerous guidance documents outlining its approach to reviewing and licensing biosimilars and interchangeable biosimilars under the PHSA, including a draft guidance issued in November 2020 that seeks to provide additional clarity to manufacturers of interchangeable biosimilars.

Under the BPCIA, a manufacturer may submit an application for a product that is "biosimilar to" a previously approved biological product, which the statute refers to as a "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and the

proposed biosimilar product in terms of safety, purity and potency. The biosimilar applicant may demonstrate that its product is biosimilar to the reference product on the basis of data from analytical studies, animal studies and one or more clinical studies to demonstrate safety, purity and potency in one or more appropriate conditions of use for which the reference product is approved. In addition, the applicant must show that the biosimilar and reference products have the same mechanism of action for the conditions of use on the label, route of administration, dosage and strength, and the production facility must meet standards designed to assure product safety, purity and potency.

For the FDA to approve a biosimilar product as interchangeable with a reference product, the FDA must find not only that the product is biosimilar to the reference product but also that it can be expected to produce the same clinical results as the reference product such that the two products may be switched without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. Upon licensure by the FDA, an interchangeable biosimilar may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product. Following approval of the interchangeable biosimilar product, the FDA may not grant interchangeability status for any second biosimilar until one year after the first commercial marketing of the first interchangeable biosimilar product.

A reference biological product is granted 12 years of exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. Even if a product is considered to be a reference product eligible for exclusivity, however, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of their product. There have been recent government proposals to reduce the 12-year reference product exclusivity period, but none has been enacted to date. At the same time, since passage of the BPCIA, many states have passed laws or amendments to laws, which address pharmacy practices involving biosimilar products.

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 exclusivity. For drug products, the six month exclusivity may be attached to the term of any existing patent or regulatory exclusivity, including the orphan exclusivity and regulatory exclusivities available under the Hatch-Waxman provisions of the FDCA. For biologic products, the six month period may be attached to any existing regulatory exclusivities but not to any patent terms. The conditions for pediatric exclusivity include the FDA's determination that information relating to the use of a new product in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric clinical trials, and the applicant agreeing to perform, and reporting on, the requested clinical trials within the statutory timeframe. 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 patents that cover the product are extended by six months. Although this is not a patent term extension, it effectively extends the regulatory period during which the FDA cannot approve another application.

Orphan Drug Designation and Exclusivity

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for treatment of rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the product for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for tax credits and potentially market exclusivity for seven years following the date of the product's approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development at the FDA based on

acceptable confidential requests. The product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first approved product. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

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 product for the same disease or condition for seven years, except in certain limited circumstances. If a product 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.

The period of market exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the disease or condition for which the product has been designated. Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if the company with orphan drug exclusivity is not able to meet market demand or the subsequent product 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. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan drug exclusivity regardless of a showing of clinical superiority. Under Omnibus legislation passed in December 2020, the requirement for a product to show clinical superiority applies to drug products that received orphan drug designation before enactment of amendments to the FDCA in 2017 but have not yet been approved by FDA.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." It is unclear how this court decision will be implemented by the FDA.

Patent Term Restoration and Extension

In the United States, a patent claiming a new product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent extension of up to five years for patent term lost during product development and FDA regulatory review. Assuming grant of the patent for which the extension is sought, the restoration period for a patent covering a product is typically one-half the time between the effective date of the IND involving human beings is begun and the submission date of the NDA or BLA, plus the time between the submission date of the 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 in the United States. 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 for which extension is sought. 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.

Companion Diagnostics

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

Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the therapeutic product and *in vitro* companion diagnostic device on issues related to co-development of the products.

The 2014 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 application alone, or both an IND and IDE application.

In April 2020, the FDA issued additional guidance which describes considerations for the development and labeling of companion diagnostic devices to support the indicated uses of multiple drug or biological oncology products, when appropriate. This guidance builds upon existing policy regarding the labeling of companion diagnostics. In its 2014 guidance, the FDA stated that if evidence is sufficient to conclude that the companion diagnostic is appropriate for use with a specific group of therapeutic products, the companion diagnostic's intended use/indications for use should name the specific group of therapeutic products, rather than specific products. The 2020 guidance expands on the policy statement in the 2014 guidance by recommending that companion diagnostic developers consider a number of factors when determining whether their test could be developed, or the labeling for approved companion diagnostics could be revised through a supplement, to support a broader labeling claim such as use with a specific group of oncology therapeutic products (rather than listing an individual therapeutic product(s)). 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 pre-notification marketing clearance or approval from the FDA prior to commercial distribution.

The FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval, or PMA, simultaneously with approval of the therapeutic product candidate. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. For federal fiscal year 2021, the standard fee is $374,858 and the small business fee is $93,714.

Healthcare 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, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians, other healthcare providers 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.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of drug and biologic products, limiting coverage and reimbursement for medical products and other changes to the healthcare system in the United States.

In March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, which, among other things, includes changes to the coverage and payment for pharmaceutical products under government healthcare programs. 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 2031. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, and subsequent legislation, these Medicare sequester reductions have been suspended through the end of March 2022. From April 2022 through June 2022 a 1% sequester cut will be in effect, with the full 2% cut resuming thereafter.

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, or the Tax Act, 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. 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 Act, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and, on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. 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 that directs federal agencies to reconsider rules and other policies that limit access to healthcare, 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 under the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. 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 pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care. In addition, in October 2020, the HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs HHS , to create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (1) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (2) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (3) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

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. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare 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.

Federal and State Data Privacy Laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, HHS has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them. Our clinical trials are regulated by the Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

At the state level, California has enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA went into effect on January 1, 2020 and requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. Additionally, effective starting on January 1, 2023, the California Privacy Rights Act, or CPRA, will significantly modify the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. The CCPA and CPRA could impact our business activities depending on how it is interpreted and exemplifies the vulnerability of our business

to not only cyber threats but also the evolving regulatory environment related to personal data and individually identifiable health information. These provisions may apply to some of our business activities. In addition, other states, including Virginia and Colorado, already have passed state privacy laws and other states will likely be considering similar laws in the near future.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the privacy or data security laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and administrative penalties, damages, fines, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any product candidates we may develop, once approved, are sold in a foreign country, we may be subject to similar foreign laws.

Review and Approval of Medical 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, or 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

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the European Union, or EU Member State, will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the EU 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

Marketing authorization applications, or MAAs, can be filed either under the so-called centralized or national authorization procedures, albeit through the Mutual Recognition or Decentralized procedure for a product to be authorized in more than one EU member state.

The centralized procedure provides for the grant of a single marketing authorization following a favorable opinion by the EMA that is valid in all EU Member States, as well as Iceland, Liechtenstein and Norway, which are part of the EEA. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, advanced-therapy medicines (such as gene-therapy, somatic cell-therapy or tissue-engineered medicines) and products with a new active substance indicated for the treatment of specified diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions and viral diseases. The centralized procedure is optional for products that represent a significant therapeutic, scientific or technical innovation, or whose authorization would be in the interest of public health. Under the centralized procedure, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use, or the CHMP. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding stop-clocks.

There are also two other possible routes to authorize medicinal products in several EU countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

- *Decentralized procedure*. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure. The applicant may choose a member state as the reference member State to lead the scientific evaluation of the application.

- *Mutual recognition procedure*. In the mutual recognition procedure, a medicine is first authorized in one EU Member State (which acts as the reference member state), in accordance with the national procedures of that

country. Following this, further marketing authorizations can be progressively sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization produced by the reference member state.

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

Conditional Approval

In particular circumstances, E.U. legislation (Article 14–a Regulation (EC) No 726/2004 (as amended by Regulation (EU) 2019/5 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables applicants to obtain a "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products), if (1) the product candidate is intended for the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening disease; (2) the product candidate is intended to meet unmet medical needs of the patients; (3) a marketing authorization may be granted prior to submission of comprehensive clinical data provided that the benefit 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; (4) the risk-benefit balance of the product candidate is positive, and (5) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data. 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 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.

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).

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.

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.

Pediatric Exclusivity

If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC, or alternatively a one year extension of the regulatory market exclusivity from ten to eleven years, as selected by the marketing authorization holder.

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.

Patent Term Extensions

The European Union also provides for patent term extension through Supplementary Protection Certificates, or SPCs. The rules and requirements for obtaining a SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. In certain circumstances, these periods may be extended for six additional months if pediatric exclusivity is obtained. Although SPCs are available throughout the European Union, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the European Union.

Reimbursement and Pricing of Prescription Pharmaceuticals

In the EU, similar political, economic and regulatory developments to those in the United States may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the U.S. and the EU, reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. 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, pharmaceutical firms may be required to conduct a clinical trial that compares the cost-effectiveness of the product to other available therapies.

General Data Protection Regulation

Many countries outside of the United States maintain rigorous laws governing the privacy and security of personal information. The collection, use, disclosure, transfer, or other processing of personal data , including personal health data, regarding individuals who are located in the EEA, and the processing of personal data that takes place in the EEA, is subject to the 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, and it imposes heightened requirements on companies that process health and other sensitive data, such as requiring in many situations that a company obtain the consent of the individuals to whom the sensitive personal data relate before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that fall within the scope of the GDPR include providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, appointing a data protection officer, 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 EEA, including the United States, 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 is 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. In July 2020, the Court of Justice of the European Union, or the Court of Justice of the European Union, or CJEU, invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. Following the withdrawal of the U.K. from the EU, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by GDPR.

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, 2021, we had a total of 192 full time employees. 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, encourages a high level of corporate employee tenure and low level of voluntary turnover. A large majority of our non-field based 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.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in July 2009. 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," 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 Recent Acquisition of Combangio

We may fail to realize the anticipated benefits of our acquisition of Combangio, those benefits may take longer to realize than expected, and we may encounter significant integration difficulties.

On November 15, 2021, we completed our acquisition, or the Acquisition, of Combangio, Inc., or Combangio, a clinical-stage biotechnology company focused on developing regenerative biotherapeutics based on mesenchymal stem cell secretomes, pursuant to an Agreement and Plan of Merger, or the Merger Agreement, dated November 15, 2021. Our ability to realize the anticipated benefits of the Acquisition will depend, to a large extent, on our ability to integrate Combangio and KPI-012 (previously known as CMB-012), a product candidate in clinical development for the treatment of persistent corneal epithelial defects, or PCED, into our business and business strategy and realize anticipated growth opportunities and synergies. We expect that the integration process will be complex, costly and time-consuming. As a result, we are devoting, and will be required to continue to devote, significant management attention and resources to integrating Combangio into our business and KPI-012 into our business strategy. The integration process may be disruptive to our business and the expected benefits may not be achieved within the anticipated time frame, or at all. The failure to meet the challenges involved and to realize the anticipated benefits of the Acquisition could cause an interruption of, or a loss of momentum in, our commercialization efforts for EYSUVIS and INVELTYS and could adversely affect our business, financial condition and results of operations.

Our ability to realize the anticipated benefits of the Acquisition is expected to entail numerous additional material potential difficulties, risks and uncertainties, including, among others:

- any delay in or failure in filing an investigational new drug, or IND, application for KPI-012 with the U.S. Food and Drug Administration, or FDA;
- if filed, the FDA may not clear our IND submission for KPI-012 and may not permit us to commence clinical trials in the United States of KPI-012 on the timeline we expect or at all;
- any clinical trials of KPI-012 that we commence in the future may fail to provide sufficient evidence that KPI-012 is both safe and effective for use;
- any delay or failure in obtaining marketing approvals for KPI-012, or any delay or failure to commercialize KPI-012 in the United States or other jurisdictions thereafter;
- increased scrutiny from third parties, including regulators, legislative bodies and enforcement agencies, including with respect to product pricing and commercialization matters;
- changes in laws or regulations that adversely impact the anticipated benefits of the Acquisition;
- challenges related to the perception by patients, the medical community and third-party payors of KPI-012 for the treatment of persistent corneal epithelial defects, or PCED;
- challenges related to the complex manufacturing process for KPI-012 and the reliance on manufacturing arrangements with third-party manufacturers;

- difficulties in managing the expanded operations of a more complex company following the Acquisition;
- the diversion of management attention to integration matters;
- difficulties in achieving the anticipated business opportunities and growth prospects from the Acquisition;
- the size of the treatable patient population for PCED may be smaller than we believe it is;
- difficulties in assimilating Combangio employees in our business, in maintaining employee morale and in attracting and retaining key personnel; and
- potential unknown liabilities, adverse consequences, unforeseen increased expenses or other unanticipated problems associated with the Acquisition.

Many of these factors are outside of our control, and any one of them could result in increased costs, decreased expected revenues and further diversion of management time and energy, which could materially adversely impact our business, financial condition and results of operations.

Also, we now possess certain liabilities and obligations, including contractual liabilities and obligations, that were assumed by us upon closing of the Acquisition. Further, it is possible that undisclosed, contingent, or other liabilities, problems or obligations may arise in the future of which we were previously unaware. These disclosed and undisclosed liabilities could have an adverse effect on our business, financial condition and results of operations.

In addition, we expect to incur expenses related to the continued development, regulatory approval process and commercialization with respect to KPI-012. As a company, we have no prior experience developing biological product candidates. Because we have limited financial resources, by investing in the Acquisition and focusing on the development of KPI-012, we may forgo or delay pursuit of other opportunities that may have proven to have greater commercial potential.

Any or all of these factors could decrease or delay the expected accretive effect of the Acquisition and negatively impact our stock price. As a result, it cannot be assured that we will be successful in the integration of Combangio with our business or that we will realize the benefits anticipated from the Acquisition or in the anticipated time frames or at all.

Our existing stockholders will experience dilution upon any future issuance of shares of our common stock to former equityholders of Combangio pursuant to the terms of the Merger Agreement.

In connection with the Acquisition, on January 3, 2022 we issued an aggregate of 6,815,072 shares of our common stock to the former Combangio equityholders. Such shares, together with 973,565 shares of our common stock that are held back by us, or the Holdback Shares, and will be issuable subject to the terms of the Merger Agreement to the Combangio equityholders on the escrow release date, constituted approximately 11.9% of our common stock as of immediately prior to the closing of the Acquisition. In addition, former Combangio equityholders are entitled to receive from us, subject to the terms and conditions of the Merger Agreement, contingent consideration of up to $5.4 million payable in shares of our common stock upon our achievement of various development and regulatory milestones, and, we may elect, subject to the Nasdaq rules, to satisfy a portion of certain milestone payments that are payable to Combangio equityholders in cash through the issuance of up to $15 million of our common stock. Our existing stockholders will experience dilution upon any future issuance of shares of our common stock to former Combangio equityholders pursuant to the Merger Agreement.

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 $142.6 million for the year ended December 31, 2021 and $104.3 million for the year ended

December 31, 2020. As of December 31, 2021, we had an accumulated deficit of $542.4 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 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 and the Loan and Security Agreement with Oxford Finance LLC, or the Loan Agreement, 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. As of result of the acquisition of Combangio, we expect to devote substantial financial resources to the research and development and potential commercialization of KPI-012. 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 for at least the next several years, including in connection with our continued development, regulatory approval efforts and commercialization, if any, of KPI-012. 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 research and development expenses will increase substantially in the future as compared to prior periods as we advance the clinical development of KPI-012. Our research and development expenses will also increase substantially in the future as we advance our preclinical development programs, including KPI-287, our Tyrosine Kinase Inhibitor product candidate, and our novel selective glucocorticoid receptor modulators, or SEGRM, program and conduct any necessary preclinical studies and clinical trials and other development activities for our product candidates. We continue to commercialize EYSUVIS and INVELTYS in the United States and expect that our selling, general and administrative expenses will increase substantially when we pursue the commercialization of KPI-012, if approved, and support commercialization of any other product candidate.

Our expenses will also increase if and as we:

- submit an IND for, and continue the clinical development of, KPI-012 for PCED;
- initiate and continue the research and development of KPI-012 for additional indications, including initiating and conducting clinical trials;
- scale up our manufacturing processes and capabilities to manufacture the clinical supply of KPI-012;
- seek regulatory approval for KPI-012 for PCED in the United States and other jurisdictions;
- seek regulatory approval for KPI-012 for additional indications;
- 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;
- seek regulatory approval for EYSUVIS and INVELTYS outside of the United States;
- progress our current and any future preclinical development programs;
- conduct clinical trials and other development activities and/or seek marketing approval for any other product candidates;
- in license or acquire the rights to other products, product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;

- integrate employees of Combangio;
- hire additional clinical, quality control, scientific, manufacturing, commercial and management personnel, including to support our operations;
- 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 these products, and we may not achieve profitability. Our lead product candidate, KPI-012, is in the early stages of clinical development and all of our other research and development programs are in preclinical development and, accordingly, we do not expect to generate revenue from KPI-012 or any other product candidate for several years, if at all. Achieving and maintaining profitability will require us to be successful in a range of challenging activities, including:

- successfully commercializing and growing EYSUVIS and 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;
- successfully integrating Combangio into our business;
- timely filing of an IND for, and completing the clinical development of, KPI-012 for PCED and any other indications we determine to pursue;
- subject to obtaining favorable results from our planned clinical trials of KPI-012, applying for and obtaining marketing approval of KPI-012;
- successfully commercializing KPI-012, if approved;
- manufacturing at commercial scale, marketing, selling and distributing EYSUVIS, INVELTYS and, if approved, KPI-012;
- maintaining regulatory and marketing approvals for EYSUVIS and INVELTYS;

- discovering, developing and successfully seeking marketing approval and commercialization of any 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. Moreover, KPI-012 is in the early stages of clinical development and all of our other research and development programs are in preclinical development and, accordingly, we do not expect to generate revenue from KPI-012 or any other product candidate for several years, if at all.

In addition, our commercialization efforts have previously been hampered by the operational restrictions on our sales force from quarantines, travel restrictions and bans and other governmental restrictions related to the COVID-19 pandemic. As a result of these restrictions, we previously suspended our sales force from substantially all in-person interactions with physicians and were limited to conducting educational and promotional activities virtually. Commencing in the fourth quarter of 2020, our sales force resumed substantially all in-person interactions in the field, but to the extent we restrict, or are restricted from, in-person interactions with physicians, we may be limited to conducting educational and promotional activities virtually, which may continue to hamper our ability to market EYSUVIS and INVELTYS. In addition, government restrictions have at times led to moratoria on elective ocular surgeries in many jurisdictions, which had 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. In addition, the COVID-19 pandemic has generally had an adverse impact on the launch of pharmaceutical products, and we believe the pandemic has impacted, and may continue to impact, the launch of EYSUVIS. We also do not know the extent to which the COVID-19 pandemic will impact our development of KPI-012 or any other product candidates that we may develop. The extent of the impact of COVID-19 on our development and commercialization efforts will depend on the length and severity of this pandemic, including the extent there is any resurgence of the COVID-19 virus or 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 and in developing biologics 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 commercialization of EYSUVIS.

Moreover, we plan to develop KPI-012 for the treatment of PCED and any other indications we determine to pursue. As a company, we have no prior experience developing biological product candidates. We may also encounter delays or difficulties in our efforts to, or fail to, successfully integrate the operations of Combangio into our business and KPI-012 into our business strategy. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had prior experience developing biological product candidates, integrating acquired businesses into our existing business or 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 integrate the operations of Combangio into our business. We also expect to incur significant additional expenses if and as we conduct further research and development activities, and initiate clinical trials of, and seek regulatory approval for, KPI-012 and any other product candidate that we identify and advance, including KPI-287, and from our 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. 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 progress, costs and results of integrating Combangio operations into our business and our planned clinical trials of KPI-012;
- the costs and timing of process development and manufacturing scale-up activities associated with KPI-012 for PCED and any other indications we determine to pursue;
- the costs, timing and outcome of regulatory review of KPI-012;
- the timing and amount of future milestone payments under the Merger Agreement;
- the costs and timing of commercialization activities for EYSUVIS, INVELTYS and, if approved, KPI-012, including establishing additional product sales, marketing, medical affairs, distribution and outsourced manufacturing capabilities;
- our ability to successfully commercialize and sell EYSUVIS, INVELTYS and, if approved, KPI-012 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 research and development of any other 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 and cash equivalents of $92.1 million as of December 31, 2021, along with anticipated revenue from EYSUVIS and INVELTYS, will enable us to fund our operations, lease and debt service obligations, and capital expenditure requirements into the second quarter of 2023. 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, 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 KPI-012 or any other product candidate. Also, even if we successfully develop KPI-012 or any other product candidate and one or more of 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, INVELTYS, KPI-012 or any other product candidate 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 Loan Agreement may limit our ability to obtain additional debt financing. Under the Loan Agreement, we are also restricted from paying dividends on our common stock, granting liens, making investments, making acquisitions, making certain restricted payments, selling assets and making certain other uses of our cash without the lenders' consent, subject in each case to certain exceptions.

In connection with the Acquisition, on January 3, 2022 we issued an aggregate of 6,815,072 shares of our common stock to the former Combangio equityholders. Such shares, together with 973,565 Holdback Shares that will be issuable subject to the terms of the Merger Agreement to the Combangio equityholders on the escrow release date, constituted approximately 11.9% of our common stock as of immediately prior to the closing of the Acquisition. . In addition, former Combangio equityholders are entitled to receive from us, subject to the terms and conditions of the Merger Agreement, contingent consideration of up to $5.4 million payable in shares of our common stock upon our achievement of various development and regulatory milestones, and we may elect, subject to the Nasdaq rules, to satisfy a portion of certain milestone payments that are payable to Combangio equityholders in cash through the issuance of up to $15 million of our common stock. Our existing stockholders will experience dilution upon any future issuance of shares of our common stock to former Combangio equityholders pursuant to the Merger Agreement. In addition, 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, 2021, we had $80.0 million of outstanding borrowings under the tranche A term loan under the Loan Agreement, bearing interest at a floating rate equal to the greater of 30-day LIBOR and 0.11%, plus 7.89%. The Loan Agreement provides for interest-only payments until December 1, 2024 if neither the tranche B term loan nor the tranche C term loan are made, and until June 1, 2025 if either the tranche B term loan or the tranche C term loan is made, or the Amortization Date. Beginning on the Amortization Date, we are required to repay the outstanding principal in monthly installments over a period of (i) 18 months if neither the tranche B term loan nor the tranche C term loan is made or (ii) 12 months if either the tranche B term loan or the tranche C term loan is made. All unpaid principal and interest is due in full on May 1, 2026, the date of maturity.

Our obligations under the Loan Agreement are secured by substantially all of our assets. We could in the future incur additional indebtedness beyond our borrowings under our Loan Agreement.

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 acquire other businesses for cash, take certain other 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 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 Loan Agreement 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 Loan Agreement, we may not be able to make accelerated payments, and the lender could seek to enforce security interests in the collateral securing such indebtedness.

Fluctuations in interest rates could materially affect the interest expense on our Loan Agreement.

Because our debt under the Loan Agreement bears interest at floating interest rates, increases in interest rates could materially increase our interest expense. Further, our Loan Agreement uses LIBOR as a reference rate. The United Kingdom's Financial Conduct Authority, or the FCA, which regulates LIBOR, announced that all LIBOR settings will either cease to be provided by any administrator or no longer be representative: (1) immediately after December 31, 2021, in the case of the one week and two month LIBOR tenors; and (2) immediately after June 30, 2023, in the case of the remaining LIBOR tenors. The United States Federal Reserve has advised that no new contracts using U.S. dollar LIBOR should be entered into after December 31, 2021. In June 2017, the Alternative Reference Rates Committee selected the Secured Overnight Financing Rate, or SOFR, a new index calculated by reference to short-term repurchase agreements backed by Treasury securities, as its preferred replacement for U.S. dollar LIBOR. Whether SOFR or any other alternative reference rates attains market acceptance as a LIBOR replacement tool remains is uncertain. As such, the future of LIBOR and the potential alternatives at this time is uncertain.

When LIBOR is no longer available or if lenders have increased costs due to the phase-out of LIBOR or changes in law, we may suffer from potential increases in interest rate costs on our floating debt rate. It is not possible to predict the effect these developments may have on our Loan Agreement. Further, we may need to renegotiate our Loan Agreement and the floating loans thereunder to replace the interest rate calculated by reference to LIBOR with an interest rate calculated by reference to a new standard that is established.

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 our 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, contingent consideration and acquired in-process research and development, 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, is believed to have impacted the commercialization of EYSUVIS and could impact the development of KPI-012 or any other product candidate we develop and may continue to adversely affect our business, results of operations and financial condition.

The outbreak of the COVID-19 pandemic and government measures taken in response to it, including from time to time quarantines, strict travel restrictions and bans, heightened border scrutiny and other measures, have 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. In light of shelter-in-place orders and other mandated local travel and social interaction prohibitions, we previously suspended substantially all in-person interactions with physicians and were limited to conducting educational and promotional activities virtually. Commencing in the fourth quarter of 2020, our sales force resumed substantially all in-person interactions in the field, but to the extent we restrict, or are restricted from, in-person interactions with physicians, we may be limited to conducting educational and promotional activities virtually, which may continue to hamper our ability to market EYSUVIS and INVELTYS. In addition, the COVID-19 pandemic has generally had an adverse impact on the launch of pharmaceutical products, and we believe the pandemic has impacted, and may continue to impact, the launch of EYSUVIS.

We and any of our contract manufacturing organizations and contract research organizations may face disruptions that may affect our ability to initiate and complete preclinical studies and clinical trials for our product candidates, including disruptions in procuring supplies that are essential for our research and development activities, manufacturing disruptions, disruptions in our ability to obtain necessary trial site approvals, as well as delays in or difficulties with enrollment and other delays at clinical trial sites. We may face impediments to regulatory meetings and clearance and approvals due to measures intended to limit in-person interactions. We do not know the extent to which the COVID-19 pandemic will impact our development of KPI-012 or any other product candidates that we develop. We plan to submit an IND application to the FDA for KPI-012 and, subject to regulatory clearance, commence a Phase 2/3 clinical trial of KPI-012 for PCED in the United States in the fourth quarter of 2022. The COVID-19 pandemic may delay our planned IND submission and/or the initiation and conduct of our planned clinical trial.

Additionally, while we currently are not experiencing interruptions in our manufacturing of EYSUVIS, INVELTYS or KPI-012, any reinstatement of 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 again 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 full extent of the impact of COVID-19 on our development and commercialization efforts will depend on the length and severity of this pandemic, the timing and extent of any resurgence of the COVID-19 virus or 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, KPI-012 or any other product candidate that receives 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, KPI-012 or any other 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™, Tyrvaya™, off-label use of branded or generic corticosteroids and various drugs that are produced by compounding pharmacies. Generic versions of Restasis have been available in the United States since February 2022. 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 products or product candidates would likely be offered at a substantially lower price than we offer our products and 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 products or 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 current market research data. 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 are available to patients. 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.

In addition, we are developing KPI-012 for PCED, which is a rare disease. Our understanding of both the number of people who have a PCED, as well as the subset of people with PCED diseases who have the potential to benefit from treatment with KPI-012, are based on estimates. These estimates may prove to be incorrect. The number of patients with PCED may turn out to be lower than expected, may not be otherwise amenable to treatment with KPI-012 or may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects.

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. In light of shelter-in-place orders and other mandated local travel prohibitions, we previously suspended substantially all in-person interactions with physicians and were limited to conducting educational and promotional activities virtually. Commencing in the fourth quarter of 2020, our sales force resumed substantially all in-person interactions in the field, but to the extent we restrict, or are restricted from, in-person interactions with physicians, we may be limited to conducting educational and promotional activities virtually, which may continue to hamper our ability to market EYSUVIS and INVELTYS.

Our assessment of the potential market opportunity for EYSUVIS, INVELTYS, KPI-012 and our other 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 and PCED 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, such as KPI-012, 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, KPI-012 or any of our other 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, INVELTYS, KPI-012 and any other product candidates we develop.

If EYSUVIS, INVELTYS, KPI-012 or any other product candidate for which we obtain marketing approval do not achieve adequate levels of acceptance by physicians and patients, 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, KPI-012 or any other product candidate 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, KPI-012 or any other 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, KPI-012 or any other product candidate 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, KPI-012 or any other 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, KPI-012 or any other 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, KPI-012 or any other 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, KPI-012 or our other 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, KPI-012 or our other 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, KPI-012 or any other product candidate 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. During late 2020 and 2021, we expanded our commercial organization,

which now includes approximately 100 field-based commercial sales personnel. Our sales representatives promote both EYSUVIS and INVELTYS.

There are risks involved with establishing, maintaining and expanding, if and when necessary, our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming, may divert our management and business development resources and could delay any future product launch. Maintaining our sales force requires us to continue to implement and improve our managerial, operational and financial systems, which we may not do effectively. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. Further, we may overestimate or underestimate the size of the sales force required for a successful product launch, including with respect to the ongoing launch of EYSUVIS. In addition, we have not yet established our own commercial organization or distribution capabilities specific to KPI-012. While we believe that we will be able to commercialize KPI-012, if approved, for the treatment of PCED with a small, targeted, internal sales force in the United States and potentially other major markets, our assumptions may prove inaccurate. In the future, we may need to expand our sales force and at a higher cost than previously anticipated. If the commercial launch of KPI-012, if approved, any other product candidate 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, KPI-012 or any other product candidate 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, if and when necessary, 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 and KPI-012 in certain markets outside the United States 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 and KPI-012 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, KPI-012 or any other product candidate 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, KPI-012 or any other product candidate 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, KPI-012 or any other product candidate 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, KPI-012 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, KPI-012 and any other product candidate 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, Tyrvaya 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 have been available in the United States since February 2022. 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, including Tyrvaya, which was commercially launched in November 2021. There are also 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 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 formulations of loteprednol suspension 0.5% (Lotemax suspension) and loteprednol ophthalmic gel 0.5% (Lotemax Gel) were launched in May 2019 and February 2021, respectively, and the first generic version of Durezol was launched in September 2021.

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 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.

If approved, we expect KPI-012 to compete with Oxervate, which is the only approved prescription pharmaceutical product in the PCED space. Oxervate (cenegermin-bkbj), was approved in August 2018 for the treatment of neurotrophic keratitis, or NK, a degenerative disease characterized by decreased corneal sensitivity and poor corneal healing, which we believe to represent approximately one-third of all PCED cases. Oxervate is a topical eye drop that is administered six times per day at two-hour intervals for eight weeks. Each administration of Oxervate requires the use of a vial containing the drug product, a vial adapter, a single-use pipette and disinfectant wipes. In addition, to our knowledge, there is currently only one product candidate in active clinical development for the treatment of a broad PCED population. ST266, an eye drop, is currently being studied in a Phase 2b clinical trial in patients with PCED and is being developed by Noveome Biotherapeutics Inc. ST266 is a secretome produced from amnion-derived epithelial cells from donated full-term placentas. A number of companies are pursuing development of product candidates for the treatment of NK.

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.

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, including KPI-012. 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 when and if we begin commercialization of KPI-012 or any other product candidate 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

If we are unable to successfully complete the clinical development of, and obtain marketing approval for, KPI-012 or any other product candidate, or experience significant delays in doing so, or if, after obtaining marketing approvals, we fail to commercialize our products and product candidates, our business will be materially harmed.

As a result of the acquisition of Combangio, we expect to devote a significant portion of our research and development resources and business efforts to the development of KPI-012, a clinical-stage product candidate for the treatment of PCED and any other indications we determine to pursue.

The success of KPI-012 and any other product candidates we develop will depend on many factors, including the following:

- timely submission and clearance of our planned IND submission for KPI-012 and for any other product candidates we develop;
- completing and obtaining favorable results from our planned clinical trials of KPI-012 and any other product candidate we develop;
- applying for and receiving marketing approvals from the FDA and any other regulatory authorities for KPI-012 and any other product candidate we develop;
- receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities from applicable regulatory authorities for KPI-012 and any other product candidate we develop;
- if approved, successful launch and commercialization of KPI-012 or any other product candidate we develop in the United States, including establishing and maintaining sales, marketing, manufacturing and distribution capabilities for KPI-012 or any other product candidate we develop or leveraging our existing sales, marketing, manufacturing and distribution capabilities if and when appropriate;
- acceptance of KPI-012 and any other product candidate 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, for our product candidates;
- obtaining and maintaining regulatory approval of our manufacturing processes and our third-party manufacturers’ facilities from applicable regulatory authorities and obtaining and maintaining adequate supply of our products;
- maintaining a workforce of experienced scientists and others with experience in eye diseases and biologics to continue to develop our product candidates;

- 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 KPI-012 or any other product candidate, which would materially harm our business. In addition, KPI-012 is still in the early stages of clinical development, and all of our other development efforts are in the early stages of preclinical development, including KPI-287 and our SEGRMs program. We may never generate the necessary data or results required to obtain regulatory approval of KPI-012 or any other product candidate we develop. 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 KPI-012 or any other product candidate may never occur.

If clinical trials of KPI-012 or any other 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.

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. For example, the results of Combangio's Phase 1b clinical trials of KPI-012 in 12 patients with PCED may not be indicative of future results in later stage clinical trials, including in our planned Phase 2/3 clinical trial. 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.

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 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 of KPI-012 or any other product candidate we develop 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 KPI-012 or any other product candidate 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 PCED, 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 KPI-012 or any other product candidate 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. In addition, we are developing KPI-012 for PCED, which is a rare condition with an estimated incidence in the United States of 100,000 cases per year, and, as such, we may have difficulty identifying and enrolling a sufficient number of patients in our planned clinical trials of KPI-012 given the limited number of patients with PCED. 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, KPI-012 or any other product candidate we develop 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 and serious adverse events reported to date following approval and commercialization have been very rare. Increases in intraocular pressure, or 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. In addition, while KPI-012 was generally well-tolerated in Combangio's Phase 1b clinical trials, it was only administered in 12 subjects. 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 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. We may never realize the anticipated benefits of the acquisition of Combangio and by investing our limited resources in the Acquisition and the development of KPI-012, we may be required to forego or delay other opportunities. In addition, 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.

KPI-012 has only been evaluated in a clinical trial outside of the United States. 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.

Combangio has in the past chosen, and 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. In 2020 and 2021, Combangio conducted Phase 1b clinical trials of KPI-012 for PCED in 12 patients in Mexico. KPI-012 has only been evaluated in clinical trials outside of the United States. Based on the results of the Phase 1b clinical trials conducted in Mexico, we plan to submit an IND application to the FDA for KPI-012 and, subject to regulatory clearance, commence a Phase 2/3 clinical trial of KPI-012 for PCED in the United States in the fourth quarter of 2022. However, if the FDA does not accept the data from Combangio's Phase 1b clinical trials of KPI-012 or any trial that we conduct in the future 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, INVELTYS and KPI-012 and plan to contract with third parties for preclinical, clinical and commercial supply of any other product candidates we develop. 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 Woodstock Sterile Solutions Inc. (formerly known as Catalent Pharma Solutions, LLC), or Woodstock, to manufacture and supply to us a minimum amount of EYSUVIS and INVELTYS bottles. We also rely on 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-party manufacturers to manufacture clinical supplies of KPI-012 and any other product candidates we develop and commercial supplies of all of our products if and when approved for marketing by applicable regulatory authorities, as well as for packaging, serialization, storage, distribution and other production logistics. We do not currently have arrangements in place for redundant supply for bulk drug substances.

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. Our third party manufacturers may 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.

While we have long-term commercial supply agreements for EYSUVIS and INVELTYS with third-party manufacturers, if these suppliers do not perform as we expect, we may be required to replace one or more of them. These manufacturers, and suppliers to these manufacturers, may also be affected by natural disasters, such as floods or fire, epidemics or pandemics, such as COVID-19, or such manufacturers could face manufacturing issues, such as contamination or regulatory concerns following a regulatory inspection of such facility, requiring us to seek replacement 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, including as a result of additional required FDA approvals. Replacements may not be readily available on acceptable terms, or at all. In addition, we do not own or operate, and currently have no plans to establish, any manufacturing facilities for KPI-012. We rely, and expect to continue to rely, on third parties for the manufacture of both drug substance and finished drug product for KPI-012 for preclinical and clinical testing, as well as for commercial manufacture of KPI-012 if it receives marketing approval. We also rely, and expect to continue to rely, on third parties for packaging, labeling, sterilization, storage, distribution and other production logistics. We have only limited supply agreements in place with respect to KPI-012, and these arrangements do not extend to commercial supply. We obtain supplies of drug substance and finished drug product for KPI-012 on a purchase order basis and do not have long term committed supply arrangements with respect to KPI-012. We may be unable to maintain our current arrangements for KPI-012 or conclude agreements for commercial supply of KPI-012 on acceptable terms or at all.

We are subject to additional risks related to our reliance on third-party manufacturers for the manufacture of the drug substance and drug product of KPI-012, a biological product candidate. Manufacturing biologics is complex, especially in large quantities. Biologic products must be made consistently and in compliance with a clearly defined manufacturing process. KPI-012 is a bone-marrow derived mesenchymal stem cell secretome therapeutic composed of biologically active components, including protease inhibitors and growth factors, and is produced from a proprietary cell bank. The manufacturing process for KPI-012 is comprised of three stages: (1) cultivation of mesenchymal stem cells from a working cell bank and production of unprocessed conditioned media (cell-free secretome), (2) production of drug substance as a chemically defined solution and (3) formulation and filling of drug product. While the drug product for Combangio's early research and Phase 1b clinical trials was cultivated using a planar culture model, we plan to implement a bioreactor cultivation model for our planned clinical trials and for commercial supply of KPI-012. We are continuing the process of scaling up our manufacturing processes and capabilities with our third-party manufacturers to support longer term clinical development. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. In addition, KPI-012 drug product is manufactured from a vial of a working cell bank, which in turn was produced from a vial of master cell bank. KPI-012 master cell bank and working cell bank is stored in two separate locations. It is possible that we could lose the cell bank in both locations and have our manufacturing severely impacted by the need to replace the cell bank.

The FDA maintains strict requirements governing the manufacturing process and 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. When a manufacturer seeks to modify or make even seemingly minor changes to the manufacturing 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. 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 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 current good manufacturing practices, or 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.

EYSUVIS, INVELTYS, KPI-012 and any other product candidate that we may develop may compete with other product candidates and products for access to a limited number of suitable manufacturing facilities that operate under cGMP regulations. For example, 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.

Our current and anticipated future dependence upon others for the manufacture of EYSUVIS, INVELTYS, KPI-012 or any other product candidate 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.

Our commitment to purchase from Woodstock a minimum amount of EYSUVIS and INVELTYS for commercial use may result in us paying for product in excess of our needs if we are not able to successfully commercialize our products and/or successfully estimate our supply needs.

Under our long-term supply agreement with Woodstock, we have agreed to purchase an annual combined minimum amount of EYSUVIS and INVELTYS for commercial use through the expiration of the initial term of the agreement in 2030. We cannot be certain that at any given point our future supply needs will meet or exceed such minimum purchase commitments. If demand for our products falls short of such minimum purchase requirements, our business, results of operation and financial condition may be adversely affected.

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

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

In addition, there are risks associated with large scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with good manufacturing practices, lot consistency and timely availability of raw materials. Even if we obtain regulatory approval for KPI-012 or any future product candidates, there is no assurance that our manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential commercial launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

We may 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, KPI-012 or any other product candidate we develop and 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-287 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, 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, including those acquired in connection with our recent acquisition of Combangio. 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, KPI-012 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, or the JHU License Agreement, that relate to our AMPPLIFY technology, JHU retains control of patent prosecution. In addition, we rely on a license from Stanford University for certain patent rights related to KPI-012. The license agreement between Combangio and Stanford University, or Stanford University License Agreement, imposes specified diligence, milestone payment, royalty and other obligations on us and requires that we meet development timelines, or to exercise diligent or commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the license. Our rights with respect to in-licensed patents and patent applications may be lost if the applicable license agreement expires or is terminated or if we fail to satisfy the obligations under the JHU License Agreement and Stanford University License Agreement. 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 KPI-012, 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 JHU License Agreement, under which we license certain of our patent rights and a significant portion of the technology for EYSUVIS, INVELTYS and certain of our product candidates imposes royalty and other financial obligations on us and other substantial performance obligations. We are subject to similar obligations under the Stanford University License Agreement, pursuant to which we license certain patent rights related to KPI-012. 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 License Agreement and might therefore terminate the agreement, thereby removing our ability to market products covered by our license agreement with JHU. If the JHU License 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 JHU License Agreement 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. Similar risks apply to the Stanford University License Agreement, pursuant to which we license intellectual property rights related to KPI-012.

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. The ability of the FDA to review and approve new drugs can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years. 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.

In addition, the COVID-19 pandemic has led to disruptions at the FDA and has prolonged the time necessary for certain new drugs to be reviewed and/or approved. The FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis, but certain FDA activities remain constrained by the COVID-19 pandemic. There can be no assurance that the FDA timely reviews applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

If 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.

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 Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and/or enforcement actions 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. Further, 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 European Union notably under Directive 2001/83EC, as amended, and are also subject to EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the European Union.

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.

Accordingly, we continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control for our approved products. We may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products.

We may not be able to obtain orphan drug exclusivity for one or more of our product candidates, and even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products. Additionally, if another company with a competing product candidate were to obtain orphan drug exclusivity for its competing product candidate before we do, we may be barred from marketing our product candidate for the same indication as the competing product candidate during the exclusivity period.

Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the European Medicines Agency, or EMA, in the European Union. KPI-012 has received orphan drug designation from the FDA for the treatment of PCED.

Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified. If a competing product candidate with an orphan designation for PCED were to obtain regulatory approval before we are able to obtain approval of KPI-012 for PCED, we could be barred from marketing KPI-012 for PCED in the United States during the seven-year orphan exclusivity period, which would have a severe adverse effect on our business.

In order for the FDA to grant orphan drug exclusivity to one of our products, the FDA must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the United States. The FDA may conclude that the condition or disease for which orphan drug exclusivity is sought does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition.

In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

The FDA Reauthorization Act of 2017, or FDARA, requires that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. FDARA reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA

may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the Court of Appeals concluded that orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

We may seek certain designations for our product candidates, including Breakthrough Therapy, Fast Track and Priority Review designations in the United States, and PRIME Designation in the European Union, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process.

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious 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. For products that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

The FDA may also 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 review 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 review product may be effective.

We may also seek a priority review designation for one or more of our product candidates. If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal is for the FDA to review a new drug application in six months, rather than the standard review period of ten months.

These designations are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to product candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

In the European Union, we may seek PRIME designation for some of our product candidates in the future. The PRIME program focuses on product candidates that target conditions for which there exists no satisfactory method of treatment in the European Union, or even if such a method exists, the product candidate may offer a major therapeutic advantage over existing treatments. To be accepted for PRIME designation, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims. The benefits of a PRIME designation include the appointment of a rapporteur of the Committee for Medicinal Products for Human Use to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME designation enables an applicant to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive

PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

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

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

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

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;

- the federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or transfers of value made to physicians, other healthcare providers and teaching hospitals, as well as information regarding ownership and investment interests held by physicians, other healthcare providers 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 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.

Existing and future legislation may increase the difficulty and cost for us to obtain reimbursement for our products and product candidates.

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 ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, in August 2021, 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, will stay in effect through 2031. 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. Pursuant to subsequent legislation, the reductions were suspended through the end of March 2022 and reduced to 1% from April 2022 through June 2022. In addition, 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 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 and continue to be numerous legal challenges and Congressional actions to repeal and replace provisions of the law and litigation and legislation over the ACA is likely to continue with unpredictable and uncertain results. 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. The Trump Administration also took executive actions to undermine or delay implementation of the ACA, but those were rescinded by the Biden Administration. President Biden issued an 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 executive 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 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. 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 products. For example, on July 9, 2021,

President Biden signed an executive order, which focuses on, among other things, the price of pharmaceuticals. The executive order directs the Department of Health and Human Services, or HHS, to create a plan to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (1) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (2) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (3) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

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.

Reporting and payment obligations under the Medicaid Drug Rebate Program and other governmental drug pricing programs are complex and may involve subjective decisions. Any failure to comply with those obligations could subject us to penalties and sanctions.

As a condition of reimbursement by various federal and state health insurance programs, pharmaceutical companies are required to calculate and report certain pricing information to federal and state agencies. The regulations governing the calculations, price reporting and payment obligations are complex and subject to interpretation by various government and regulatory agencies, as well as the courts. Reasonable assumptions have been made where there is lack of regulations or clear guidance and such assumptions involve subjective decisions and estimates. Pharmaceutical companies are required to report any revisions to their calculation, price reporting and payment obligations previously reported or paid. Such revisions could affect liability to federal and state payers and also adversely impact reported financial results of operations in the period of such restatement.

Uncertainty exists as new laws, regulations, judicial decisions, or new interpretations of existing laws, or regulations related to our calculations, price reporting or payments obligations increases the chances of a legal challenge, restatement or investigation. If a company becomes subject to investigations, restatements, or other inquiries concerning compliance with price reporting laws and regulations, it could be required to pay or be subject to additional reimbursements, penalties, sanctions or fines, which could have a material adverse effect on the business, financial condition and results of operations. In addition, it is possible that future healthcare reform measures could be adopted, which could result in increased pressure on pricing and reimbursement of products and thus have an adverse impact on financial position or business operations.

Further, state Medicaid programs may be slow to invoice pharmaceutical companies for calculated rebates resulting in a lag between the time a sale is recorded and the time the rebate is paid. This results in a company having to carry a liability on its consolidated balance sheets for the estimate of rebate claims expected for Medicaid patients. If

actual claims are higher than current estimates, the company's financial position and results of operations could be adversely affected.

In addition to retroactive rebates and the potential for 340B Program refunds, if a pharmaceutical firm is found to have knowingly submitted any false price information related to the Medicaid Drug Rebate Program to the CMS, it may be liable for civil monetary penalties. Such failure could also be grounds for CMS to terminate the Medicaid drug rebate agreement, pursuant to which companies participate in the Medicaid program. In the event that CMS terminates a rebate agreement, federal payments may not be available under government programs, including Medicaid or Medicare Part B, for covered outpatient drugs.

Additionally, if a pharmaceutical company overcharges the government in connection with the FSS program or Tricare Retail Pharmacy Program, whether due to a misstated Federal Ceiling Price or otherwise, it is required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against a company under the FCA and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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.

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 are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies, contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the U.S., EU and U.K. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards

and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future.

If we are unable to properly protect the privacy and security of protected health information, we could be found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

Similar to the laws in the United States, there are significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area, or EEA, and the processing of personal data that takes place in the EEA, is regulated by the General Data Protection Regulation, or GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross-border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.

While we continue to address the implications of the recent changes to data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the United States regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

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, 2021, we had federal net operating loss, or NOL, carryforwards of $364.4 million, which may be available to offset future federal tax liabilities and expire at various dates beginning in 2030. As of December 31, 2021, we also had state NOL carryforwards of $352.9 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 $3.6 million, which begin to expire in 2040 (federal) and 2035 (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 previously completed an analysis and determined that an ownership change has materially limited our net operating loss carryforwards and research and development tax credits available to offset future tax liabilities, which

limitation is reflected in the numbers presented above. We may be further limited by any changes that may have occurred or may occur subsequent to December 31, 2021. 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 Chief Executive Officer, Todd Bazemore, our President and Chief Operating Officer, Mary Reumuth, our Chief Financial Officer, Kim Brazzell, Ph.D., our Head of Research and Development and Chief Medical Officer, Darius Kharabi, our Chief Business 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. In addition, we are highly dependent on the employees who joined us in connection with the Acquisition and their expertise developing biologics.

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, clinical and regulatory 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 our development, regulatory, commercial and manufacturing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We have experienced 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. To manage growth, we must continue to implement and improve our managerial, operational and financial systems and continue to recruit and train additional qualified personnel. In addition, the change in our business in connection with the Acquisition, including the addition of a biological product candidate and employees who joined us in connection with the Acquisition, has imposed added responsibilities on members of our management, including the

need to recruit, hire, retain, motivate and integrate additional employees and business operations, including employees with experience developing biologics should KPI-012 advance through the various stages of development.

Due to our limited financial resources and our limited experience in managing such growth, we may not be able to effectively integrate Combangio into our business and KPI-012 into our business strategy, manage our recently expanded operations, 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 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.

A partially or fully remote workplace could negatively impact our business.

We terminated our lease for office and laboratory space at our former corporate headquarters in Watertown, Massachusetts, effective January 11, 2022. While we have retained a nominal amount of office space on a short-term

basis to conduct in-person meetings from time-to-time in Arlington, Massachusetts and acquired a sublease for a nominal amount of office and laboratory space in Menlo Park, California in connection with our acquisition of Combangio, the vast majority of our employees no longer have individual offices or access to dedicated laboratory space. We plan to outsource all laboratory activities, other than certain activities related to KPI-012, until such time, if ever, that we maintain our own dedicated laboratory space. As a result, our management team and the vast majority of our employees will work remotely and without dedicated office space, until such time as we determine to obtain a new operating lease. By migrating to a remote workforce, our employees are accessing our servers remotely through home or other networks to perform their job responsibilities, which may be less secure. The risk of cyber incidents or other privacy or data security incidents may be heightened as a result of our remote work environment. Remote working arrangements could also impact employee productivity and morale, impede employee training, strain our technology resources and introduce operational risks, all of which could negatively impact our business. Furthermore, our transition to a largely remote workplace will increase our reliance on third parties to conduct a significant portion of our research and development activities. We have limited ability to control the amount or timing of resources that any such third party will devote to our research and development activities, and such third parties may terminate their engagements with us at any time. We also expect to have to negotiate budgets and contracts with such third parties, and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs.

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 March 28, 2022, our executive officers and directors and their affiliates in the aggregate, owned shares representing approximately 15.99% 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 ability to achieve the anticipated benefits of the Acquisition and to successfully implement our proposed business strategy;
- 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 development of KPI-012 and any other product candidate we develop;
- 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, KPI-012 or any other product candidate we develop. 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 March 28, 2022, we had outstanding 72,594,005 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.

In connection with the Acquisition, on January 3, 2022 we issued an aggregate of 6,815,072 shares of our common stock to the former Combangio equityholders, and we held back 973,565 Holdback Shares that will be issuable subject to the terms of the Merger Agreement to the Combangio equityholders on the escrow release date. In addition, former Combangio equityholders are entitled to receive from us, subject to the terms and conditions of the Merger Agreement, contingent consideration of up to $5.4 million payable in shares of our common stock upon our achievement of various development and regulatory milestones, and we may elect, subject to the Nasdaq rules, to satisfy a portion of certain milestone payments that are payable to Combangio equityholders in cash through the issuance of up to $15 million of our common stock. While the shares of common stock issued to former Combangio equityholders will be restricted as a result of securities laws, following expiration of applicable holding periods, these shares will be able to be

freely sold in the public market, subject to any requirements and restrictions, including any applicable volume limitations, imposed by Rule 144 under the Securities Act.

In addition, the Merger Agreement obligates us to file a registration statement with respect to public resale of our shares of common stock that may become issuable upon the achievement of certain of the milestones.

The sale or resale of these shares in the public market, or the market's expectation of such sales, may result in an immediate and substantial decline in our stock price. Such a decline will adversely affect our investors and also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

If we fail to comply with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

We must satisfy Nasdaq's continued listing requirements, including, among other things, a minimum closing bid price of $1.00 per share, or risk delisting, which would have a material adverse effect on our business. A delisting of our common stock from Nasdaq could materially reduce the liquidity of our common stock and result in a corresponding material reduction in the price of our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the potential loss of confidence by investors, suppliers, customers and employees and fewer business development opportunities. Any potential delisting of our common stock from Nasdaq would also make it more difficult for our stockholders to sell their shares in the public market.

On March 2, 2022, we received a deficiency letter from Nasdaq notifying us that, for the last 30 consecutive business days, the bid price of our common stock had closed below the $1.00 per share minimum bid price requirement for continued inclusion on Nasdaq pursuant to Nasdaq Listing Rule 5450(a)(1), or the Bid Price Requirement. We were provided a period of 180 calendar days, or until August 29, 2022, to regain compliance with the Bid Price Requirement. On March 22, 2022, we received a letter from the Listing Qualifications Department of the Nasdaq Stock Market notifying us that we had regained compliance with the Bid Price Requirement as we had a closing bid price of at least $1.00 per share for a minimum of ten consecutive business days from March 8, 2022 through March 21, 2022.

Although the matter is now closed, there can be no assurance that we will be able to continue to comply with the Nasdaq continued listing requirements.

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 Loan Agreement 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 deduction for NOLs to 80% of current year taxable income and elimination of NOL carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such NOLs may be carried forward indefinitely).

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, COVID relief provisions were included in the Consolidated Appropriations Act, 2021, or CAA, which was enacted on December 27, 2020, and the American Rescue Plan Act of 2021, or ARPA, was enacted on March 11, 2021. 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 NOLs, which was enacted as part of the 2017 Tax Act. It also provides that NOLs 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.

Regulatory guidance under the 2017 Tax Act, the FFCR Act, the CARES Act, the CAA and the ARPA 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 or otherwise. Any such legislation 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 , the CAA or the ARPA.

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

On February 28, 2018, we entered into a lease for our former corporate headquarters located in Watertown, Massachusetts, which consisted of 66,052 rentable square feet. We began to occupy this space on January 28, 2019, and the initial term of this lease was eight years with an option to extend for an additional term of five years. On November 12, 2021, we entered into a lease termination agreement with the landlord of this facility, which was amended on December 22, 2021. Pursuant to the lease termination agreement, we vacated the premises on January 11, 2022. We currently lease a limited amount of office space in Arlington, Massachusetts, which serves as our corporate headquarters.

Combangio, our wholly-owned subsidiary as a result of the Acquisition, entered into a space sharing agreement with Lagunita, LLC on October 11, 2019, pursuant to which it subleases 1,550 square feet of shared office and lab space. The term of the space-sharing agreement expires on June 30, 2023.

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 March 28, 2022, there were approximately 31 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 Loan and Security Agreement with Oxford Finance LLC, 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 2022 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, 2021 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 18, 2021, we granted stock options to ten new employees to purchase an aggregate of 70,000 shares of our common stock at an exercise price of $1.85 per share. On November 15, 2021, we granted stock options to four new employees to purchase an aggregate of 135,200 shares of our common stock at an exercise price of $2.10 per share. On December 15, 2021, we granted stock options to four new employees to purchase an aggregate of 13,500 shares of our common stock at an exercise price of $1.44 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. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and 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 products utilizing our proprietary mucus penetrating particle drug delivery technology, which we refer to as our AMPPLIFY® technology, to address medical needs for the front of the eye. Our product candidates and programs include a proprietary regenerative biotherapy for severe ocular diseases and a pipeline of preclinical 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, 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, and we commenced a full promotional launch of EYSUVIS in January 2021. 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 offer 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 are 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.

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. The FDA approved INVELTYS in August 2018, and we commercially launched the product in January 2019. INVELTYS 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.

Upon the consummation of our acquisition of Combangio, Inc., or Combangio, on November 15, 2021, we acquired Combangio's product candidate, CMB-012, which we now refer to as KPI-012. KPI-012 is our lead product candidate and is currently in clinical development for the treatment of persistent corneal epithelial defects, or PCED, a rare disease of impaired corneal healing. We believe the multifactorial mechanism of action of KPI-012 also makes it a platform technology, and we are evaluating KPI-012 for potential expansion to indications for rare front of the eye diseases, such as limbal stem cell deficiency, chemical burns and Sjogren's Syndrome, as well as select rare back of the eye diseases, such as retinitis pigmentosa and optic neuritis. For a further description of our acquisition of Combangio, see "Acquisition of Combangio, Inc." below and for a further description of KPI-012 and PCED, see Item 1, Business.

We are also progressing our pipeline of proprietary NCE preclinical development programs targeted to address both front and back of the eye diseases. These preclinical development programs include KPI-287, our receptor Tyrosine Kinase Inhibitor and our selective glucocorticoid receptor modulators, or SEGRMs.

KPI-287 is designed to inhibit the vascular endothelial growth factor and platelet derived growth factor pathways, and is administered by suprachoroidal injection for the treatment of retinal diseases, including wet age-related macular degeneration diabetic macular edema and retinal vein occlusion. SEGRMs are a novel class of therapies designed to modify the downstream activity of the glucocorticoid receptors to exhibit the anti-inflammatory and immunomodulatory properties of the corticosteroid class of therapies while markedly reducing their associated side effects, which we are developing for the treatment of inflammatory diseases.

We have retained worldwide commercial rights for EYSUVIS, INVELTYS, KPI-012 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 approximately 100 field-based commercial sales personnel. 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, utilizing a variety of collaboration, distribution and other marketing arrangements with one or more third parties.

Since inception, we have incurred significant losses from operations and negative cash flows from operations. Our net losses were $142.6 million for the year ended December 31, 2021 and $104.3 million for the year ended December 31, 2020. As of December 31, 2021, we had an accumulated deficit of $542.4 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 initial public offering, or IPO, follow-on public common stock offerings and sales of our common stock under our sales agreement with Jefferies, LLC, or Jefferies, in at-the-market offerings, or ATM Offerings, private placements of preferred stock, borrowings under credit facilities and our Loan and Security Agreement, or Loan Agreement, with Oxford Finance LLC, or Oxford Finance, 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. As a result of the acquisition of Combangio, we expect to devote substantial financial resources to the research and development and potential commercialization of KPI-012. 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 for at least the next several years, including in connection with our continued development, regulatory approval efforts and commercialization, if any, of KPI-012. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year.

Acquisition of Combangio, Inc.

On November 15, 2021, pursuant to the terms and conditions of an Agreement and Plan of Merger, or the Merger Agreement, we acquired Combangio, a clinical-stage biotechnology company focused on developing regenerative biotherapeutics for severe ocular diseases based on mesenchymal stem cell, or MSCs, secretomes, including, its lead product candidate, CMB-012 for the treatment of PCED, or the Acquisition. Following the Acquisition, Combangio became our wholly-owned subsidiary and we refer to CMB-012 as KPI-012.

In connection with the closing of the Acquisition on November 15, 2021, or the Closing, we made an upfront payment of an aggregate of $5.0 million in cash to former Combangio stockholders and other equityholders, or the Combangio Equityholders, subject to customary adjustments, and agreed to issue an aggregate of 7,788,637 shares, or the Deferred Purchase Consideration, of our common stock to the Combangio Equityholders with an aggregate value of approximately $16.1 million, consisting of (i) an aggregate of 6,815,072 shares of common stock which were issued on January 3, 2022 and (ii) an aggregate of 973,565 shares of common stock that have been held back by us and will be issuable subject to the terms of the Merger Agreement to the Combangio Equityholders on the Escrow Release Date (as defined below), or the Initial Holdback Shares. The aggregate value of the Deferred Purchase Consideration was

calculated using the closing price of our common stock on the Nasdaq Global Select Market on November 12, 2021, the last trading day prior to the Closing.

In addition, pursuant to the Merger Agreement, the Combangio Equityholders, in the aggregate and subject to the terms and conditions of the Merger Agreement, will also be entitled to receive from us the following contingent consideration, or the Contingent Consideration:

- up to $105.0 million in contingent milestone consideration, of which (i) $2.3 million would become payable in cash and $2.7 million would be payable in shares of our common stock upon the first patient dosed with any product candidate whose active ingredient comprises one or more biological factors secreted by MSCs or their progenitors, including KPI-012, or the Product Candidate, in a Phase 2 clinical trial, or the Dosing Milestone, (ii) $2.3 million would become payable in cash and $2.7 million would be payable in shares of our common stock upon the first patient dosed with a Product Candidate in a pivotal clinical trial, (iii) $12.5 million would become payable (with up to $6.25 million payable, at our option, in shares of our common stock and the remainder in cash) upon regulatory approval by the FDA of marketing and sale of a Product Candidate in the United States, subject to certain specified reductions; (iv) $17.5 million would become payable (with up to $8.75 million payable, at our option, in shares of our common stock and the remainder in cash) upon the first commercial sale of a Product Candidate in the United States, subject to certain specified reductions, and (v) an aggregate of up to $65.0 million would become payable in cash upon the achievement of specified sales milestones, or the Net Sales Milestone Payments;
- tiered cash royalties at percentage rates in the mid-to-high single digits payable on annual net sales of all Product Candidates; and
- a cash payment at a percentage rate in the high single digits of all income, including earnout payments, received by us or any of our affiliates from a product license granted by us to a third party to sell or otherwise commercialize the Product Candidate in countries where neither we nor our affiliates conduct sales of such Product Candidate, subject to certain exceptions set forth in the Merger Agreement.

The portion of any payment of Contingent Consideration payable in shares of our common stock is referred to herein as “Contingent Stock Consideration” and the portion of any payment of Contingent Consideration payable in cash is referred to herein as “Contingent Cash Consideration”.

If the issuance of the Deferred Purchase Consideration or any Contingent Stock Consideration would result in the aggregate number of shares of our common stock issued under the Merger Agreement equaling or exceeding 19.9% of the total number of shares of our common stock issued and outstanding immediately prior to the Closing, or the Share Cap, then we will be required to pay the portion of the Deferred Purchase Consideration or any Contingent Stock Consideration in excess of the Share Cap in cash. If the aggregate amount of Contingent Cash Consideration payable in any calendar year (after giving effect to the Share Cap) exceeds $2,500,000, or the Excess Cash Cap, such excess portion, or the Carry Forward Contingent Cash Consideration, will be carried forward and, subject to application of the Excess Cash Cap in the following calendar year, become payable on the first business day of the following calendar year. Any Carry Forward Contingent Cash Consideration outstanding on June 1, 2026 is payable in full on June 1, 2026.

Former Combangio Equityholders who are non-accredited investors will receive cash in lieu of any of our common stock that otherwise would be issuable to them pursuant to the Merger Agreement.

In connection with the Closing, we placed $625,000 of the cash purchase price in an escrow account, or the Escrow Account, to be disbursed in accordance with an escrow agreement with Computershare Corporate Trust Company, N.A., or the Escrow Agreement, as escrow agent, and subject to the terms of the Merger Agreement, we will place 12.5% of any Contingent Cash Consideration that becomes payable prior to the date that is fifteen months after the Closing, or the Escrow Release Date, into such Escrow Account to be disbursed in accordance with the Escrow Agreement. Subject to the terms of the Merger Agreement, 12.5% of any Contingent Stock Consideration that becomes payable in common stock prior to the Escrow Release Date will be held back by us, or the Contingent Holdback Shares, and, together with the Initial Holdback Shares, which we collectively referred to herein as the Holdback Shares, will serve as partial security for the satisfaction of indemnification obligations and other payment obligations of the Combangio Equityholders and, subject to reduction in respect of these obligations, the Holdback Shares will be issued to the Combangio Equityholders on the Escrow Release Date.

Business Impact of COVID-19 Pandemic

In order to safeguard the health of our employees from the ongoing COVID-19 pandemic, we are 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. We previously suspended our sales force from substantially all in-person interactions with physicians and were limited to conducting educational and promotional activities virtually. Commencing in the fourth quarter of 2020, our sales force resumed substantially all in-person interactions in the field, but if we suspend all or some in-person interactions with physicians in the future, or to the extent physicians limit in-person interactions, we may be limited to conducting educational and promotional activities virtually, which may continue to hamper our ability to market and commercialize EYSUVIS and INVELTYS.

In addition, government restrictions have at times led to moratoria on elective ocular surgeries in many jurisdictions, which had 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. In addition, the COVID-19 pandemic has generally had an adverse impact on the launch of pharmaceutical products, and we believe the pandemic has impacted, and may continue to impact, the launch of EYSUVIS. We also do not know the extent to which the COVID-19 pandemic will impact our development of KPI-012 or any other product candidate we develop. The extent of the impact of the COVID-19 pandemic on our commercialization efforts of EYSUVIS and INVELTYS, our clinical development efforts for KPI-012 and our preclinical developments programs, and our operational and financial performance will depend on certain developments, including the length and severity of this pandemic, the timing and extent of any resurgence of the COVID-19 virus or any variant strains of the virus, the availability and effectiveness of vaccines, and the full extent of 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 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, is believed to have impacted the ongoing commercialization of EYSUVIS and could impact the development of KPI-012 or any other product candidate we develop, 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. Full promotional launch of EYSUVIS began 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 programs, 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, prescriptions of INVELTYS and related revenue are still being adversely affected by the ongoing COVID-19 pandemic and 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 the COVID-19 pandemic. We also cannot project the full extent of the impact that the COVID-19 pandemic may have on the commercialization of EYSUVIS. Moreover, KPI-012 is in the early stages of clinical development and all of our other research and development programs are in

preclinical development and, accordingly, we do not expect to generate revenue from KPI-012 or any other product candidate for several years, if at all.

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, losses on inventory purchase commitments, 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 the COVID-19 pandemic.

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, compliance, information technology and business development functions. Selling, general and administrative expenses also include external selling and marketing costs, 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 expect that our selling, general and administrative expenses will decrease in 2022 as compared to the year ended December 31, 2021 as we have completed the buildout of our commercial infrastructure to support the commercialization of INVELTYS and EYSUVIS, have incurred launch-related expenses during 2021 that we do not expect to incur again in the future related to EYSUVIS or INVELTYS and have terminated the lease for our corporate headquarters, effective January 11, 2022. Until we pursue the commercialization of KPI-012 or any other product candidate, if approved, we anticipate that our selling, general and administrative expenses will remain largely consistent beyond 2022 and for the foreseeable future as we continue to commercialize EYSUVIS and INVELTYS and as we support our continued research and development activities and seek marketing approval for our product candidates, including KPI-012. We expect that our selling, general and administrative expenses will increase substantially if and when we pursue the commercialization of KPI-012, if approved, and support commercialization of any other product candidate. Our sales force has resumed substantially all in-person interactions in the field with physicians, which were previously suspended due to the restrictions with respect to the ongoing COVID-19 pandemic. 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 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 certain 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, 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 research and development costs will increase in 2022 as compared to the year ended December 31, 2021 as we continue to advance our development programs and conduct any necessary preclinical studies and clinical trials and other development activities for product candidates, including KPI-012, KPI-287 and our SEGRM program. 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 the 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.

KPI-012 is in the early stages of clinical development and all of our other research and development programs are in preclinical 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.

Acquired In-Process Research and Development Expenses

We include costs to acquire or in-license product candidates in acquired in-process research and development, or IPR&D, expenses. When we acquire the right to develop and commercialize a new product candidate, any upfront payments or any future milestone payments that are recorded at fair value that relate to the acquisition or licensing of such a right are immediately expensed as acquired IPR&D in the period in which they are incurred. These costs are immediately expensed provided that the payments do not also represent processes or activities that would constitute a "business" as defined under U.S. generally accepted accounting principles, or U.S. GAAP, or provided that the product candidate has not achieved regulatory approval for marketing and, absent obtaining such approval, has no alternative future use.

Gain on Fair Value Remeasurement of Deferred Purchase Consideration

Consideration payable for our acquisitions may include future issuances of our common stock. We record an obligation for such Deferred Purchase Consideration at fair value on the acquisition date. We then revalue our Deferred Purchase Consideration obligations each reporting period. Changes in the fair value of our Deferred Purchase Consideration obligations, other than changes due to issuance, are recognized as a (gain) loss on fair value remeasurement of Deferred Purchase Consideration in our consolidated statements of operations and comprehensive loss.

Interest Income

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

Interest Expense

Interest expense primarily consists of contractual coupon interest, amortization of debt discounts and debt issuance costs and accretion of the final payment fee recognized on our debt arrangements.

Loss on Extinguishment of Debt

Loss on extinguishment of debt primarily consists of unamortized debt discount and issuance costs, a prepayment premium and unaccreted exit fees on the credit agreement, or the Athyrium Credit Facility, with Athyrium Opportunities III Acquisition LP, or Athyrium.

Gain on Lease Modification

Gain on lease modification represents the gain recognized in connection with the lease termination agreement we entered into in November 2021 with the landlord for our office and laboratory space at our former corporate headquarters in Watertown, Massachusetts, which was amended on December 22, 2021. In connection with the modification of this lease, we remeasured the operating right-of-use asset and liability balances and recognized a gain of $1.3 million.

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. GAAP. 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 critical accounting estimates 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. Our allowance for product returns has increased in the year ended December 31, 2021 as a result of an increase in the actual returns received.

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.

Acquisition Accounting

We are required to make significant judgments and estimates to determine whether an acquisition constitutes an acquisition of a business or assets. For asset acquisitions, this includes whether substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or a group of similar identifiable assets. We are also required to make several significant judgments and estimates in order to determine the total consideration transferred for the asset acquisition and then allocate it to the assets that we have acquired and the liabilities that we have assumed on a relative fair value basis. If the asset related to acquired IPR&D has no alternative future use, it is expensed immediately upon the completion of the transaction.

In addition to upfront consideration, our asset acquisitions may also include contingent consideration payments to be made for future milestone events or royalties on net sales of future products. We assess whether such contingent consideration is required to be recorded at fair value on the date of the acquisition and subsequently remeasured to fair value at each reporting date. Contingent consideration payments in an asset acquisition not required to be recorded at fair value are recognized when the contingency is resolved, and the consideration is paid or becomes payable. Changes in the fair value of the contingent milestone payments can result from changes to one or more inputs, including adjustments to the probability of achievement, timing of the contingent milestone payments and changes to the applicable discount rates. Significant judgment is used in determining these assumptions during each reporting period. Reasonable changes in these assumptions can cause material changes to the fair value of our contingent consideration liability. Any changes in the fair value of these contingent consideration liabilities are included in loss from operations in the consolidated statements of operations and comprehensive loss. For information related to the unobservable inputs related to the contingent consideration, see Note 4 of our consolidated financial statements.

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, 2021 and 2020

The following table summarizes the results of our operations for the years ended December 31, 2021 and 2020:

	Year Ended December 31,		
	2021	2020	Change
	(in thousands)		
Product revenues, net	$ 11,240	$ 6,362	$ 4,878
Costs and expenses:			
Cost of product revenues	4,097	3,173	924
Selling, general and administrative	105,061	81,068	23,993
Research and development	11,515	18,352	(6,837)
Acquired in-process research and development	26,617	—	26,617
Gain on fair value remeasurement of deferred purchase consideration	(5,805)	—	(5,805)
Total operating expenses	141,485	102,593	38,892
Loss from operations	(130,245)	(96,231)	(34,014)
Other income (expense)			
Interest income	104	493	(389)
Interest expense	(8,380)	(8,589)	209
Loss on extinguishment of debt	(5,395)	—	(5,395)
Gain on lease modification	1,311	—	1,311
Net loss	$ (142,605)	$ (104,327)	$ (38,278)

Product revenues, net

Product revenues, net was $11.2 million for the year ended December 31, 2021, consisting of $6.3 million from EYSUVIS sales and $4.9 million from INVELTYS sales, compared to $6.4 million for the year ended December 31, 2020, which consisted of $0.3 million from EYSUVIS sales and $6.1 million from INVELTYS sales. The increase in product revenues, net of $4.8 million is primarily the result of sales of EYSUVIS, which we began shipping to wholesalers in the United States in late December 2020 and for which we commenced a full commercial launch in January 2021, an increase in the total units of INVELTYS sold in the year ended December 31, 2021 as well as a higher per unit gross selling price of INVELTYS as compared to those sold during the year ended December 31, 2020. These increases in INVELTYS sales were offset by higher estimated allowances per unit during the year ended December 31, 2021 as compared to those allowances per unit during the year ended December 31, 2020. 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 2022 as a result of the COVID-19 pandemic.

Cost of product revenues

Cost of product revenues was $4.1 million for the year ended December 31, 2021, compared to $3.2 million for the year ended December 31, 2020. Cost of product revenues increased $0.9 million due to an increase in total INVELTYS units sold during the year ended December 31, 2021, compared to the year ended December 31, 2020 as well as a higher INVELTYS cost per unit as a result of the units sold during the year ended December 31, 2020 being partially manufactured prior to its FDA approval and for which costs were expensed as research and development prior to such FDA approval as compared to those units sold during the year ended December 31, 2021. Partially offsetting these increases was an additional reserve for excess or obsolete inventory of $0.5 million recorded during the year ended December 31, 2020, as compared to the year ended December 31, 2021. The cost of product revenues attributable to EYSUVIS was $0.8 million for the year ended December 31, 2021, compared to $0.3 million in the year ended December 31, 2020. We expect the aggregate cost of product revenues to increase as we continue to commercialize EYSUVIS and INVELTYS.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $105.1 million for the year ended December 31, 2021, compared to $81.1 million for the year ended December 31, 2020, which was an increase of $24.0 million. Selling, general and administrative expenses for the year ended December 31, 2021 included a $6.9 million increase in external sales and marketing costs as compared to the year ended December 31, 2020, primarily as a result of the launch of EYSUVIS. External sales and marketing costs incurred during the year ended December 31, 2020 primarily related to commercial activities for INVELTYS. Also contributing to the increase in selling, general and administrative expenses for the year ended December 31, 2021 was a $14.6 million increase in employee-related expenses primarily due to an increase in employee headcount related to the launch of EYSUVIS and merit-based pay, a $2.4 million increase in stock-based compensation costs and a $1.7 million increase in other selling, general and administrative expenses, which included facility related costs and certain medical affairs costs attributable to our commercial products. These increases were partially offset by a $1.6 million decrease in costs for administrative and professional service fees.

We expect our selling, general and administrative expenses to decrease in 2022 as compared to the year ended December 31, 2021 as we have completed the buildout of our commercial infrastructure to support the commercialization of EYSUVIS and INVELTYS, have incurred launch-related expenses in 2021 that we do not expect to incur again in the future related to EYSUVIS or INVELTYS and have terminated the lease for our former corporate headquarters, effective January 11, 2022. Until we pursue the commercialization of KPI-012 or any other product candidate, if approved, we anticipate that our selling, general and administrative expenses will remain largely consistent beyond 2022 and for the foreseeable future as we continue to commercialize EYSUVIS and INVELTYS and as we support our continued research and development activities and seek marketing approval for our product candidates, including KPI-012. We expect that our selling, general and administrative expenses will increase substantially when we pursue the commercialization of KPI-012, if approved, and support commercialization of any other product candidate.

Research and Development Expenses

The following table summarizes the research and development expenses incurred during the years ended December 31, 2021 and 2020:

	Year Ended December 31,		
	2021	2020	Change
	(in thousands)		
KPI-121 development costs	$ 384	$ 4,686	$ (4,302)
Employee-related costs	7,417	10,607	(3,190)
Other research and development costs	3,714	3,059	655
Total research and development	$ 11,515	$ 18,352	$ (6,837)

Research and development expenses were $11.5 million for the year ended December 31, 2021 compared to $18.4 million for the year ended December 31, 2020, a decrease of $6.8 million. The decrease was primarily the result of a $4.3 million decrease in EYSUVIS development costs related to a decrease in external spend on STRIDE 3, our Phase 3 clinical trial of EYSUVIS, a $3.2 million decrease in employee-related costs largely due to the decrease in the allocation of employee time dedicated to research and development, partially offset by a $0.7 million increase in other research and development costs, which included preclinical studies and other facility related costs. We expect research and development costs to increase as we advance our development programs and conduct any necessary preclinical studies and clinical trials and other development activities for product candidates, including KPI-012.

Acquired In-Process Research and Development Expenses

Acquired IPR&D expenses for the year ended December 31, 2021 were $26.6 million. Acquired IPR&D for the year ended December 31, 2021 includes costs associated with the acquisition of acquired in-process research and development from the Acquisition. There were no acquired IPR&D expenses for the year ended December 31, 2020.

Gain on fair value remeasurement of deferred purchase consideration

Gain on fair value remeasurement of deferred purchase consideration for the year ended December 31, 2021 was $5.8 million and was primarily due to a change in the fair value of our underlying stock price. There was no gain or loss on fair value remeasurement of deferred purchase consideration for the year ended December 31, 2020.

Interest Income

Interest income was $0.1 million for the year ended December 31, 2021, compared to $0.5 million for the year ended December 31, 2020, a decrease of $0.4 million. Interest income consists of interest earned on our cash, cash equivalents and short-term investments, if any. The decrease was attributable to lower interest rates and lower cash, cash equivalents and short-term investments balances during the year ended December 31, 2021.

Interest Expense

Interest expense was $8.4 million for the year ended December 31, 2021, compared to $8.6 million for the year ended December 31, 2020, a decrease of $0.2 million. Interest expense for the year ended December 31, 2021 was comprised of the contractual coupon interest expense, the amortization of the debt discount and the accretion of the final payment fee associated with our Loan Agreement with Oxford Finance LLC and our Athyrium Credit Facility. Interest expense for the year ended December 31, 2020 was comprised of the contractual coupon interest expense, the amortization of the debt discount and the accretion of the final payment fee associated with our Athyrium Credit Facility. During the year ended December 31, 2021, $75.0 million of indebtedness was outstanding under the Athyrium Credit Facility until we repaid such indebtedness in full on May 4, 2021. During the year ended December 31, 2021, $80.0 million of indebtedness was outstanding under our Loan Agreement after we drew down the tranche A term loan on May 4, 2021. During the year ended December 31, 2020, $75.0 million of indebtedness was outstanding under the Athyrium Credit Facility.

Loss on extinguishment of debt

The loss of extinguishment of debt was $5.4 million for the year ended December 31, 2021. Upon the repayment in full of all amounts owed under the Athyrium Credit Facility, the unamortized debt discount and issuance costs, prepayment premium and unaccreted exit fee were recorded as loss on extinguishment of debt for the year ended December 31, 2021. There was no loss on extinguishment of debt for the year ended December 31, 2020.

Gain on lease modification

The gain on lease modification was $1.3 million for the year ended December 31, 2021 and represents the gain recognized in connection with the lease termination agreement entered into in November 2021 with the landlord for our office and laboratory space at our former corporate headquarters in Watertown, Massachusetts, which was amended on December 22, 2021. There was no gain on lease modification for the year ended December 31, 2020.

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 and the Loan Agreement, 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 shelf registration statement on Form S-3 that was declared effective by the SEC on August 27, 2018, or the 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. The 2018 Shelf Registration is now expired.

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 which we did not draw down. On May 4, 2021, concurrently with the closing of the Loan Agreement with Oxford Finance LLC and the borrowing of the tranche A loan, we utilized substantially all of the proceeds from the tranche A term loan to repay in full all outstanding amounts owed under the Athyrium Credit Facility, under which we had an aggregate principal amount of $75.0 million of indebtedness outstanding. We terminated all commitments by Athyrium to extend further credit under the Athyrium Credit Facility and all guarantees and security interests granted by us thereunder. In connection with the termination of the Athyrium Credit Facility, we paid to the lenders a prepayment premium of $2.25 million and an exit fee of $0.8 million. The transaction resulted in a loss on extinguishment of debt of $5.4 million, consisting of the prepayment premium, the unamortized debt discount and the unaccreted exit fee.

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. Through the first quarter of 2020, we issued an aggregate of 4,945,605 shares of our common stock under the ATM Offering, resulting in net proceeds to us of $25.6 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, commissions and offering expenses, of $125.4 million.

Under the 2018 Shelf Registration, which has now expired, we 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 our shelf registration statement on Form S-3 that was declared effective by the SEC on May 7, 2020, or the 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 the year ended December 31, 2021, we issued and sold an additional 5,760,198 shares of our common stock under our ATM Offering, resulting in net proceeds to us of $41.2 million. As of December 31, 2021, there was $11.3 million of shares of common stock remaining under the ATM Offering that we may issue and sell in the future and, excluding the shares of common stock that may be offered under our ATM Offering, there was $275.0 million of securities available to be issued under the 2020 Shelf Registration.

On May 4, 2021, we entered into the Loan Agreement with Oxford Finance, in its capacity as lender, or the Lender, and in its capacity as collateral agent, pursuant to which a term loan of up to an aggregate principal amount of $125.0 million is available to us, consisting of (i) a tranche A term loan that was disbursed on the closing date of the Loan Agreement in the aggregate principal amount of $80.0 million; (ii) a contingent tranche B term loan in the aggregate principal amount of $20.0 million available to us through June 30, 2023 and within 90 days of our achieving trailing 6-month product revenue equal to or greater than $75.0 million, subject to certain other terms and conditions; and (iii) a contingent tranche C term loan in the aggregate principal amount of $25.0 million available to us through December 31, 2023 and within 90 days of our achieving trailing 6-month product revenue equal to or greater than $100 million, subject to certain other terms and conditions. The term loans bear interest at a floating rate equal to the greater of 30-day LIBOR and 0.11%, plus 7.89%. Certain of the customary negative covenants limit our and certain of our subsidiaries' ability, among other things, to incur future debt, grant liens, make investments, make acquisitions, distribute dividends, make certain restricted payments and sell assets, subject in each case to certain exceptions. The Loan Agreement provides for interest-only payments until December 1, 2024 if neither the tranche B term loan nor the tranche C term loan are made, and until June 1, 2025 if either the tranche B term loan or the tranche C term loan is made, or the Amortization Date. The aggregate outstanding principal balance of the term loans are required to be repaid in monthly installments starting on the Amortization Date based on a repayment schedule equal to (i) 18 months if neither the tranche B term loan nor the tranche C term loan is made and (ii) 12 months if either the tranche B term loan or the tranche C term loan is made. All unpaid principal and accrued and unpaid interest with respect to each term loan is due and payable in full on May 1, 2026, or the Maturity Date.

We paid a facility fee of $400,000 on the closing date of the Loan Agreement and have agreed to pay a facility fee of $100,000 upon closing of the tranche B term loan and a $125,000 facility fee upon the closing of the tranche C term loan. We will be required to make a final payment fee of 7.00% of the original principal amount of any funded term loan payable on the earlier of (i) the prepayment of the term loan in full or (ii) the Maturity Date. At our option, we may elect to prepay all, but not less than all, of the outstanding loans, subject to a prepayment fee equal to the following percentage of the principal amount being prepaid: 3.00% if an advance is prepaid during the first 12 months following the applicable advance date, 2.00% if an advance is prepaid after 12 months but prior to 24 months following the applicable advance date, and 1.00% if an advance is prepaid any time after 24 months following the applicable advance date but prior to the Maturity Date. For further information about the Loan Agreement, see Note 11 of our consolidated financial statements.

As a result of the Acquisition, we may be required to pay additional contingent consideration to the former Combangio Equityholders. Pursuant to the Merger Agreement, former Combangio Equityholders are entitled to receive from us, subject to the terms and conditions of the Merger Agreement, Contingent Cash Consideration and Contingent Stock Consideration, which would become payable upon our achievement of various development, regulatory and sales milestones and as a result of certain cash royalty payment obligations. At our option, we may satisfy a portion of certain of the milestone payments through either the payment of cash or the issuance of additional shares of our common stock up to the Share Cap. For a full description of the consideration payable as a result of the Acquisition of Combangio, see "Acquisition of Combangio, Inc." above.

Our other material cash requirements from known contractual and other obligations as of December 31, 2021 primarily related to lease obligations and licensing and commercial supply agreements. For information related to our future commitments for our lease related obligations, see Note 10 of our consolidated financial statements. For information related to our future commitments relating to our licensing and commercial supply agreements, see Note 17 of our consolidated financial statements.

Cash Flows

As of December 31, 2021, we had $92.1 million in cash and cash equivalents and as of December 31, 2020, we had $153.5 million in cash, cash equivalents and short-term investments. As of December 31, 2021, we had $80.0 million in indebtedness, which represented the aggregate principal amount that was outstanding under the Loan Agreement with Oxford Finance LLC. As of December 31, 2020, we had $75.0 million in indebtedness, which represented the aggregate principal amount that was outstanding under the Athyrium Credit Facility.

On November 12, 2021, we entered into a lease termination agreement with the landlord for our office and laboratory space at our former corporate headquarters in Watertown, Massachusetts, which was amended on December 22, 2021, modifying the lease to accelerate the lease termination date to January 11, 2022, or the Lease Termination

Date. Under the terms of the lease termination agreement, we received a payment of $2.0 million from the landlord in January 2022 and released $2.0 million of restricted cash on the Lease Termination Date that was pledged as collateral under a letter of credit with cash on deposit required by the terminated lease.

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

	Year Ended December 31,		
	2021	2020	Change
	(in thousands)		
Net cash used in operating activities	$ (108,235)	$ (90,694)	$ (17,541)
Net cash provided by (used in) investing activities	70,803	(78,209)	149,012
Net cash provided by financing activities	42,554	160,628	(118,074)
Increase (decrease) in cash and restricted cash	$ 5,122	$ (8,275)	$ 13,397

Operating Activities

Net cash used in operating activities for the year ended December 31, 2021 was $108.2 million compared to $90.7 million for the year ended December 31, 2020, an increase of $17.5 million, primarily due to a $10.5 million increase in the net loss adjusted for non-cash charges and the timing of working capital fluctuations which accounted for $7.0 million of the increase. Notable working capital fluctuations include an increase to accounts receivable in the year ended December 31, 2021 of $5.8 million driven by an increase in sales largely due to the launch of EYSUVIS, whereas accounts receivable had decreased by $2.0 million in the year ended December 31, 2020 driven by improved days outstanding in the year ended December 31, 2020. Inventory increased by a greater amount during the year ended December 31, 2021 due to an increase in manufacturing activity for EYSUVIS and INVELTYS. Partially offsetting these increases was an increase in accounts payable, accrued expenses and other current liabilities during the year ended December 31, 2021 of $4.9 million, as compared to a decrease in accounts payable, accrued expenses and other current liabilities in the year ended December 31, 2020 of $2.7 million.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2021 was $70.8 million compared to net cash used of $78.2 million for the year ended December 31, 2020, an increase of $149.0 million. Net cash provided by investing activities for the year ended December 31, 2021 was due to the sales or maturities of short-term investments of $76.3 million and proceeds from sales of property and equipment of $0.1 million, partially offset by cash paid for the acquisition of IPR&D, net of cash acquired, of $4.7 million and purchases of property and equipment and other assets of $0.9 million. Net cash used in investing activities for the year ended December 31, 2020 consisted of the purchases of short-term investments of $113.6 million and purchases of property and equipment and other assets of $1.9 million, partially offset by proceeds from sales or maturities of short-term investments of $37.3 million.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 was $42.6 million, a decrease of $118.0 million compared to $160.6 million in the year ended December 31, 2020. Net cash provided by financing activities for the year ended December 31, 2021 included $77.8 million of net proceeds from the tranche A term loan under our Loan Agreement, $41.2 million of net proceeds from the sale of shares of our common stock under the ATM Offering and $1.6 million of proceeds from the exercise of stock options and the issuance of common stock under our employee stock purchase plan, partially offset by the repayment of indebtedness under our Athyrium Credit Facility of $78.0 million. Net cash provided by financing activities for the year ended December 31, 2020 consisted of $125.4 million of net proceeds from the sale of shares of our common stock in an underwritten offering pursuant to 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.

Funding Requirements

We anticipate that our research and development expenses will increase substantially in the future as compared to prior periods as we advance the clinical development of KPI-012. Our research and development expenses will also increase substantially in the future as we advance our preclinical development programs, including KPI-287 and our novel SEGRM program, and conduct any necessary preclinical studies and clinical trials and other development activities for our product candidates. We continue to commercialize EYSUVIS and INVELTYS in the United States and expect selling, general and administrative expenses will increase substantially when we pursue the commercialization of KPI-012, if approved, and support commercialization of any other product candidate.

Our expenses will also increase if and as we:

- submit an IND for, and continue the clinical development of, KPI-012 for PCED;
- initiate and continue the research and development of KPI-012 for additional indications, including initiating and conducting clinical trials;
- scale up our manufacturing processes and capabilities to manufacture the clinical supply of KPI-012;
- seek regulatory approval for KPI-012 for PCED in the United States and other jurisdictions;
- seek regulatory approval for KPI-012 for additional indications;
- 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;
- seek regulatory approval for EYSUVIS and INVELTYS outside of the United States;
- progress our current and any future preclinical development programs;
- conduct clinical trials and other development activities and/or seek marketing approval for any other product candidates;
- in-license or acquire the rights to other products, product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- integrate employees of Combangio;
- hire additional clinical, quality control, scientific, manufacturing, commercial and management personnel, including to support our operations;
- 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 and cash equivalents as of December 31, 2021, along with anticipated revenue from EYSUVIS and INVELTYS, will enable us to fund our operations, lease and debt service obligations, and capital expenditure requirements into the second quarter of 2023. 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 these products, and we may not achieve profitability. Our lead product candidate, KPI-012, is in the early stages of clinical development and all of our other research and development programs are in preclinical development and, accordingly, we do not expect to generate revenue from KPI-012 or any other product candidate for several years, if at all. Achieving and maintaining profitability will require us to be successful in a range of challenging activities, including:

- successfully commercializing and growing EYSUVIS and 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;
- successfully integrating Combangio into our business;
- timely filing of an IND for, and completing the clinical development of, KPI-012 for PCED and any other indications we determine to pursue;
- subject to obtaining favorable results from our planned clinical trials of KPI-012, applying for and obtaining marketing approval of KPI-012;
- successfully commercializing KPI-012, if approved;
- manufacturing at commercial scale, marketing, selling and distributing EYSUVIS, INVELTYS and, if approved, KPI-012;
- maintaining regulatory and marketing approvals for EYSUVIS and INVELTYS;
- discovering, developing and successfully seeking marketing approval and commercialization of any 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. Moreover, KPI-012 is in the early stages of clinical development and all of our other research and development programs are in preclinical development and, accordingly, we do not expect to generate revenue from KPI-012 or any other product candidate for several years, if at all.

In addition, our commercialization efforts have previously been hampered by the operational restrictions on our sales force from quarantines, travel restrictions and bans and other governmental restrictions related to the COVID-19 pandemic. As a result of these restrictions, we previously suspended our sales force from substantially all in-person interactions with physicians and were limited to conducting educational and promotional activities virtually. Commencing in the fourth quarter of 2020, our sales force resumed substantially all in-person interactions in the field, but to the extent we restrict, or are restricted from, in-person interactions with physicians, we may be limited to conducting educational and promotional activities virtually, which may continue to hamper our ability to market EYSUVIS and INVELTYS. In addition, government restrictions have at times led to moratoria on elective ocular surgeries in many jurisdictions, which had 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. In addition, the COVID-19 pandemic has generally had an adverse impact on the launch of pharmaceutical products, and we believe the pandemic has impacted, and may continue to impact, the launch of EYSUVIS. We also do not know the extent to which the COVID-19 pandemic will impact our development of KPI-012 or any other product candidates that we may develop. The extent of the impact of COVID-19 on our development and commercialization efforts will depend on the length and severity of this pandemic, including the extent there is any resurgence of the COVID-19 virus or 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 Loan Agreement may limit our ability to obtain additional debt financing. Under our Loan Agreement, we are also restricted from incurring future debt, granting liens, making investments, making acquisitions, distributing dividends on our common stock, making certain restricted payments and selling assets and making certain other uses of our cash, without the lenders' consent, subject in each case to certain exceptions.

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 again 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.

Recently Issued Accounting Pronouncements

From time to time the Financial Accounting Standards Board 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 accounting pronouncements 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 as of December 31, 2021 consisted primarily of cash equivalents which consisted of money market accounts that have contractual maturities of less than 90 days from the date of acquisition. Due to the short-term maturities of our cash equivalents, 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.

As of December 31, 2021, the aggregate principal amount outstanding under the Loan Agreement was $80.0 million, which bears interest at a floating rate equal to the greater of 30-day LIBOR and 0.11%, plus 7.89% per annum. An immediate 10% change in the 30-day LIBOR rate would not have a material impact on our operating results or cash flows. As of December 31, 2020, the aggregate principal amount outstanding under the Athyrium Credit Facility was $75.0 million, which bore interest at a fixed rate of 9.875% per annum. On May 4, 2021, we utilized substantially all of the proceeds from the tranche A term loan under the Loan Agreement to repay in full all outstanding amounts under the Athyrium Credit Facility.

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-36 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, 2021. 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, 2021, 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, 2021. 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, 2021, 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, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

Part III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2022 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 2022 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 2022 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 2022 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 2022 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
2.1#	Agreement and Plan of Merger, dated as of November 15, 2021, by and among Kala Pharmaceuticals, Inc., Ceres Merger Sub, Inc., Combangio, Inc. and, solely in its capacity as Combangio Equityholder Representative, Fortis Advisors LLC. (incorporated by reference to Exhibit 2.1 of the Registrant's current report on Form 8-K (File No. 001-38150) filed on November 15, 2021)
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 (incorporated by reference to Exhibit 4.2 to the Registrant's annual report on Form 10-K (File No. 001-38150) filed on February 25, 2021)
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)

Exhibit Number	Description of Exhibit
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)
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 10.2 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on August 5, 2021)
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 10.3 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on August 5, 2021)
10.18#*	Exclusive License Agreement, dated October 11, 2019, by and between Combangio, Inc. and The Board of Trustees of the Leland Stanford Junior University
10.19+	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)
10.20+	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)

Exhibit Number	Description of Exhibit
10.21+	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)
10.22+	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)
10.23+	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)
10.24+	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)
10.25+	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)
10.26†	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)
10.27#	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) (incorporated by reference to Exhibit 10.26 of the Registrant's annual report on Form 10-K (File No. 001-38150) filed on February 25, 2021)
10.28†	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)
10.29†	Commercial Supply Agreement, dated June 27, 2016, by and between the Registrant and Woodstock Sterile Solutions, Inc. (formerly known as 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)
10.30†	Amendment No. 1 to Commercial Supply Agreement, dated February 16, 2018, by and between the Registrant and Woodstock Sterile Solution, Inc. (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)
10.31#	Amendment No. 2 to Commercial Supply Agreement, dated March 27, 2020, by and between the Registrant and Woodstock Sterile Solution, Inc. (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)
10.32#	Amendment No. 3 to Commercial Supply Agreement, dated December 11, 2020, by and between the Registrant and Woodstock Sterile Solution, Inc. (incorporated by reference to Exhibit 10.31 of the Registrant's annual report on Form 10-K (File No. 001-38150) filed on February 25, 2021)
10.33*#	Amendment No. 4 to Commercial Supply Agreement, effective January 6, 2021, by and between the Registrant and Woodstock Sterile Solution, Inc.
10.34	Lease Termination Agreement, dated November 12, 2021, by and between the Registrant and Columbia Massachusetts Arsenal Office Properties, LLC. (incorporated by reference to Exhibit 10.1 of the Registrant's current report on Form 8-K (File No. 001-38150) filed on November 15, 2021)
10.35*	First Amendment to Lease Termination Agreement, dated December 22, 2021, by and between the Registrant and Columbia Massachusetts Arsenal Office Properties, LLC
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#	Loan and Security Agreement, dated May 4, 2021, by and among the Registrant and Oxford Finance LLC, as collateral agent and lender (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38150) filed on May 5, 2021)
10.38	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

Exhibit Number	Description of Exhibit
23.1*	Consent of Deloitte & Touche LLP
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: March 29, 2022

By: /s/ Mark Iwicki
Mark Iwicki
Chief Executive Officer 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	Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer)	March 29, 2022
/s/ Mary Reumuth Mary Reumuth	Chief Financial Officer (Principal Financial and Accounting Officer)	March 29, 2022
/s/ Mark Blumenkranz Mark Blumenkranz	Director	March 29, 2022
/s/ Gregory Grunberg Gregory Grunberg, M.D.	Director	March 29, 2022
/s/ Andrew I. Koven Andrew I. Koven	Director	March 29, 2022
/s/ C. Daniel Myers Daniel C. Myers	Director	March 29, 2022
/s/ Robert Paull Robert Paull	Director	March 29, 2022
/s/ Gregory Perry Gregory Perry	Director	March 29, 2022
/s/ Howard Rosen Howard Rosen	Director	March 29, 2022

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders 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 subsidiaries (the "Company") as of December 31, 2021 and 2020, 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, 2021 and 2020, 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
March 29, 2022

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

KALA PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share amounts)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 92,136	$ 77,264
Short-term investments	—	76,276
Short-term restricted cash	2,042	—
Accounts receivable, net	15,345	9,604
Inventory	8,639	5,229
Prepaid expenses and other current assets	6,204	3,006
Total current assets	124,366	171,379
Non-current assets:		
Property and equipment, net	2,722	3,166
Long-term inventory	9,578	6,219
Right-of-use assets	1,299	27,853
Restricted cash and other long-term assets	1,462	12,989
Total assets	$ 139,427	$ 221,606
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 4,899	$ 1,724
Accrued expenses and other current liabilities	20,986	18,971
Current portion of lease liabilities	711	1,530
Current portion of contingent consideration	3,817	—
Current portion of deferred purchase consideration	7,009	—
Total current liabilities	37,422	22,225
Long-term liabilities:		
Long-term lease liabilities	548	27,143
Long-term debt	78,929	72,243
Long-term contingent consideration	4,841	—
Long-term deferred purchase consideration	883	—
Total long-term liabilities	85,201	99,386
Total liabilities	122,623	121,611
Commitments and Contingencies (Note 17)		
Stockholders' equity:		
Common stock, $0.001 par value; 120,000,000 shares authorized as of December 31, 2021 and December 31, 2020; 65,500,275 and 58,915,375 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	66	59
Additional paid-in capital	559,126	499,715
Accumulated other comprehensive income	—	4
Accumulated deficit	(542,388)	(399,783)
Total stockholders' equity	16,804	99,995
Total liabilities and stockholders' equity	$ 139,427	$ 221,606

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,	
	2021	2020
Product revenues, net	$ 11,240	$ 6,362
Costs and expenses:		
Cost of product revenues	4,097	3,173
Selling, general and administrative	105,061	81,068
Research and development	11,515	18,352
Acquired in-process research and development	26,617	—
Gain on fair value remeasurement of deferred purchase consideration	(5,805)	—
Total costs and expenses	141,485	102,593
Loss from operations	(130,245)	(96,231)
Other income (expense):		
Interest and other income	104	493
Interest and other expense	(8,380)	(8,589)
Loss on extinguishment of debt	(5,395)	—
Gain on lease modification	1,311	—
Total interest and other expense	(12,360)	(8,096)
Net loss	$ (142,605)	$ (104,327)
Net loss per share—basic and diluted	$ (2.19)	$ (1.99)
Weighted average shares outstanding—basic and diluted	65,202,832	52,377,526
Net loss	$ (142,605)	$ (104,327)
Other comprehensive loss:		
Change in unrealized gains on investments	(4)	4
Total other comprehensive loss	(4)	4
Total comprehensive loss	$ (142,609)	$ (104,323)

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, 2019	36,086,254	$ 36	$ 325,112	$ —	$ (295,456)	$ 29,692
At the market offering, net of offering costs of $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 issuance cost and underwriting fees of $8,475	16,979,371	17	125,406	—	—	125,423
Issuance of common stock 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
At the market offering, net of offering costs $1,176	5,760,198	6	41,226	—	—	41,232
Exercise of stock options	88,888	—	248	—	—	248
Issuance of vested restricted stock units	460,090	1	—	—	—	1
Issuance of common stock under employee stock purchase plan	275,724	—	1,337	—	—	1,337
Stock-based compensation expense	—	—	16,600	—	—	16,600
Change in fair value of investments	—	—	—	(4)	—	(4)
Net loss	—	—	—	—	(142,605)	(142,605)
Balance as of December 31, 2021	65,500,275	$ 66	$ 559,126	$ —	$ (542,388)	$ 16,804

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,	
	2021	**2020**
Cash flows from operating activities:		
Net loss	$ (142,605)	$ (104,327)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation and amortization	975	912
Non-cash operating lease cost	1,335	1,928
Loss on extinguishment of debt	5,395	—
Gain on lease modification	(1,311)	—
Acquired in-process research and development	26,617	—
Gain on fair value remeasurement of deferred purchase consideration	(5,805)	—
Amortization of debt discount and other non-cash interest	1,519	1,059
Stock-based compensation	16,088	13,312
Amortization of discount on available-for-sale securities	22	(5)
Other non-cash charges	151	—
Change in operating assets and liabilities:		
Accounts receivable	(5,756)	1,959
Prepaid expenses and other current assets	(2,859)	818
Inventory	(6,257)	(2,368)
Accounts payable	3,231	(924)
Accrued expenses and other current liabilities	1,714	(1,763)
Lease liabilities and other long-term liabilities	(689)	(1,295)
Net cash used in operating activities	(108,235)	(90,694)
Cash flows from investing activities:		
Cash paid for acquisition of in-process research and development, net of cash acquired	(4,653)	—
Purchases of property and equipment and other assets	(886)	(1,942)
Proceeds from sale of property and equipment	92	—
Purchases of short-term investments	—	(113,592)
Proceeds from sales or maturities of short-term investments	76,250	37,325
Net cash provided by (used in) investing activities	70,803	(78,209)
Cash flows from financing activities:		
Proceeds from issuance of debt, net of debt issuance costs of $2,218	77,782	—
Payment of principal, prepayment premium and exit fee on debt	(78,010)	—
Proceeds from common stock offerings, net of offering costs	41,232	158,557
Payment of principal on finance lease	(35)	(32)
Proceeds from exercise of stock options and issuance of common stock under employee stock purchase plan	1,585	2,103
Net cash provided by financing activities	42,554	160,628
Net increase (decrease) in cash, cash equivalents and restricted cash:	5,122	(8,275)
Cash, cash equivalents and restricted cash at beginning of period	89,756	98,031
Cash, cash equivalents and restricted cash at end of period	$ 94,878	$ 89,756
Reconciliation of cash, cash equivalents and restricted cash:		
Cash, cash equivalents, and restricted cash at end of period	$ 94,878	$ 89,756
Less restricted cash (Notes 10 and 11)	(2,742)	(12,492)
Cash and cash equivalents at end of period	$ 92,136	$ 77,264
Non-cash investing and financing activities:		
Purchases of property and equipment in accounts payable and accrued expenses	$ 139	$ 130
Supplemental disclosure:		
Cash paid for interest	$ 6,837	$ 7,528
Right-of-use assets obtained in exchange of operating lease obligations	1,210	—

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 worldwide rights to a portfolio of innovative products and product candidates that include two marketed products utilizing its proprietary mucus penetrating particle drug delivery technology, which it refers to as its AMPPLIFY® technology, to address medical needs for the front of the eye. The Company's product candidates and programs include a proprietary regenerative biotherapy for severe ocular diseases and a pipeline of preclinical new chemical entities ("NCEs"), targeted to address front and back of the eye diseases.

The Company's 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 the Company's AMPPLIFY technology to loteprednol etabonate, a corticosteroid designed for ocular applications. The AMPPLIFY technology uses selectively-sized nanoparticles that each have a proprietary coating. The Company believes 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.

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 for its clinical-stage product candidate, KPI-012 for the treatment of persistent corneal epithelial defects ("PCED"), 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 NCE preclinical development programs targeted to address both front and back of the eye diseases. These preclinical development programs include KPI-287, its receptor Tyrosine Kinase Inhibitor and its selective glucocorticoid receptor modulators ("SEGRMs").

KPI-287 is designed to inhibit the vascular endothelial growth factor and platelet derived growth factor pathways, and is administered by suprachoroidal injection for the treatment of retinal diseases, including wet age-related macular degeneration, diabetic macular edema, and retinal vein occlusion. SEGRMs are a novel class of therapies designed to modify the downstream activity of the glucocorticoid receptors to exhibit the anti-inflammatory and immunomodulatory properties of the corticosteroid class of therapies while markedly reducing their associated side effects, which we are developing for the treatment of inflammatory diseases.

Combangio, Inc. Acquisition—On November 15, 2021, the Company and its newly formed, direct wholly owned subsidiary, Ceres Merger Sub, Inc. (the "Merger Subsidiary"), entered into an Agreement and Plan of Merger (the "Merger Agreement") with Combangio, Inc. ("Combangio") and Fortis Advisors LLC, solely in its capacity as Combangio Equityholder Representative in connection with the Merger Agreement, pursuant to which on November 15, 2021, the Merger Subsidiary merged with and into Combangio with Combangio surviving such merger and becoming a direct wholly owned subsidiary of the Company (the "Acquisition"). Combangio is a clinical-stage biotechnology company focused on developing regenerative biotherapeutics for severe ocular diseases based on mesenchymal stem cell

("MSCs") secretomes, including, its lead product candidate, CMB-012 for the treatment of PCED. Following the Acquisition, the Company refers to CMB-012 as KPI-012.

Refer to Note 3 for further discussion of the Acquisition.

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"). In connection with the filing of the 2018 Shelf Registration, the Company entered into a sales agreement (the "2018 Sales Agreement") with Jefferies, LLC ("Jefferies") 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. Through the first quarter of 2020, the Company issued an aggregate of 4,945,605 shares of its common stock under the ATM Offering, resulting in net proceeds to the Company of $25,605. 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 (the "2020 Offering Shares") 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, which expired in August 2021, the Company issued an aggregate of 30,549,976 shares of common stock, including under the ATM Offering, resulting in aggregate gross proceeds of $231,666.

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. During the year ended December 31, 2021, the Company issued and sold an additional 5,760,198 shares of its common stock under its ATM Offering resulting in net proceeds of $41,232. As of December 31, 2021, there were $11,344 of shares of common stock remaining under the ATM Offering, and excluding the shares of common stock that may be offered under the ATM Offering, there was approximately $275,000 of securities available to be issued under the 2020 Shelf Registration.

Refer to Note 11 for a discussion of debt financing activity.

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

COVID-19 – In order to safeguard the health of its employees from the ongoing novel coronavirus pandemic, or COVID-19, 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. The Company previously suspended its sales force from substantially all in-person interactions with physicians and was limited to conducting educational and promotional activities virtually. Commencing in the fourth quarter of 2020, the Company's sales force resumed substantially all in-person interactions in the field, but if the Company suspends all or some in-person interactions with physicians in the future, or to the extent physicians limit in-person interactions, the Company may be limited to conducting educational and promotional activities virtually, which may continue to hamper its ability to market and commercialize EYSUVIS and INVELTYS.

In addition, government restrictions have at times led to moratoria on elective ocular surgeries in many jurisdictions, which had 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. In addition, the COVID-19 pandemic has generally had an adverse impact on the launch of pharmaceutical products, and the Company believes the pandemic has impacted, and may continue to impact, the launch of EYSUVIS. The Company also does not know the extent to which the COVID-19 pandemic will impact its development of KPI-012 or any other product candidate we develop. The extent of the impact of the COVID-19 pandemic on the Company's commercialization efforts of EYSUVIS and INVELTYS, its clinical development of KPI-012 and its preclinical developments programs, and its operational and financial performance will depend on certain developments, including the length and severity of this pandemic, the timing and extent of any resurgence of the COVID-19 virus or any variant strains of the virus, the availability and effectiveness of vaccines, and the impact of the foregoing 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 subsidiaries, Kala Pharmaceuticals Security Corporation, which is a Massachusetts subsidiary created to buy, sell and hold securities, and Combangio, Inc. 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 $142,605 and $104,327, for the years ended December 31, 2021 and 2020, respectively, and used cash in operations of $108,235 and $90,694, in the years ended December 31, 2021 and 2020, 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 and the Loan and Security Agreement with Oxford Finance LLC, (the "Loan Agreement"), convertible promissory notes 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.

The Company expects that its cash and cash equivalents as of December 31, 2021, together with anticipated net revenue from sales of EYSUVIS and 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. The Company believes the COVID-19 pandemic has impacted and may continue to impact anticipated net revenues in the future. 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, contingent consideration and acquired in-process research and development ("IPR&D"), 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.

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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, 2021 and 2020:

	Trade Discounts, Allowances and Chargebacks (1)	Product Returns (2)	Rebates and Incentives (3)
Balance as of January 1, 2020	$ 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
Provision related to current period sales	9,443	973	48,007
Changes in estimate related to prior period sales	44	1,338	(646)
Credit/payments made	(7,972)	(1,771)	(40,985)
Balance as of December 31, 2021	$ 2,672	$ 1,140	$ 11,280

(1) Trade discounts, allowances and chargebacks include fees for distribution service fees, prompt pay and other discounts, and chargebacks. Estimated 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) Estimated 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. Estimated 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, 2021 and 2020, 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.

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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, 2021 or December 31, 2020. The Company recorded an allowance of $2,672 and $1,157 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, 2021 and December 31, 2020, respectively.

Acquired IPR&D—A key provision within ASC 805*, Business Combinations,* is the single or similar asset threshold. When substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets, the acquired set is not a business. In evaluating the Acquisition, the Company concluded that substantially all of the fair value of the gross assets acquired was concentrated in a single asset, KPI-012, and the Company accounted for the transaction as an asset acquisition.

Acquired IPR&D expense consists of the initial up-front payments and any future milestone payments that are recorded at fair value incurred in connection with the acquisition or licensing of product candidates that do not meet the definition of a business. Acquired IPR&D is expensed immediately in the period in which it is incurred. For the year ended December 31, 2021, the Company recorded an expense for the IPR&D acquired in the Acquisition of $26,617 as there is no alternative future use.

Contingent Consideration—In addition to upfront consideration and Deferred Purchase Consideration (as defined below) (see Note 3), the Company's asset acquisitions may also include contingent consideration payments to be made for future milestone events or royalties on net sales of future products. The Company assesses whether such contingent consideration is required to be recorded at fair value on the date of the acquisition and subsequently remeasured to fair value at each reporting date. Contingent consideration payments in an asset acquisition not required to be accounted for at fair value are recognized when the contingency is resolved, and the consideration is paid or becomes payable. Changes to contingent consideration obligations can result from changes to discount rates, accretion of the liability due to the passage of time, changes in our estimates of the likelihood or timing of achieving certain milestones. Any changes in the fair value of these contingent consideration liabilities are included in loss from operations in the consolidated statements of operations and comprehensive loss.

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 recorded the cost of product revenues related to INVELTYS as research and development expenses prior to regulatory approval and recorded the 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, 2021 and 2020. These Customers comprised 44%, 31% and 24% of the accounts receivable balance, respectively, as of December 31, 2021 and 39%, 33% and 25% of the accounts receivable balance, respectively, as of December 31, 2020. To date, losses with respect to the collection of the Company's accounts receivable have been *de minimis* and the Company believes that its entire accounts receivable balances is collectible as of December 31, 2021. The same three Customers comprised 10% or more of the Company's revenue during the years ended December 31, 2021 and 2020. These Customers comprised 48%, 29% and 22% of revenue, respectively, during the year ended December 31, 2021 and 40%, 29% and 28% of revenue, respectively, during the year ended December 31, 2020. 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, 2021, the Company had short-term restricted cash of $2,042, which represented cash held to serve as collateral for its facility lease in Watertown, Massachusetts (see Note 10) and long-term restricted cash of $700 which primarily represented cash held to serve as collateral for its vehicle fleet lease (see Note 10). As of December 31, 2020, the Company had long-term restricted cash of $12,492, which represented cash held to satisfy its prior financial covenant (see Note 11) and serve as collateral for the Company's vehicle fleet lease, credit cards and its facility lease in Watertown, Massachusetts (see Note 10).

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 years ended December 31, 2021 or 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.

The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, including quality control and assurance reserves for defective inventories, and also writes-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 the Company's 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 based on the Company's forecasted expectations.

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 had 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

resulted 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.

Advertising Costs—Advertising costs are expensed as incurred. For the years ended December 31, 2021 and 2020, advertising expenses were $11,962 and $7,593, respectively, and are included in selling, general and administrative expenses in the accompanying 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 year ended December 31, 2021, impairment charges recorded were *de minimis*. For the year ended December 31, 2020, 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.

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 in addition to its own historical volatility 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.

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.

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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, 2021 and 2020. (See Note 15).

Recent Accounting Pronouncements

In June 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("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. The Company is currently evaluating the impact of the adoption of ASU 2016-13, beginning January 1, 2023, on its consolidated financial statements. The Company does not expect that the adoption of this standard will have a material impact on its consolidated financial statements.

Note 3: Acquisition of Combangio, Inc.

In connection with the closing of the Acquisition on November 15, 2021 (the "Closing"), the Company made an upfront payment of an aggregate of $5,000 in cash to former Combangio stockholders and other equityholders (the "Combangio Equityholders"), subject to customary adjustments, and agreed to issue an aggregate of 7,788,637 shares (the "Deferred Purchase Consideration") of the Company's common stock to the Combangio Equityholders with an aggregate value of approximately $16,123, consisting of (i) an aggregate of 6,815,072 shares of common stock issued on January 3, 2022 (the "Upfront Shares") and (ii) an aggregate of 973,565 shares of common stock that have been held back by the Company and will be issuable subject to the terms of the Merger Agreement to the Combangio Equityholders (the "Holdback Shares") on the date that is fifteen months after the Closing (the "Escrow Release Date). The aggregate value of the Deferred Purchase Consideration was calculated using the closing price of the Company's common stock on the Nasdaq Global Select Market on November 12, 2021, the last trading day prior to the Closing.

In addition, pursuant to the Merger Agreement, the Combangio Equityholders, in the aggregate and subject to the terms and conditions of the Merger Agreement, will also be entitled to receive from the Company the following contingent consideration (the "Contingent Consideration"):

- up to $105,000 in contingent milestone consideration, of which (i) $2,300 would become payable in cash and $2,700 would be payable in shares of the Company's common stock upon the first patient dosed with any product candidate whose active ingredient comprises one or more biological factors secreted by MSCs or their progenitors, including KPI-012 (the "Product Candidate") in a Phase 2 clinical trial (the "Dosing Milestone"), (ii) $2,300 would become payable in cash and $2,700 would be payable in shares of the Company's common stock upon the first patient dosed with a Product Candidate in a pivotal clinical trial, (iii) $12,500 would become payable (with up to $6,250 payable, at the option of the Company, in shares of the Company's common stock and the remainder in cash) upon regulatory approval by the U.S. Food and Drug Administration (the "FDA") of marketing and sale of a Product Candidate in the United States, subject to certain specified

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reductions; (iv) $17,500 would become payable (with up to $8,750 payable, at the option of the Company, in shares of the Company's common stock and the remainder in cash) upon the first commercial sale of a Product Candidate in the United States, subject to certain specified reductions, and (v) an aggregate of up to $65,000 would become payable in cash upon the achievement of specified sales milestones;

- tiered cash royalties at percentage rates in the mid-to-high single digits payable on annual net sales of all Product Candidates; and

- a cash payment at a percentage rate in the high single digits of all income, including earnout payments, received by the Company or any of its affiliates from a product license granted by the Company to a third party to sell or otherwise commercialize the Product Candidate in countries where neither the Company nor its affiliates conduct sales of such Product Candidate, subject to certain exceptions set forth in the Merger Agreement.

The portion of any payment of Contingent Consideration payable in shares of the Company's common stock is referred to herein as "Contingent Stock Consideration" and the portion of any payment of Contingent Consideration payable in cash is referred to herein as "Contingent Cash Consideration".

If the issuance of the Deferred Purchase Consideration or any Contingent Stock Consideration would result in the aggregate number of shares of the Company's common stock issued under the Merger Agreement equaling or exceeding 19.9% of the total number of shares of the Company's common stock issued and outstanding immediately prior to the Closing (the "Share Cap"), then the Company will be required to pay the portion of the Deferred Purchase Consideration or any Contingent Stock Consideration in excess of the Share Cap in cash. If the aggregate amount of Contingent Cash Consideration payable in any calendar year (after giving effect to the Share Cap) exceeds $2,500 (the "Excess Cash Cap"), such excess portion ("Carry Forward Contingent Cash Consideration") will be carried forward and, subject to application of the Excess Cash Cap in the following calendar year, become payable on the first business day of the following calendar year. Any Carry Forward Contingent Cash Consideration outstanding on June 1, 2026 is payable in full on June 1, 2026.

For accounting purposes, the transaction was accounted for as an asset acquisition, as substantially all of the fair value of the gross assets acquired was concentrated in a single asset, KPI-012.

Pursuant to the Merger Agreement, following the Acquisition, the Company owns 100% of the outstanding common stock of Combangio. The cost of the Acquisition, which represents the total consideration transferred to Combangio stockholders in the Acquisition consists of the following:

Cash	$	3,821
Transaction expenses		901
Deferred Purchase Consideration (1)		13,698
Contingent consideration (2)		8,658
Total consideration	$	27,078

(1) Deferred Purchase Consideration consists of 6,815,072 Upfront Shares issued on January 3, 2022 recorded at $1.79 per share and 973,565 Holdback Shares, which will not be issued until the Escrow Release Date of February 15, 2023 recorded at $1.58 per share based on the transaction date fair value.

(2) Contingent consideration consists of the fair value of certain milestone payments. The total potential maximum payout for the milestone payments, which are recorded at fair value is $40,000 and such milestone payments and are contingent upon the achievement of specified development and regulatory milestones. Additionally, pursuant to the Merger Agreement, the Company could trigger potential future sales-based milestone payments of up to $65,000. Because the achievement of these sales-based milestones related to KPI-012 was not considered probable as of December 31, 2021, such contingencies have not been recorded in the Company's financial statements.

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The following is the allocation of the purchase consideration based on the fair value of assets acquired and the liabilities assumed by the Company in the Acquisition:

Cash and cash equivalents	$	69
Prepaid expense and other current assets		121
Property and equipment		38
Other assets		46
Workforce		307
Acquired in-process research and development		26,617
Liabilities		(120)
Total consideration	$	27,078

Note 4: Fair Value of Financial Instruments

The Company from time to time 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 as of December 31, 2021 consisted primarily of cash equivalents and contingent consideration. The Company's financial instruments as of December 31, 2020 consisted primarily of cash equivalents and short-term investments in money market funds and short-term securities. Cash equivalents, short-term investments and contingent consideration are reported at their respective fair values on the Company's consolidated balance sheets. See Note 5, "Investments" for additional information.

As discussed in Notes 2 and 3, the Company acquired Combangio in November 2021 and in connection with the closing of the Acquisition, the Company agreed to issue Deferred Purchase Consideration for which the Company has established liabilities for these considerations. The Deferred Purchase Consideration related to the Acquisition is measured at fair value each reporting period using Level 3 unobservable inputs. The fair value of the Deferred Purchase Consideration was based on the fair value of the underlying stock and a discount for lack of marketability. Changes in these estimates and assumptions could have a significant impact on the fair value of the Deferred Purchase Consideration. Any change in the fair value of the Deferred Purchase Consideration is included in loss from operations in the consolidated statements of operations and comprehensive loss. During the year ended December 31, 2021, the change in the fair value of the Deferred Purchase Consideration was $5,805 primarily due to the change in the fair value of the underlying stock price and is recognized as the gain on fair value remeasurement of deferred purchase consideration in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2021.

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Additionally, the purchase price of the Acquisition included potential future payments that are contingent upon the achievement of specified development, regulatory and commercialization milestones and are required to recorded at fair value. Contingent consideration liabilities related to acquisitions are measured at fair value each reporting period using Level 3 unobservable inputs. The fair values of the contingent consideration liabilities were based on a probability-adjusted discounted cash flow calculation using Level 3 fair value measurements. Changes in these estimates and assumptions could have a significant impact on the fair value of the contingent consideration liabilities. Any changes in the fair value of these contingent consideration liabilities are included in loss from operations in the consolidated statements of operations and comprehensive loss. During the year ended December 31, 2021, the change in the fair value of the contingent consideration liabilities was *de minimis*.

The following table sets forth the fair value of the Company's financial instruments by level within the fair value hierarchy as of December 31, 2021 and 2020:

	December 31, 2021			
	Fair Value	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$ 86,135	$ 86,135	$ —	$ —
Total Assets	$ 86,135	$ 86,135	$ —	$ —
Liabilities:				
Deferred purchase consideration	$ 7,892	$ —	$ —	$ 7,892
Contingent consideration	8,658	—	—	8,658
Total Liabilities	$ 16,550	$ —	$ —	$ 16,550

	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	$ —	$ —

The following tables summarizes quantitative information and assumptions pertaining to the fair value measurement of the Level 3 inputs as of December 31, 2021:

Financial Instrument	Fair Value at December 31, 2021	Valuation Technique	Unobservable Input	Range (Average)
Deferred purchase consideration	$ 7,892	Option pricing model	Discount for lack of marketability	15.0% - 25.0% (20.0%)
Contingent consideration	8,658	Probability-adjusted discounted cash flow model	Period of expected milestone achievement	2022 - 2027 (2025)
			Probabilities of achievement	18.9% - 90.0% (42.5%)
			Discount rate	10.3%
			Discount for lack of marketability	12.0%

During the year ended December 31, 2021 and 2020 there were no transfers between Level 1, Level 2, and Level 3.

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 11) 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.

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Note 5: Investments

The Company held no short-term investments as of December 31, 2021. 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.

Note 6: Inventory

Inventory consists of the following:

	December 31, 2021	December 31, 2020
Raw materials	$ 1,328	$ 801
Work in progress	9,799	6,437
Finished goods	7,090	4,210
Total inventory	$ 18,217	$ 11,448

As of December 31, 2021, the Company had $8,639 of current inventory and $9,578 of long-term inventory. As of December 31, 2020, the Company had $5,229 of current inventory and $6,219 of long-term inventory.

Note 7: Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets, consists of the following:

	December 31, 2021	December 31, 2020
Non-trade receivables	$ 2,110	$ 250
Insurance	1,307	1,201
Deposits	911	606
Other	1,876	949
Prepaid expenses and other current assets	$ 6,204	$ 3,006

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Note 8: Property and Equipment, Net

Property and equipment, net, consists of the following:

	December 31, 2021	December 31, 2020
Equipment	$ 2,647	$ 2,652
Computer hardware and software	1,184	1,108
Furniture and office equipment	37	1,144
Leasehold improvements	—	356
Construction in progress	1,715	1,330
Property and equipment—at cost	5,583	6,590
Less: Accumulated depreciation	(2,861)	(3,424)
Property and equipment—net	$ 2,722	$ 3,166

Depreciation expense for the years ended December 31, 2021 and 2020 was $933 and $908, respectively.

In connection with the lease termination agreement entered into in November 2021 to accelerate the lease termination of the Company's Watertown Lease (as defined below) (see Note 10), the Company disposed of and sold certain property and equipment. Additionally, in conjunction with the termination of the Watertown Lease, the Company had $211 of assets held for sale as of December 31, 2021 included within prepaid expenses and other current assets on the consolidated balance sheet, which were subsequently sold in the first quarter of 2022.

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Note 9: Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2021	December 31, 2020
Accrued revenue reserves (1)	$ 10,300	$ 5,224
Compensation and benefits	6,324	9,676
Commercial costs	2,134	2,103
Professional services	881	926
Contract manufacturing	396	336
Development costs	127	154
Other	824	552
Accrued expenses	$ 20,986	$ 18,971

(1) As of December 31, 2021 and 2020, $2,120 and $280 of additional revenue reserves were in accounts payable, respectively.

Note 10: Lease

Operating leases

Terminated Watertown Lease

On February 28, 2018, the Company entered into a lease agreement with 480 Arsenal Group LLC 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 was eight years with an option to extend for an additional five years, which were 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.

On November 12, 2021, the Company entered into the Lease Termination Agreement with the landlord of the Watertown Lease, which Lease Termination Agreement was amended on December 22, 2021, modifying the lease to accelerate the lease termination date to January 11, 2022 (the "Lease Termination Date"). Under the terms of the Lease Termination Agreement, the Company was entitled to receive a payment of $2,000 due from the landlord in January 2022, which was collected after December 31, 2021. The Company was obligated to make rent payments outlined in the lease agreement until the Lease Termination Date.

In connection with the signing of the Lease Termination Agreement, the Company remeasured the lease liability and right-of-use asset and recognized a gain of approximately $1,311, which is included in gain on lease modification in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2021. Additionally, pursuant to the Lease Termination Agreement, $2,042 of restricted cash was released on the Lease Termination Date that was pledged as collateral under a letter of credit with cash on deposit required by the terminated lease. The restricted cash was included within short-term restricted cash on the consolidated balance sheet as of December 31, 2021 and included within restricted cash and other long-term assets on the consolidated balance sheet as of December 31, 2020.

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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, 2021 and December 31, 2020. The Vehicle Fleet Lease has an expected term of three years, which commenced upon the delivery of the vehicles in March 2019.

During the year ended December 31, 2021, the Company modified the Vehicle Fleet Lease to add 54 additional vehicles to the fleet. The new component of the lease has an expected term of approximately three years, which commenced upon the delivery of the additional vehicles in March 2021.

The components of lease expense and related cash flows were as follows:

	Year Ended December 31,	
	2021	2020
Lease cost		
Operating lease cost	$ 3,822	$ 4,741
Short-term lease cost	20	—
Variable lease cost	2,270	1,848
Total lease cost	$ 6,112	$ 6,589
Operating cash outflows from operating leases	$ 7,350	$ 5,981

Maturities of lease liability due under these operating lease agreements as of December 31, 2021 are as follows:

Years Ending December 31,	
2022	$ 727
2023	406
2024	141
Total minimum lease payments	1,274
Less: amount representing interest	(15)
Present value of lease liabilities	$ 1,259

The weighted average remaining lease term and weighted average discount rate of operating leases are as follows:

	December 31, 2021	December 31, 2020
Weighted average remaining lease term	2.4 years	10.3 years
Weighted average discount rate	2.6%	9.8%

Note 11: Debt

Athyrium Credit Facility

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 which bore interest at a rate of 9.875% per annum, with quarterly, interest-only payments until the fourth anniversary of the Term Loan A. The maturity date of the Athyrium Credit Facility was October 1, 2024, the six-year anniversary of the close.

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.

As of December 31, 2020, the unpaid principal balance under the Athyrium Credit Facility was $75,000 and the unamortized debt discount was $3,088. On May 4, 2021, the Company repaid all amounts owed under the Athyrium Credit Facility and terminated all commitments by Athyrium to extend further credit thereunder and all guarantees and security interests granted by the Company to the lenders thereunder. In connection with the termination of the Athyrium Credit Facility, the Company paid to the lenders a prepayment premium of $2,250 and an exit fee of $750. The transaction resulted in a loss on extinguishment of debt of $5,395, consisting of the prepayment premium, the unamortized debt discount and issuance costs and the unaccreted exit fee. Additionally, the Company released $10,000 of restricted cash previously recorded to comply with a financial covenant required by the Athyrium Credit Facility.

Oxford Finance Loan and Security Agreement

On May 4, 2021 (the "Closing Date"), the Company entered into a Loan and Security Agreement (the "Loan Agreement") with Oxford Finance LLC, in its capacity as lender (in such capacity, the "Lender"), and in its capacity as collateral agent (in such capacity, the "Agent"), pursuant to which a term loan of up to an aggregate principal amount of $125,000 is available to the Company, consisting of (i) a tranche A term loan that was disbursed on the Closing Date in the aggregate principal amount of $80,000; (ii) a contingent tranche B term loan in the aggregate principal amount of $20,000 available to the Company through June 30, 2023 and within 90 days of the Company achieving trailing 6-month product revenue equal to or greater than $75,000, subject to certain other terms and conditions; and (iii) a contingent tranche C term loan in the aggregate principal amount of $25,000 available to the Company through December 31, 2023 and within 90 days of the Company achieving trailing 6-month product revenue equal to or greater than $100,000, subject to certain other terms and conditions. The Company utilized substantially all of the proceeds from the tranche A term loan to repay the Athyrium Credit Facility (as more fully described above).

The term loans bear interest at a floating rate equal to the greater of (i) 30-day LIBOR and (ii) 0.11%, plus 7.89%. The Loan Agreement provides for interest-only payments until December 1, 2024 if neither the tranche B term loan nor the tranche C term loan are made, and until June 1, 2025 if either the tranche B term loan or the tranche C term loan is made (the "Amortization Date"). The aggregate outstanding principal balance of the term loans are required to be repaid in monthly installments starting on the Amortization Date based on a repayment schedule equal to (i) 18 months if neither the tranche B term loan nor the tranche C term loan is made and (ii) 12 months if either the tranche B term loan or the tranche C term loan is made. All unpaid principal and accrued and unpaid interest with respect to each term loan is due and payable in full on May 1, 2026 (the "Maturity Date").

The Company paid a facility fee of $400 on the Closing Date and has agreed to pay a facility fee of $100 upon closing of the tranche B term loan and a $125 facility fee upon the closing of the tranche C term loan. The Company will be required to make a final payment fee of 7.00% of the original principal amount of any funded term loan payable on the earlier of (i) the prepayment of the term loan in full or (ii) the Maturity Date. At the Company's option, the Company may elect to prepay all, but not less than all, of the outstanding loans, subject to a prepayment fee equal to the following percentage of the principal amount being prepaid: 3.00% if an advance is prepaid during the first 12 months following

the applicable advance date, 2.00% if an advance is prepaid after 12 months but prior to 24 months following the applicable advance date, and 1.00% if an advance is prepaid any time after 24 months following the applicable advance date but prior to the Maturity Date.

In connection with its entry into the Loan Agreement, the Company granted the Agent a security interest in substantially all of the Company's personal property owned or later acquired, including intellectual property. The Loan Agreement also contains customary representations and warranties and affirmative and negative covenants, as well as customary events of default. Certain of the customary negative covenants limit the ability of the Company and certain of its subsidiaries, among other things, to incur future debt, grant liens, make investments, make acquisitions, distribute dividends, make certain restricted payments and sell assets, subject in each case to certain exceptions.

The Loan Agreement includes features requiring (i) additional interest rate upon an event of default accrued at an additional 5%, and (ii) 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, 2021. 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 condensed consolidated statements of operations and comprehensive loss.

In addition, in connection with the Loan Agreement, the Company paid certain fees to the Lender and other third-party service providers. The fees paid to the Lender were recorded as a debt discount while the fees paid to other third-party service providers were recorded as debt issuance cost. These costs were amortized using the effective interest method over the term of the Loan Agreement. The amortization of debt discount and debt issuance cost is included in interest expense within the condensed consolidated statements of operations and comprehensive loss. As of December 31, 2021, the effective interest rate was 10.41%, 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, 2021, the Company recognized interest expense of $7,446 for the Loan Agreement and the Athyrium Credit Facility. This consisted of amortization of debt discount of $613 and the contractual coupon interest expense of $6,833. During the year ended December 31, 2020, the Company recognized interest expense of $8,440 for the Athyrium Credit Facility. This consisted of amortization of debt discount of $910 and the contractual coupon interest expense of $7,530.

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The components of the carrying value of the debt as of December 31, 2021 and December 31, 2020 are detailed below:

	December 31, 2021	December 31, 2020
Principal loan balance	$ 80,000	$ 75,000
Unamortized debt discount and issuance cost	(1,927)	(3,088)
Cumulative accretion of exit fee	856	331
Long-term debt, net	$ 78,929	$ 72,243

The annual principal payments due under the Loan Agreement as of December 31, 2021 were as follows:

Years Ending December 31,	
2022	$ —
2023	—
2024	4,445
2025	53,333
2026	22,222
Total	$ 80,000

Note 12: 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 11.

The following table summarizes the common stock warrants outstanding as of December 31, 2021 and 2020, each exercisable into the number of shares of common stock set forth below as of the specified dates:

				Shares Exercisable at	
Issued	Exercise Price	Expiration Date	Exercisable From	December 31, 2021	December 31, 2020
2013	$ 7.50	April 2021	July 2017	—	33,333
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
				215,172	248,505

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Note 13: 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, 2021 and 2020. There was no preferred stock outstanding as of December 31, 2021 and 2020.

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, 2021 and 2020. The Company had 65,500,275 and 58,915,375 shares of common stock issued and outstanding as of December 31, 2021 and 2020, 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.

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.

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Reserved Shares

As of December 31, 2021 and 2020, 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, upon the vesting of RSUs and PSUs and upon the issuance of Upfront Shares and Holdback Shares in connection with the Acquisition as follows (see Note 14):

	December 31, 2021	December 31, 2020
Warrant rights to acquire common stock	215,172	248,505
ESPP	798,201	484,772
Outstanding inducement stock option awards	1,291,909	945,842
2009 Plan	2,142,661	2,251,570
2017 Plan	9,734,830	7,813,784
Deferred Purchase Consideration	7,788,637	—
Total	21,971,410	11,744,473

Note 14: 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, 2021, there were 2,266,601 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 2,142,661 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, 2021 and December 31, 2020, the Company granted non-statutory stock options to purchase an aggregate of 649,400 shares and 350,800 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

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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).

A summary of option activity for employee awards under the 2009 Plan, the 2017 Plan and inducement grants for the year ended December 31, 2021 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, 2021	8,745,127	$ 7.03	7.3	$ 16,275
Granted	2,239,664	5.66		
Exercised	(88,888)	2.79		
Forfeited	(894,973)	6.92		
Outstanding as of December 31, 2021	10,000,930	$ 6.77	6.4	$ 14
Vested or expected to vest as of December 31, 2021	10,000,930	$ 6.77	6.4	$ 14
Options exercisable as of December 31, 2021	6,826,887	$ 7.49	5.5	$ 14

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, 2021 and 2020 are as follows:

	Year Ended December 31,	
	2021	2020
Expected volatility	72.7% – 74.2%	79.6% – 82.5%
Risk-free interest rate	0.50% – 1.39%	0.37% – 1.73%
Expected dividend yield	0%	0%
Expected term (in years)	5.13 – 6.10	5.91 – 6.08

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 the Company as well as the volatility of comparable companies with publicly available share prices. The impact of forfeitures on compensation expense is recorded as they occur.

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The weighted average grant-date fair value of options granted during the years ended December 31, 2021 and 2020, was $3.63 and $3.20, 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, 2021, there was $10,408 of unrecognized compensation cost related to the stock options granted, which is expected to be expensed over a weighted-average period of 2.40 years. Stock-based compensation expense was classified in the consolidated statements of operations and comprehensive loss as follows:

	Year Ended December 31,	
	2021	2020
Cost of product revenues	$ 169	$ 92
Research and development	3,145	3,083
Selling, general and administrative	12,774	10,137
Total	$ 16,088	$ 13,312

Stock-based compensation costs capitalized into inventory totaled $1,157 and $888 for the years ended December 31, 2021 and 2020, 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 $248 and $1,087 during the years ended December 31, 2021 and 2020, respectively. The total intrinsic value of options exercised for the year ended December 31, 2021 and 2020, was $406 and $2,124, 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. In 2020, 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 vested upon the date of the 2021 Annual Meeting of Stockholders. In 2020, 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 not all of the awards have vested as of December 31, 2021.

In 2021, the Company issued 431,333 RSUs to certain executives and other employees which will vest no sooner than one-third per year over three years on the anniversary of the date of grant as well as 125,000 RSUs to members of the Board which will vest upon the earlier of the first anniversary of the 2021 Annual Meeting of Stockholders or the date of the 2022 Annual Meeting of Stockholders.

As of December 31, 2021, a total of 813,869 RSUs and PSUs were unvested and outstanding, which results in unrecognized stock-based compensation of $3,291 to be recognized as stock-based compensation expense over the remaining weighted-average vesting period of 1.27 years.

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A summary of activity for RSUs and PSUs for the year ended December 31, 2021 is as follows:

	Shares	Weighted Average Grant Date Fair Value
Unvested and outstanding balance as of January 1, 2021	942,222	$ 11.70
Changes during the period:		
Granted	556,333	6.51
Vested	(548,090)	$ 11.35
Forfeited	(136,596)	$ 9.01
Unvested and outstanding balance as of December 31, 2021	813,869	$ 8.84
Vested and deferred balance as of December 31, 2021	88,000	

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, 2021, employees of the Company purchased an aggregate of 275,724 shares under the ESPP. During the year ended December 31, 2020, employees of the Company purchased an aggregate of 314,397 shares under the ESPP.

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Note 15: Loss Per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
Numerator:		
Net loss attributable to common stockholders	$ (142,605)	$ (104,327)
Denominator:		
Weighted-average common shares outstanding, basic and diluted (1)	65,202,832	52,377,526
Net loss per share attributable to common stockholders, basic and diluted	$ (2.19)	$ (1.99)

(1) Included in the weighted-average common shares outstanding, basic and diluted for the year ended December 31, 2021 is an aggregate of 6,815,072 shares of common stock issued to Combangio Equityholders on January 3, 2022 and an aggregate of 973,565 shares of common stock that have been held back by the Company and will be issuable subject to the terms of the Merger Agreement to the Combangio Equityholders on the Escrow Release Date of February 15, 2023.

The following potential common stock equivalents, presented based on amounts outstanding at each period end, were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2021	2020
Options to purchase shares of common stock	10,000,930	8,745,127
Unvested RSUs and PSUs	813,869	942,222
Unexercised warrants	215,172	248,505
	11,029,971	9,935,854

Note 16: Income Taxes

The Company has had no income tax expense due to operating losses incurred for the years ended December 31, 2021 and 2020. 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.

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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,	
	2021	2020
Federal statutory income tax rate	21.0 %	21.0 %
Effect of:		
Change in valuation allowance	(23.0)	(22.2)
Acquired in-process research and development	(3.9)	—
Stock-based compensation	(1.3)	(0.9)
State income taxes, net of federal benefit	4.8	1.2
Losses limited by Section 382	1.3	—
Research and development tax credits	0.5	0.9
Other	0.6	—
Effective income tax rate	— %	— %

Net deferred tax assets as of December 31, 2021 and 2020 consisted of the following:

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 102,935	$ 67,368
Stock-based compensation	8,408	7,413
Capitalized research and development and start-up expenditures	4,615	5,258
Research and development tax credit carryforwards	3,591	2,398
Rebates, incentives, trade discounts and allowances	3,334	2,177
Lease liabilities	321	8,152
Other	1,260	2,609
Total deferred tax assets	$ 124,464	$ 95,375
Deferred tax liabilities:		
Right-of-use assets	(331)	(7,810)
Total deferred tax liabilities	$ (331)	$ (7,810)
Valuation allowance	$ (124,133)	$ (87,565)
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, 2021 and 2020. The valuation allowance increased by $36,568 and $17,492 during the years ended December 31, 2021 and 2020, respectively, 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, 2021 and 2020, the Company had federal net operating loss carryforwards of $364,425 and $243,155, respectively, which may be available to offset future federal tax liabilities and expire at various dates beginning in 2030. As of December 31, 2021 and 2020, the Company had state net operating loss carryforwards of $352,863 and $214,989, respectively, which may be available to offset future state income tax liabilities and expire at various dates beginning in 2030. As of December 31, 2021 and 2020, the Company also had federal and state research

and development credit carryforwards of approximately $3,591 and $2,398, respectively, which begin to expire in 2040 (federal) and 2035 (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, which limitation is reflected in the numbers presented above.

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.

As of December 31, 2021 and 2020 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, 2021 and 2020.

Note 17: Commitments and Contingencies

JHU 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. During the years ended December 31, 2021 and 2020, amounts paid to JHU for royalties were *de minimis*. The Company also has an obligation to pay JHU certain one-time development and commercial milestone payments. The Company paid JHU a $150 milestone payment during the year ended December 31, 2021, which was triggered by the first commercial sale of EYSUVIS in the United States in December 2020. Additional amounts paid to JHU during the years ended December 31, 2021 and 2020 were *de minimis*.

Stanford License Agreement —In October 2019, Combangio entered into a license agreement with The Board of Trustees of The Leland Stanford Junior University ("Stanford"), which was amended in February 2020 and subsequently transferred to the Company by operation of law upon the Acquisition. Pursuant to the license agreement with Stanford (the "Stanford Agreement"), the Company has a worldwide, exclusive, sublicensable license under certain patent rights, or licensed patents, directed to methods to promote eye wound healing, to make, have made, use, import, offer to sell and sell products that are covered by the licensed patents ("licensed products") for use in all fields. Under the Stanford Agreement, the Company is required to pay Stanford annual license maintenance fees and milestone payments upon the achievement of specified development, regulatory and sales milestones, as well as tiered royalties on net sales of licensed products that are covered by a valid claim of a licensed patent.

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The Company's minimum obligations due under its license agreements as of December 31, 2021, are as follows:

Years Ending December 31,		
2022	$	131
2023		143
2024		143
2025		178
2026		178
Thereafter		1,240
Total minimum license payments	$	2,013

Commercial Supply Agreement — The Company entered into a commercial supply agreement with Woodstock Sterile Solutions, Inc. (formerly known as Catalent Pharma Solutions, LLC) to manufacture commercial supplies of EYSUVIS and INVELTYS. The commercial supply agreement contains annual minimum purchase requirements, which follow the contract year from July 1st to June 30th. The minimum purchase requirements increased upon FDA approval of EYSUVIS on October 26, 2020.

The Company has the following minimum purchase obligations for EYSUVIS and INVELTYS:

Years Ending December 31,		
2022 (1)	$	4,044
2023		6,190
2024		6,380
2025 (2)		9,370
2026 (2)		7,028
Thereafter (2)		14,411
Total minimum purchase commitments	$	47,423

(1) Amount presented is net of amounts paid towards the minimum purchase obligation as of December 31, 2021.
(2) Beginning with the contract year July 1, 2025 to June 30, 2026, the minimum contract amounts above are 75% of the actual dollar value of the units ordered for commercial products, in the aggregate, in the contract year immediately prior to the applicable contract year. The table above assumes each contract year beginning July 1, 2025, purchases are 75% of the prior year purchases.

Contingencies related to the Merger Agreement—In connection with the acquisition of Combangio, the Company agreed to make additional payments based on the achievement of certain milestone events related to KPI-012. The Company recognized certain contingent consideration liabilities at fair value on the acquisition date, and revalues the remaining obligations each reporting period. The total potential maximum payout for the milestone payments, which have been recorded as liabilities at fair value, is $40,000 and the milestone payments are contingent upon the achievement of specified development, regulatory and commercialization milestones. Additionally, pursuant to the Merger Agreement, the Company could trigger potential future sales-based milestone payments of up to $65,000. Because the achievement of these sales-based milestones related to KPI-012 was not considered probable as of December 31, 2021, such contingencies have not been recorded in the Company's financial statements. Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain development, regulatory or commercial milestones.

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.

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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, 2021 and 2020, 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 18: 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 $612 and $446 to the 401(k) Plan during for the years ended December 31, 2021 and 2020, respectively.

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

EXCLUSIVE LICENSE AGREEMENT

This Agreement between THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY ("Stanford"), an institution of higher education having powers under the laws of the State of California, and Combangio, Inc., a corporation having a principal place of business at is effective on the 11th day of October, 2019 ("Effective Date").

1. BACKGROUND

Stanford and the University of Illinois ("UIC") have an assignment of an invention entitled "Methods to promote eye wound healing," which was invented in the laboratory of [**], an employee of Stanford and the United States Department of Veterans Affairs ("VA"), and by UIC inventor [**] and is described in Stanford docket [**].

The Invention is administered by Stanford under an Interinstitutional Agreement between Stanford and UIC effective August 7, 2018.

The invention was made in the course of research supported by the DOD, NIH and the Stanford Spark program.

Stanford and UIC want to have the invention perfected and marketed as soon as possible so that resulting products may be available for public use and benefit.

The invention is subject to a Cooperative Technology Administration Agreement between Stanford and the VA, effective August 24, 2017, that authorizes Stanford to exclusively manage certain inventions on behalf of both Stanford and the VA.

Combangio is hereby exercising its Option dated February 11, 2019.

Combangio is a biotechnology company with a program in regenerative therapy and which is in the portfolio of Lagunita Biosciences, an early stage life sciences incubator and venture capital company.

2. DEFINITIONS

Whenever used in this Agreement with an initial capital letter, the following terms, whether used in the singular or the plural, shall have the meanings specified below.

2.1 "**Affiliate**" means as to any person or entity, any other person or entity which controls, is controlled by or is under common control with such person or entity. A person or entity shall be regarded as in control of another entity only if it owns or controls, directly or indirectly, at least fifty percent (50%) of the equity securities or other ownership interests in the subject entity entitled to vote in the election of directors or with the power to direct or elect management of such subject entity.

2.2 "**Change of Control**" means the following, as applied only to the entirety of that part of Combangio's business that exercises all of the rights granted under this Agreement:

(A) acquisition of ownership—directly or indirectly, beneficially or of record—by any person or group (within the meaning of the Exchange Act and the rules of the SEC or equivalent body under a different jurisdiction) of the capital stock of Combangio representing more than 50% of either the aggregate ordinary voting power or the aggregate equity value represented by the issued and outstanding capital stock of Combangio; and/or

(B) the sale of all or substantially all Combangio's assets and/or business in one transaction or in a series of related transactions.

2.3 "**Commercially Reasonable Efforts**" means that Combangio will use the level of effort that would be undertaken by a similarly situated company in the same industry if it were entrusted with the exercise of rights under an Exclusive patent license. Under no circumstances will the level of effort will be less than: (a) marketing Licensed Products in quantities calculated to address anticipated market demand once marketing has begun and (b) seeking any needed governmental approvals for marketing Licensed Products with diligence in supplying indicated information to, and replying to, appropriate governmental offices in the process. Commercially Reasonable Efforts shall in no case involve a shelving of the development, marketing or sale of Licensed Products or a suspension of the diligent pursuit of any needed governmental approval for Licensed Products.

2.4 "**Exclusive**" means that, subject to Sections 3 and 5, Stanford will not grant further licenses under the Licensed Patents in the Licensed Field of Use in the Licensed Territory.

2.5 "**Fully Diluted Basis**" means the total number of shares of Combangio's issued and outstanding common stock, assuming:

(A) the conversion of all issued and outstanding securities convertible into common stock;

(B) the exercise of all issued and outstanding warrants or options, regardless of whether then exercisable; and

(C) the issuance, grant, and exercise of all securities reserved for issuance pursuant to any Combangio stock or stock option plan then in effect.

2.6 "**Indemnitees**" means the VA, Stanford, Stanford Health Care and Lucile Packard Children's Hospital at Stanford and their respective trustees, officers, employees, students, agents, faculty, representatives, and volunteers.

2.7 "**Licensed Field of Use**" means all fields.

2.8 "**Licensed Patents**" means Stanford, UIC and the VA patent applications as listed below:

Stanford	Country	Patent Type	Patent Status	Serial Number	Date Filed	Expiration Date
[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]
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[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]

Licensed Patents shall include any US or foreign patent application corresponding or claiming priority thereto, and any divisional, substitution, continuation, reexamination application or extension of the foregoing, and each patent that issues or reissues from any of these patent applications. "Licensed Patent" includes only those claims in a continuation-in-part (CIP) patent application that are entirely supported in the parent application's original specification and entitled to the parent application's priority date.

2.9 "**Licensed Product**" means a product in the Licensed Field of Use the making, having made, using, importing or selling of which, absent this license, infringes, induces infringement, or contributes to infringement of a Valid Claim of a Licensed Patent.

2.10 "**Licensed Territory**" means worldwide.

2.11 "**Net Sales**" means all gross revenue received by Combangio, its Affiliates or any tier of its Sublicensees, from the sale, or other commercial transfer or disposition of Licensed Products to a third party customer. Net Sales excludes the following items (but only as they pertain to the making, using, importing or selling of Licensed Products, are included in gross revenue, and are separately accounted for):

(A) import, export, excise, value-added, sales and other direct taxes, and custom duties and other similar governmental charges;

(B) costs of insurance, packing, and transportation from the place of manufacture to the customer's premises or point of installation;

(C) costs of installation at the place of use;

(D) credit for returns, allowances, trades and similar adjustments; and

(E) trade, quantity or cash discounts and customary rebates and chargebacks (including without limitation, those granted to managed-care entities and government agencies, as well as entities that manage patient benefits).

In the event that a Licensed Product or a Licensed Service is sold in combination with another product, component or service for which no royalty would be due hereunder if

sold separately (together as a combination, "Combination Product"), Net Sales from such Combination Product sales for purposes of calculating the amounts due under Article 7 shall be calculated by multiplying the Net Sales of the Combination Product by the fraction (A-B)/A, where A is the market value of the Combination Product as determined by its separately listed sale price and B is the market value of the other products, components or services as determined by their separately listed sale price. In the event that separate sales of the Licensed Product and such other product/s, component/s or service/s were not made during the preceding calendar quarter in the applicable country, then the Net Sales on the Combination Product shall be reasonably allocated between such Licensed Product or Licensed Service, and such other product/s, component/s or service/s based upon their relative importance and proprietary protection as mutually agreed upon by Stanford and Combangio. In no event will the applicable royalty rate be reduced by more than [**] percent ([**]%). For the removal of doubt, Net Sales shall not include sales by Combangio to its Affiliates or Sublicensees; provided that if Combangio sells a Licensed Product to an Affiliate or Sublicensee for resale, Net Sales shall include the amounts invoiced by such Affiliate or Sublicensee to third parties on the resale of such Licensed Product.

2.12 "**Nonroyalty Sublicensing Consideration**" means any consideration received by Combangio from any tier of its Sublicensees hereunder but excluding any consideration for:

(A) royalties on products sales (royalties on product sales by any tier of its Sublicensees will be treated as if Combangio made the sale of such product);

(B) investments in Combangio stock;

(C) research and development expenses calculated on a fully burdened basis, incurred for development of the Licensed Product after the effective date of the Sublicense; and

(D) debt;

(E) reimbursement of out-of pocket patent prosecution and maintenance expenses for Patent Matters; and

(F) the sale of substantially all of the business or assets of Combangio (or its assignee) whether by merger, sale of stock or assets or otherwise but provided that Stanford has received the Change of Control Fee as defined under Section 16 of the agreement.

2.13 "**Patent Matters**" means preparing, filing, and prosecuting broad and extensive patent claims (including any interference or reexamination actions) for Stanford's benefit in the Licensed Territory and for maintaining all Licensed Patents.

2.14 "**Sublicense**" means any agreement between Combangio and a third party that contains a grant to Stanford's Licensed Patents regardless of the name given to the agreement by the

parties; however, an agreement to make, have made, use or sell Licensed Products on behalf of Combangio is not considered a Sublicense.

2.15 "**Sublicensee**" means a non-Affiliate third party to whom Combangio or any tier of its Sublicensees has granted a Sublicense; provided that a wholesaler or distributor that does not market or promote the Licensed Product shall not be deemed a Sublicensee.

2.16 "**Valid Claim**" means any claim of an issued patent or pending patent application within the Licensed Patents that has not lapsed, expired, been canceled, or become abandoned and has not been held to be invalid by a court of competent jurisdiction and is unappealable or unappealed within the time allowed for appeal, and which has not been admitted to be invalid or unenforceable through reissue, disclaimer or otherwise, which would be infringed by the making, having made, using, offering for sale, selling or importing of Licensed Product, but for the licenses granted to Combangio under the License Agreement; (each, a "Valid Claim") provided that if the claim of a pending application has not issued within [**] after the priority date of such application, the same shall thereafter not be deemed a Valid Claim until such claim issues except if Combangio chooses to put the issued patent into a reissue proceedings.

3. GRANT

3.1 **Grant**. Subject to the terms and conditions of this Agreement, Stanford grants Combangio an Exclusive license under the Licensed Patents in the Licensed Field of Use to make, have made, use, import, offer to sell and sell Licensed Product in the Licensed Territory. Such license includes the right by Combangio to have any of the foregoing activities performed on its behalf by a third party. Combangio shall have the right to exercise the foregoing licenses through an Affiliate only if such Affiliate has agreed in writing to comply with this entire Agreement. Combangio shall remain fully responsible for such Affiliate's compliance and performance under this Agreement, and for any breach of this Agreement by such Affiliate. Any such Affiliates will be considered to be Combangio for purposes of this Agreement, with all the same rights and obligations as Combangio. An exercise of the licensed rights by such an Affiliate shall not require a Sublicense.

3.2 **Exclusivity.** The license to the Licensed Patents is Exclusive, including the right to sublicense under Section 4, in the Licensed Field of Use beginning on the Effective Date and continuing until the last to expire of a Valid Claim in the Licensed Patents.

3.3 **Retained Rights.** Stanford retains the right, on behalf of itself, Stanford Health Care, Lucile Packard Children's Hospital at Stanford and all other non-profit research institutions, to practice the Licensed Patent for any non-profit purpose, including sponsored research and collaborations. Combangio agrees that, notwithstanding any other provision of this Agreement, it has no right to enforce the Licensed Patent against any such institution. Stanford and any such other institution have the right to publish any information included in a Licensed Patent.

3.4 **Specific Exclusion**. Stanford does not:

(A) grant to Combangio any other licenses, implied or otherwise, to any patents or other rights of Stanford or the VA other than those rights granted under the Licensed Patents, regardless of whether the patents or other rights are dominant or subordinate to any Licensed Patent, or are required to exploit any Licensed Patent.

(B) commit to Combangio to bring suit against third parties for infringement, except as described in Section 14; and

(C) agree to furnish to Combangio any or technological information or to provide Combangio with any assistance.

4. SUBLICENSING

4.1 **Permitted Sublicensing.** Combangio may grant sublicenses through multiple tiers in the Licensed Field of Use and Licensed Territory. Sublicenses with any exclusivity must include diligence requirements commensurate with the diligence requirements of Appendix A. Stanford agrees that Combangio may apportion without discrimination between Combangio patents and Stanford patents a commercially reasonable percentage of sublicensing payments made to Stanford pursuant to Section 4.6, provided however that Combangio provides Stanford with the proposed apportionment and justification prior to Combangio's payment pursuant to Section 8.1. Stanford and Combangio agree to meet to discuss such proposed apportionment if in Stanford's opinion the apportionment does not reasonably reflect the value of the Licensed Patents. Negotiation of any Sublicense must be an arms-length transaction.

4.2 **Required Sublicensing.** If Combangio is unable or unwilling to serve or develop a potential market or market territory for which there is a company with adequate resources willing to be a sublicensee and which has adequate resources and (a) such potential sublicensee has provided Stanford and Combangio with a bona fide, detailed proposal to develop a Licensed Product for such potential market, and (b) such proposed development is not within or detrimental to Combangio's current or planned Licensed Products, as reasonably demonstrated by Combangio in a material communication to its Board of Directors or to third parties such as an investor presentation or a public disclosure, Combangio will, at Stanford's request, use Commercially Reasonable Efforts to negotiate in good faith a Sublicense within [**] with any such company. Stanford would like licensees to address unmet needs, such as those of neglected patient populations or geographic areas, giving particular attention to improved therapeutics, diagnostics and agricultural technologies for the developing world.

4.3 **Sublicense Requirements**. Any Sublicense:

(A) is subject to this Agreement;

(B) will prohibit Sublicensee from paying royalties to an escrow or other similar account;

(C) will expressly include the provisions of Sections 8, 9, and 10 for the benefit of Stanford; and

(D) will include the provisions of Section 4.4 and require that Sublicensee pay the amounts that would be due under this Agreement for the Sublicensee's exercise of its Sublicense, including applicable Earned Royalties, to Stanford or its designee, if this Agreement is terminated and the Sublicense survives pursuant to Section 15.3(c) below. If the Sublicensee is a spin-out from Combangio, so long as the Sublicense survives pursuant to Section 15.3(c) below, Combangio must guarantee the Sublicensee's performance with respect to the payment of Stanford's share of Sublicense royalties.

4.4 **Litigation by Sublicensee**. Any Sublicense must include the following clauses:

(A) In the event Sublicensee brings an action seeking to invalidate any Licensed Patent:

(1) Sublicensee will [**] the payment paid to Combangio during the pendency of such action. Moreover, should the outcome of such action determine that any claim of a patent challenged by the Sublicensee is both valid and infringed by a Licensed Product, Sublicensee will pay [**] times the payment paid under the original Sublicense;

(2) Sublicensee will have no right to recoup any royalties paid before or during the period challenge;

(3) any dispute regarding the validity of any Licensed Patent shall be litigated in the courts located in Santa Clara County, and the parties agree not to challenge personal jurisdiction in that forum; and

(4) Sublicensee shall not pay royalties into any escrow or other similar account.

(B) Sublicensee will provide written notice to Stanford at least [**] prior to bringing an action seeking to invalidate a Licensed Patent. Sublicensee will include with such written notice an identification of all prior art it believes invalidates any claim of the Licensed Patent.

4.5 **Copy of Sublicenses and Sublicensee Royalty Reports.** Combangio will submit to Stanford copies of each Sublicense within [**] of signing, any subsequent amendments and all copies of Sublicensees' royalty reports; provided, however, that Combangio may redact sensitive information in such Sublicenses and royalty reports to the extent it is not necessary for Stanford's confirmation of Combangio's and Sublicensees' compliance with the requirements of this Agreement. Beginning with the first Sublicense, the Chief Financial Officer or equivalent will certify [**] regarding the name and number of Sublicensees.

4.6 **Sharing of Nonroyalty Sublicensing Consideration.** Combangio will pay to Stanford a portion of all Nonroyalty Sublicensing Consideration for the Sublicense of Licensed Patents, specifically for sublicense of all or substantially all of the Licensed Patents, at a rate determined based on the timing of execution of the sublicense agreement as follows:

(A) Sublicense executed prior to [**]% of Nonroyalty Sublicensing Consideration;

(B) Sublicense executed after [**]% of Nonroyalty Sublicensing Consideration; and

(C) Sublicense executed after [**]% of Nonroyalty Sublicensing Consideration.

A pro rata reduction of the percentage of Nonroyalty Sublicensing Consideration will be payable to Stanford under this Agreement where, in addition to the Sublicense of any rights granted by Combangio hereunder, Combangio also grants Sublicensee a license under its own or a third party's intellectual property rights that are applicable to a Licensed Product. The amount of the pro rata reduction shall be calculated by Combangio based on a commercial reasonable allocation of value among the Sublicense of Patent Rights and sublicense of other rights. In some situations, it may be appropriate to make this calculation based on the [**]. By way of example, if utilizing this methodology was deemed to be commercially reasonable in a given circumstance, then if Combangio sublicenses [**], the Nonroyalty Sublicensing Consideration upon which Stanford would receive a sublicense fee would be [**]% of the total Nonroyalty Sublicensing Consideration received by Combangio in consideration of the sublicense rights [**]. Such intellectual property must have Valid Claims that read on the Licensed Product. Stanford shall be provided copies of any patents with such Valid Claims and written rationale justifying the request to reduce Nonroyalty Sublicensing Consideration. Notwithstanding the foregoing, if Stanford does not believe that Combangio's calculation of the pro rata reduction of the percentage of Nonroyalty Sublicensing Consideration is commercially reasonable, parties will meet to discuss a mutually agreeable reduction of the Nonroyalty Sublicensing Consideration, and the dispute over what constitutes a commercially reasonable pro rata reduction may be submitted by either party at any time for final determination under arbitration pursuant to Section 17 below.

4.7 For purposes of this Section 4.6, a [**] shall be deemed to be completed on the date that the [**].

4.8 **Royalty-Free Sublicenses**. If Combangio pays all royalties due Stanford from a Sublicensee's Net Sales, Combangio may grant that Sublicensee a royalty-free or noncash:

(A) Sublicense or

(B) cross-license.

5. GOVERNMENT RIGHTS

5.1 This Agreement is subject to Title 35 Sections 200-204 of the United States Code. Among other things, these provisions provide the United States Government with

nonexclusive rights in the Licensed Patent. They also impose the obligation that Licensed Product sold or produced in the United States be "manufactured substantially in the United States." Combangio will ensure all obligations of these provisions are met.

5.2 The United States Government shall have the nonexclusive, nontransferable, irrevocable, royalty-free, paid-up right to practice or have practiced the Licensed Patent throughout the world by or on behalf of the United States Government and on behalf of any foreign government or international organization pursuant to any existing or future treaty or agreement to which the United States Government is a signatory.

5.3 Combangio certifies that Combangio is in good standing to do business with the federal government regarding debarment, suspension, proposed debarment or other matters rendering them ineligible.

6. DILIGENCE

6.1 **Milestones.** Because the invention is not yet commercially viable as of the Effective Date, Combangio will diligently develop, manufacture, and sell Licensed Product and will diligently develop markets for Licensed Product. In addition, Combangio will use Commercially Reasonable Efforts to pursue the milestones shown in Appendix A, and notify Stanford in writing as each milestone is met. For clarity, Combangio may satisfy its diligence obligations under this Agreement through its Affiliates and Sublicensees.

6.2 **Progress Report.** By [**] of each year and during the term of the Agreement Combangio will submit a written annual report to Stanford covering the preceding calendar year. The report will include information sufficient to enable Stanford to satisfy reporting requirements of the U.S. Government and for Stanford to ascertain progress by Combangio toward meeting this Agreement's diligence requirements. Each report will describe, where relevant: [**]. Combangio will specifically describe [**].

6.3 **Clinical Trial Notice.** Combangio will notify the Stanford University Office of Licensing prior to commencing any clinical trials at Stanford. If Combangio does not notify Stanford University Office of Licensing at least [**] prior to enrolling the first patient in a clinical study at Stanford, Combangio agrees that it will pay $[**] to Stanford within [**] of being invoiced.

7. ROYALTIES

7.1 **Issue Fee.** Combangio will pay to Stanford a noncreditable, nonrefundable license issue fee of $15,000 upon signing this Agreement.

7.2 **Purchase Right**.

(A) Stanford shall have the right, but not the obligation, to purchase for cash up to its Share of the securities issued in any Qualifying Offering on the terms, and subject to the conditions, set forth in this Section 7.2 and Section 7.3 (the "Purchase Right"). For purposes of this Section 7.2 and Section 7.3:

(1) "Adjustment Event" means the final closing of the first Threshold Qualifying Offering occurring after the date of this Agreement.

(2) "Board of Directors" means (i) if Combangio is organized as a corporation, its board of directors, and (ii) if Combangio is organized as a limited liability company, Combangio manager(s) or member(s) or both that have the power to direct the principal management and activities of Combangio, whether through ownership of voting securities, by agreement, or otherwise.

(3) "Qualifying Offering" means a private offering of Combangio's equity securities (or securities convertible into or exercisable for Combangio's equity securities) for cash (or in satisfaction of debt issued for cash) having its final closing on or after the date of this Agreement and which includes investment by one or more venture capital, professional angel, corporate or other similar institutional investors other than Stanford. For the avoidance of doubt, if Combangio is a limited liability company, then "equity securities" means limited liability company interests in Combangio.

(4) "Share" means:

(i) [**]% with respect to any Qualifying Offering having a closing on or before the date of an Adjustment Event; or

(ii) with respect to any Qualifying Offering having a closing after an Adjustment Event, but before a Termination Event, the percentage necessary for Stanford to maintain its pro rata ownership interest in Combangio on a Fully-Diluted Basis.

(5) "Threshold Qualifying Offering" means any Qualifying Offering which either (i) is at least $[**] in size or (ii) involves the sale to outside investors of at least [**]% of the equity securities outstanding after such round on a Fully-Diluted Basis.

(6) The parties shall construe the term "Fully-Diluted Basis" mutatis mutandis in the case where Combangio is organized as a limited liability company.

(B) The Purchase Right shall terminate upon the earliest to occur of the following (each a "Termination Event"):

(1) Stanford's execution of an investor rights agreement or similar agreement (each a "Rights Agreement") in connection with a Threshold Qualifying Offering so long the Rights Agreement satisfies the terms of this Section and Section 7.3 below;

(2) Stanford purchases less than its entire Share of a Qualifying Offering;

(3) Stanford fails to give an election notice within the Notice Period for a Qualifying Offering which has its final closing within [**] of the date such notice is received by Stanford and which is closed on terms that are the same or less favorable to the investors as the terms stated in Combangio's notice to Stanford;

(4) The closing of a firm commitment underwritten public offering of Combangio's common stock; or

(5) The closing of the sale of all or substantially all of Combangio's assets to a company publicly traded on one of the major recognized exchanges.

(C) The Purchase Right shall not apply to the issuance of securities: (i) to employees, individuals who are members of Combangio's Board of Directors as of the time of issuance, and service providers to Combangio pursuant to a plan approved by Combangio's Board of Directors; or (ii) as additional consideration in lending or leasing transactions; or (iii) to an entity pursuant to an arrangement that Combangio's Board of Directors determines in good faith is a strategic partnership or similar arrangement of Combangio (i.e., an arrangement in which the entity's purchase of securities is not primarily for the purpose of financing Combangio); or (iv) to owners of another entity in connection with the acquisition of that entity by Combangio.

(D) If Combangio has entered into more than one Exclusive (Equity) Agreement or other agreement to license intellectual property from Stanford, and Stanford has fully exercised its right to purchase its Share in connection with a Qualifying Offering under any such agreement, Stanford will waive its right to purchase its Share in connection with a Qualifying Offering under all other applicable agreements. In the event that Stanford has not fully exercised its right to purchase its Share in connection with a Qualifying Offering under any agreement, then Stanford may only exercise its right to purchase under a single agreement, and will waive its right to purchase under all others.

7.3 **Rights Agreements; Information Rights; Notice; Elections**.

(A) Combangio shall ensure that each Rights Agreement executed by Stanford in connection with a Qualifying Offering will grant to Stanford the same rights as all other investors who are parties to that Rights Agreement. In particular, Combangio shall ensure that each such Rights Agreement will grant to Stanford the same right to purchase additional securities in future offerings, the same information rights, and the same registration rights as are granted to other parties thereto, including all such rights granted to any investor designated as a "Major Investor" or other similar designation, even if Stanford is not so designated.

(B) Notwithstanding any terms to the contrary contained in any applicable Rights Agreement:

(1) Stanford shall not have any representation on the Board of Directors or rights to attend meetings of the Board of Directors;

(2) In connection with all Qualifying Offerings, Combangio shall give Stanford notice of the terms of the offering, including: (i) the names of the investors, the allocation of equity securities among them and the total amounts to be invested by each of them in such offering; (ii) pre- and post-projected) financing capitalization table; (iii) investor presentation (if available); (iv) an introduction to the lead investor in such offering for the purpose of discussing the lead investor's due diligence process; and (v) such other documents and information as Stanford may reasonably request for the purpose of making an investment decision or verifying the amount of equity securities it is entitled to purchase in such offering; and

(3) Stanford may elect to exercise its Purchase Right, in whole or in part, by notice given to Combangio within [**] after receipt of Combangio's notice ("Notice Period').

(C) If Stanford has no information rights under a Rights Agreement and to the extent that such information has been prepared by Combangio for other purposes, so long as Stanford holds Combangio securities, Combangio shall furnish to Stanford, upon request and as promptly as reasonably practicable, Combangio's annual consolidated financial statements and annual operating plan, including an annual report of the holders of Combangio's securities, and such other information as Stanford may reasonably request from time to time for the purpose of valuing its interest in Combangio.

(D) Notwithstanding any notice provision in this Agreement to the contrary, any notice given under this Agreement that refers or relates to any of Section 7.2 above or this Section 7.3 shall be copied concurrently to [**]; provided, however, that delivery of the copy will not by itself constitute notice for any purpose under this Agreement.

7.4 **License Maintenance Fee.** Combangio will pay Stanford annual minimum license maintenance fees as follows:

(a) [**] through [**] anniversary of Effective Date - $[**] per year;

(b) [**] Anniversary of Effective Date - $[**] per year; and

(c) [**] anniversary of the Effective Date and thereafter until Combangio makes its first commercial sale —$[**] per year.

Yearly maintenance payments are nonrefundable but they are creditable each year as described in Section 7.8.

7.5 **Milestone Payments**. Combangio will pay Stanford the following one-time milestone payments with respect to the first Licensed Product to achieve each such milestone.

(A) [**];

(B) [**];

(C) [**]; and

(D) Upon first achieving cumulative Net Sales of $[**] in a calendar year: $[**].

For purposes of clarity, it is understood and agreed that each of the foregoing milestone payments shall be payable only once, irrespective of the number of Licensed Products Combangio may ultimately develop. It is further understood and agreed that Combangio's total obligation to Stanford under this Section 7.5 shall in no event exceed two million one hundred and seventy-five thousand Dollars ($2,175,000).

7.6 **Earned Royalty.** Combangio will pay Stanford earned royalties (Y%) on Net Sales as follows (''Earned Royalties"):

Amount of Annual Net Sales	**Royalty Percentage (Y%) of Net Sales**
≤ $USD [**]	[**] percent ([**]%)
> $USD [**] ≤ $USD [**]	[**] percent ([**]%)
> $USD [**] ≤ $USD [**]	[**] percent ([**]%)
$USD [**] ≤ $USD [**]	[**] percent ([**]%)
$USD [**] ≤ $USD [**]	[**] percent ([**]%)
$USD [**]	[**] percent ([**]%)

For clarity, Earned Royalties will be paid on a tiered structure based on the portion of Net Sales of Licensed Products in each such tier. By way of example only, in the event that Net Sales in a given year are $USD [**].

Earned Royalties will be payable on a country-by-country basis and Licensed Product-by-Licensed Product basis on Net Sales of Licensed Products in each such country until the last to occur of the following: (i) the last to expire Valid Claim covering such Licensed Product in the Licensed Field of Use in the country of sale; and (ii) the last to expire Valid Claim covering such Licensed Product in the Licensed Field of Use in the country of manufacture. For clarity, in the event that there are no Valid Claims in either i) or ii) above for a given Licensed Product in a given country, no Earned Royalty will be payable with respect to the sale of such Licensed Product in such country.

In no event shall more than one Earned Royalty be due hereunder with respect to any Licensed Product unit; nor shall an Earned Royalty be payable hereunder with respect to sales of Licensed Product for use in research and/or development, in clinical trials or as samples.

In the event that the total annual Earned Royalties that Combangio is required to pay to Stanford, and all other royalties payable by Combangio, its Affiliates and Sublicensees to any third parties in connection with the development, manufacture or commercialization of a given Licensed Product exceed [**] percent ([**]%) of Net Sales in aggregate, the

royalties payable to Stanford and each of the third party royalty recipients (each, a "Royalty Recipient") shall be reduced on a proportional basis according to each Royalty Recipient's share of the total percentage royalty payable on such Net Sales of such Licensed Product, so that the aggregate royalties payable to all Royalty Recipients does not exceed [**] percent ([**]%) of Net Sales of such Licensed Product. But in no event shall the applicable Stanford Earned Royalty above be reduced by more than [**]%.

7.7 **Earned Royalty if Combangio Challenges the Patent.** Notwithstanding the above, should Combangio bring an action seeking to invalidate any Licensed Patent, Combangio will pay Earned Royalties to Stanford at [**] the rates specified under Section 7.6 during the pendency of such action. Moreover, should the outcome of such action determine that any claim of a patent challenged by Combangio is both valid and infringed by a Licensed Product, Combangio will [**] the rates specified under Section 7.6.

7.8 **Creditable Payments.** The license maintenance fee for a year may be offset against Earned Royalty payments due on Net Sales occurring in that year.

For example:

(A) if Combangio pays Stanford a $[**] maintenance payment for year Y, and according to Section 7.6 [**].

(B) if Combangio pays Stanford a $[**] maintenance payment for year Y, and according to Section 7.6 [**].

7.9 **Obligation to Pay Royalties**. If certain quantities of Licensed Products are made, or imported before the date this Agreement terminates, and those Licensed Products quantities are sold after the termination date and an Earned Royalty would have been due on such Licensed Products at the time of their sale had this Agreement not been terminated, Combangio will pay Stanford an Earned Royalty for its exercise of rights based on the Net Sales of those Licensed Products quantities.

7.10 **No Escrow.** Combangio shall not pay royalties into any escrow or other similar account.

7.11 **Currency.** Combangio will calculate the Earned Royalty on sales in currencies other than U.S. Dollars using the appropriate foreign exchange rate for the currency quoted by the Wall Street Journal on the close of business on the last banking day of each calendar quarter. Combangio will make Earned Royalty payments to Stanford in U.S. Dollars.

7.12 **Non-U.S. Taxes.** Combangio will pay all non-U.S. taxes related to Earned Royalty payments. These payments are not deductible from any payments due to Stanford.

7.13 **Interest.** Any payments not made when due will bear interest at the lower of (a) the Prime Rate published in the Wall Street Journal plus [**] or (b) the maximum rate permitted by law.

8. ROYALTY REPORTS, PAYMENTS, AND ACCOUNTING

8.1 **Earned Royalty Payment and Report.** Beginning with the first sale of a Licensed Product by Combangio or a Sublicensee, or with the first receipt of any Nonroyalty Sublicensing Consideration by Combangio, Combangio will submit to Stanford a written report, an Earned Royalty payment and/or Nonroyalty Sublicensing Consideration payment due Stanford within [**] after each calendar period, where the period is initially on a per-year basis, and changes to a per-quarter basis when annual Earned Royalty payments to Stanford exceed $[**]. This report will be in the form of Appendix B and will state the number, description, and aggregate Net Sales of Licensed Product during the completed calendar time period and details about any Sublicenses. The report will include an overview of the process and documents relied upon to permit Stanford to understand how the Earned Royalties and Nonroyalty Sublicensing Consideration are calculated. With each report, Combangio will include any Earned Royalty payment and Nonroyalty Sublicensing Consideration payment due Stanford for the completed time period (as calculated under Section 7.6 and Section 4.6).

8.2 **No Refund.** In the event that a validity or non-infringement challenge of a Licensed Patent brought by Combangio is successful, Combangio will have no right to recoup any royalties paid before or during the period challenge.

8.3 **Termination Report.** Combangio will pay to Stanford all applicable royalties and submit to Stanford a written report within [**] after the license terminates. Combangio will continue to submit earned royalty payments and reports to Stanford after the license terminates, until all Licensed Products made or imported under the license have been sold.

8.4 **Accounting**. Combangio will maintain records showing manufacture, importation, sale, and use of a Licensed Product for [**] from the date of sale of that Licensed Product. Records will include general-ledger records showing cash receipts and expenses, and records that include: production records, customers, invoices, serial numbers, and related information in sufficient detail to enable Stanford to determine the royalties payable under this Agreement.

8.5 **Audit by Stanford.** Combangio will allow Stanford or its designee to examine Combangio's records to verify payments made by Combangio under this Agreement.

8.6 **Paying for Audit.** Stanford will pay for any audit done under Section 8.5. But if the audit reveals an underreporting of earned royalties due Stanford of [**]% or more for the period being audited, Combangio will pay the audit costs.

8.7 **Self-audit.** Combangio will conduct an independent audit of sales and royalties at least every [**] if annual sales of Licensed Product are over $[**]. The audit will address, at a minimum, the amount of Licensed Product gross sales by or on behalf of Combangio during the audit period, the amount of funds owed to Stanford under this Agreement, and whether the amount owed has been paid to Stanford and is reflected in the records of Combangio. Combangio will submit the auditor's report promptly to Stanford upon completion. Combangio will pay for the entire cost of the audit.

9. EXCLUSIONS AND NEGATION OF WARRANTIES

9.1 **Negation of Warranties**.

As of the Effective Date, Stanford represents that to the knowledge of Stanford's Office of Technology Licensing representative and without conducting any further investigation:

(a) Stanford has assignments from all inventors known as of the Effective Date on the Licensed Patents; and

(b) Stanford has the right to grant the rights in the Licensed Patents to Combangio in this Agreement.

Stanford provides Combangio **the rights granted in this Agreement AS IS and WITH ALL FAULTS. Stanford makes no representations and extends no warranties of any kind, either express or implied. Among other things, Stanford disclaims any express or implied warranty:**

(A) of merchantability, of fitness for a particular purpose;

(B) of non-infringement; or

(C) arising out of any course of dealing.

9.2 **No Representation of Licensed Patent**. Combangio also acknowledges that Stanford does not represent or warrant:

(A) the validity or scope of any Licensed Patent; or

(B) that the exploitation of Licensed Patent will be successful.

10. INDEMNITY

10.1 **Indemnification.** Combangio will indemnify, hold harmless, and defend all Indemnitees against any third party claim of any kind arising out of or related to the exercise of any rights granted Combangio under this Agreement or the breach of this Agreement by Combangio, except to the extent such claim is determined with finality by a court of competent jurisdiction to result from the gross negligence or willful misconduct of any Indemnitee.

10.2 **No Indirect Liability.** Neither party is liable for any special, consequential, lost profit, expectation, punitive or other indirect damages in connection with any claim arising out of or related to this Agreement, whether grounded in tort (including negligence), strict liability, contract, or otherwise.

10.3 **Workers' Compensation.** Combangio will comply with all statutory workers' compensation and employers' liability requirements for activities performed under this Agreement.

10.4 **Insurance.** During the term of this Agreement, Combangio will maintain Commercial General Liability Insurance with a reputable and financially secure insurance carrier to cover the activities of Combangio and its affiliates and sublicensees. The insurance will provide minimum limits of liability of $[**] per occurrence and will include all Indemnitees as additional insureds. Prior to any use of a Licensed Product in or for humans, the insurance coverage will be increased to provide minimum limits of liability of $[**] per occurrence. Prior to any clinical trial using the Licensed Product, the insurance will include Clinical Trial Insurance in addition to the increased minimum limits of liability of $[**] per occurrence. Prior to any offering for sale of Licensed Product by Combangio, or its affiliates or sublicensees, the insurance will include Product Liability Insurance, and will have minimum limits of liability of $[**] per occurrence. Insurance must cover claims incurred, discovered, manifested, or made during or after the expiration of this Agreement and must be placed with carriers with ratings of at least A- as rated by A.M. Best. Within [**] of the Effective Date of this Agreement, and for each instance in which the coverage is changed as per the requirements above, Combangio will furnish a Certificate of Insurance evidencing primary coverage and additional insured requirements. Combangio will provide to Stanford [**] prior written notice of cancellation or material change to this insurance coverage. Combangio will advise Stanford in writing that it maintains a combination of excess liability coverage (following form) over primary insurance for at least the minimum limits set forth above. All insurance of Combangio will be primary coverage; insurance of Indemnitees will be excess and noncontributory.

11. EXPORT

Combangio and its Affiliates and Sublicensees will comply with all applicable United States laws and regulations controlling the export of licensed commodities and technical data relating to this Agreement. (For the purpose of this paragraph, "licensed commodities" means any article, material or supply but does not include information; and "technical data" means tangible or intangible technical information that is subject to U.S. export regulations, including blueprints, plans, diagrams, models, formulae, tables, engineering designs and specifications, manuals and instructions.) These laws and regulations may include, but are not limited to, the Export Administration Regulations (15 CFR 730-774), the International Traffic in Arms Regulations (22 CFR 120-130) and the various economic sanctions regulations administered by the U.S. Department of the Treasury (31 CFR 500-600).

Among other things, these laws and regulations may prohibit or require a license for the export or retransfer of certain commodities and technical data to specified countries, entities and persons. Combangio hereby gives written assurance that it will comply with, and will cause its Sublicensees and Affiliates to comply with all United States export control laws and regulations, that it understands it may be held responsible for any violation of such laws and regulations by itself or its Sublicensees and Affiliates, and that it will indemnify, defend and hold Stanford harmless for the consequences of any such violation.

12. MARKING

Before any Licensed Patent issues, Combangio will mark Licensed Product with the words "Patent Pending." Otherwise, Combangio will mark Licensed Product with the number of any issued Licensed Patent.

13. STANFORD NAMES AND MARKS

Combangio will not use (i) Stanford's or the VA's name or other trademarks, (ii) the name or trademarks of any organization related to Stanford or the VA, or (iii) the name of any Stanford faculty member, employee, student or volunteer, or any VA employee. This prohibition includes, but is not limited to, use in press releases, advertising, marketing materials, other promotional materials, presentations, case studies, reports, websites, application or software interfaces, and other electronic media. Notwithstanding the foregoing, Combangio may include Stanford's name in factual statements in legal proceedings, patent applications and other regulatory filings. In addition, Combangio may make a short factual statement that identifies Stanford as the licensor of the rights granted under this Agreement to actual or potential investors or acquirers, as well as in the "About Combangio" or other similar section of the Combangio website.

14. PROSECUTION AND PROTECTION OF PATENTS

14.1 **Patent Prosecution**.

(A) Following the Effective Date and subject to Stanford's approval, Combangio will be responsible for Patent Matters. Combangio will use its diligent efforts with respect to the Patent Matters and in doing so will act in good faith irrespective of other patents, patent applications, or other rights that Combangio may possess. Combangio will notify Stanford before taking any substantive actions in prosecuting the claims, and Stanford will have final approval on how to proceed with any such actions. To aid Combangio in this process, Stanford will provide information, execute and deliver documents and do other acts as Combangio shall reasonably request from time to time. In the event that Combangio decides to abandon any patent right within the Licensed Patents (which it may do so at any time in its sole discretion), it will provide reasonable prior notice to Stanford and provide Stanford with an opportunity to assume responsibility for the prosecution and maintenance of such patent right. Following such notice by Combangio, prosecution and maintenance of such patent right shall be at the cost of Stanford (or VA, to the extent separately agreed to between Stanford and VA), and such patent right shall no longer be within the Licensed Patents. If Stanford at any time believes that Combangio has failed to satisfy the standards of this Section 14.1 (A), Stanford may, upon [**], terminate this Section 14.1 (A).

(B) Combangio will reimburse Stanford for Stanford's reasonable costs (and VA's reasonable costs, to the extent applicable) incurred in complying with such requests. Stanford and Combangio agree that Stanford is the client of record for the attorney prosecuting the Licensed Patents and agree to have Appendix C fully

executed by the appropriate parties upon execution of this Agreement. At Stanford's request, Combangio will provide all information and assistance to Stanford to ensure that Licensed Patent is as extensive as reasonably possible. If Combangio gives notice to Stanford of intent to abandon a patent right within the Licensed Patents pursuant to Section 14.1(A), Combangio will assist Stanford in the transfer of the prosecution materials for such patent right to the law firm of Stanford's choice. If Stanford has terminated Section 14.1(A), any agreement in the form of Appendix C will be deemed to be amended immediately without prior action by any party to revise Appendix C, Section 1 to require the Firm (as defined in Appendix C) to interact directly with Stanford only (i.e., with respect to the Licensed Patents).

14.2 **Patent Costs**. Within [**] after receiving a statement from Stanford, Combangio will reimburse Stanford:

(A) $[**] to offset Licensed Patent's patenting expenses, including but not limited to interference or reexamination matters, inventorship disputes and opposition proceedings incurred by Stanford before the Effective Date; and

(B) for all Licensed Patent's patenting expenses, including but not limited to interference or reexamination matters, inventorship disputes and opposition proceedings incurred by Stanford after the Effective Date. In all instances, Stanford will pay the fees prescribed for large entities to the United States Patent and Trademark Office.

14.3 **Infringement Procedure.** Each party will promptly notify the other if it believes a third party infringes a Licensed Patent or if a third party files a declaratory judgment action with respect to any Licensed Patent. During the Exclusive term of this Agreement and if Combangio (or its Sublicensee) is diligently developing or selling Licensed Product, Combangio may have the right to institute a suit against or defend any declaratory judgment action initiated by this third party, but only within fields of use where this Agreement is Exclusive, as provided in Section 14.4 through and including Section 14.8.

14.4 **Combangio Suit.** Combangio has the first right (itself or through others) to institute and prosecute a suit to enforce the Licensed Patents and/or defend any declaratory judgment action with respect thereto, but only within fields of use where this Agreement is Exclusive, and only if Combangio provides a claim chart evidence of the infringement to Stanford and if Combangio is (or its Sublicensee is) diligently developing, offering for sale, or selling Licensed Product, then Combangio may institute and prosecute a suit or defend any declaratory judgment action so long as it conforms with the requirements of this Section. Stanford agrees to cooperate fully in connection with such suit. If Combangio decides to institute suit, it will notify Stanford in writing and give Stanford and the VA the opportunity to institute suit jointly as provided in Section 14.5. Combangio will diligently pursue the suit and Combangio will bear the entire cost of the litigation, including reasonable expenses and counsel fees incurred by Stanford and the VA in connection with Stanford's and the VA's cooperation in such suit. Combangio will keep Stanford reasonably apprised of all developments in the suit and will make a

good faith effort to incorporate Stanford's input (including input from the VA that Stanford provides to Combangio) on any substantive submissions or positions taken in the litigation regarding the scope, validity and enforceability of the Licensed Patent. Combangio will not initiate, prosecute, settle or otherwise compromise any such suit in a manner that materially adversely affects Stanford's or the VA's interests without Stanford's prior written consent, not to be unreasonably withheld or delayed. Stanford or the VA may be named as a party only if:

(A) Combangio's and Stanford's respective counsel recommend that such action is necessary in their reasonable opinion to achieve standing;

(B) Neither Stanford nor the VA are the first named party in the action; and

(C) the pleadings and any public statements about the action state that Combangio is pursuing the action and that Combangio has the right to join Stanford and the VA as a party.

14.5 **Joint Suit**. If Stanford and Combangio so agree, they may institute suit or defend the declaratory judgment action jointly. If so, they will:

(A) prosecute the suit in both their names;

(B) bear the out-of-pocket costs equally;

(C) share any recovery or settlement equally; and

(D) agree how they will exercise control over the action.

14.6 **Stanford Suit.** If neither Section 14.4 nor 14.5 apply, and in the event Combangio elects not to initiate an action to enforce the Licensed Patents against a commercially significant infringement by a third party by written notice to Stanford in [**] upon a request by Stanford to do so after a notice of infringement as provided in Section 14.3, Stanford has the right to institute and prosecute a suit or defend any declaratory judgment action, and may name Combangio as a party for standing purposes. If Stanford decides to institute suit, it will notify Combangio in writing. If Combangio does not notify Stanford in writing that it desires to jointly prosecute the suit within [**] after the date of the notice, Combangio will assign and hereby does assign to Stanford all rights, causes of action, and damages resulting from the alleged infringement. Stanford will bear the entire cost of the litigation and will retain the entire amount of any recovery or settlement.

14.7 **Recovery.** Any recovery or settlement received in connection with any suit will first be shared by Stanford, VA and Combangio equally to cover the litigation costs each incurred, and next shall be paid to Stanford, VA or Combangio to cover any litigation costs it incurred in excess of the litigation costs of the other. In any suit initiated by Combangio, any recovery in excess of litigation costs will be shared between Combangio and Stanford as follows:

(A) any payment for past sales will be deemed Net Sales, and Combangio will pay Stanford Earned Royalties at the rates specified in Section 7.6;

(B) any payment for future sales will be deemed a payment under a Sublicense, and Earned Royalties will be shared as specified in Article 4; and

(C) Combangio and Stanford will negotiate in good faith appropriate compensation to Stanford for any non-cash settlement or non-cash cross-license.

In any suit initiated by Stanford, any recovery in excess of litigation costs will belong to Stanford. Stanford and Combangio agree to be bound by all determinations of patent infringement, validity, and enforceability (but no other issue) resolved by any adjudicated judgment in a suit brought in compliance with this Section 14.

14.8 **Abandonment of Suit.** If either Stanford or Combangio commences a suit and then wants to abandon the suit, it will give timely notice to the other party. The other party may continue prosecution of the suit after Stanford and Combangio agree on the sharing of expenses and any recovery in the suit.

14.9 **VA Cooperation**. The VA's cooperation in litigation proceedings instituted under this Agreement is subject to U.S. Department of Justice approval on a case-by-case basis.

14.10 **No Implied Obligations**. Except as expressly provided in this Article 14, neither party has any obligation to bring or prosecute actions or suits against any third party for patent infringement.

15. TERMINATION

15.1 **Termination by Combangio.** Combangio may terminate this Agreement by giving Stanford written notice at least 30 days in advance of the effective date of termination selected by Combangio.

15.2 **Termination by Stanford**.

(A) Stanford may also terminate this Agreement if Combangio:

(1) is delinquent on any report or payment;

(2) is not diligently developing and commercializing Licensed Product;

(3) misses a milestone described in Appendix A;

(4) is in breach of any provision; or

(5) provides any false report.

(B) Termination under this Section 15.2 will take effect 60 days after written notice by Stanford unless Combangio remedies the problem in that 60-day period.

Notwithstanding the foregoing, if Combangio disputes in good faith any payment obligation (including but not limited to a dispute regarding the amount of Nonroyalty Sublicensing Consideration to pay in a particular case) during such 60-day period, Stanford shall not have the right to terminate this Agreement unless and until it is finally determined pursuant to Article 17 that such default or breach occurred, and Combangio fails to cure such default or breach within [**] after such determination.

15.3 **Surviving Provisions.** Surviving any termination or expiration are:

(A) Combangio's obligation to make all payments, accrued or accruable, including but not limited to fees, royalties and patent costs;

(B) any claim of Combangio or Stanford, accrued or to accrue, because of any breach or default by the other party; and

(C) the provisions of Articles 1, 2, 8, 9, 10 and 17-19, and Section 15.3; and any Sublicenses granted by Combangio or its Sublicensees hereunder, provided that the applicable Sublicensee is not in breach with respect to its obligations under such sublicense and provided such Sublicensee promptly agrees in writing to be bound by the applicable terms of this Agreement.

16. CHANGE OF CONTROL, ASSIGNMENT AND NON-ASSIGNABILITY

16.1 **Change of Control.** If there is a Change of Control or if this Agreement is assigned to a third party that was not an Affiliate prior to the Change of Control, Combangio will pay Stanford a $100,000 ("Change of Control/Assignment Fee") per Section 16.2.

16.2 **Conditions of Assignment.** Combangio may assign this Agreement upon prior and complete performance of the following conditions:

(A) Combangio must give Stanford written notice of the assignment within [**], including the new assignee's contact information; and

(B) the new assignee must agree in writing to Stanford to be bound by this Agreement; and

(C) Stanford must have received the full Change of Control/Assignment Fee (except in the case of an assignment to an Affiliate).

16.3 **After the Assignment.** Upon a permitted assignment of this Agreement pursuant to Section 15.3(C), Combangio will be released of liability under this Agreement and the term "Combangio" in this Agreement will mean the assignee.

16.4 **Bankruptcy.** In the event of a bankruptcy or insolvency, assignment is permitted only to a party that can provide adequate assurance of future performance, including diligent development and sales of Licensed Product.

16.5 **Nonassignability of Agreement.** Except in conformity with Section 16.2 and Section 16.4, this Agreement is not assignable by Combangio under any other circumstances and any attempt to assign this Agreement by Combangio is null and void.

17. DISPUTE RESOLUTION

17.1 **Dispute Resolution by Arbitration.** Any dispute between the parties regarding any payments made or due under this Agreement will be settled by arbitration in accordance with the JAMS Arbitration Rules and Procedures, provided that in the case of a good faith dispute as to the amount due, the cure period under Section 15.2 will be tolled until the amount due has been finally determined in such an arbitration. The parties are not obligated to settle any other dispute that may arise under this Agreement by arbitration.

17.2 **Request for Arbitration.** Either party may request such arbitration. Stanford and Combangio will mutually agree in writing on a third-party arbitrator within [**] of the arbitration request. The arbitrator's decision will be final and nonappealable and may be entered in any court having jurisdiction.

17.3 **Discovery**. The parties will be entitled to discovery as if the arbitration were a civil suit in the California Superior Court. The arbitrator may limit the scope, time, and issues involved in discovery.

17.4 **Place of Arbitration**. The arbitration will be held in Stanford, California unless the parties mutually agree in writing to another place.

17.5 **Patent Validity**. Any dispute regarding the validity of any Licensed Patent shall be litigated in the courts located in Santa Clara County, California, and the parties agree not to challenge personal jurisdiction in that forum.

18. NOTICES

18.1 **Legal Action**. Combangio will provide written notice to Stanford at least three months prior to bringing an action seeking to invalidate any Licensed Patent or a declaration of non-infringement. Combangio will include with such written notice an identification of all prior art it believes invalidates any claim of the Licensed Patent.

18.2 **All Notices.** All notices under this Agreement are deemed fully given when written, addressed, and sent as follows:

All general notices to Combangio are mailed or emailed to:

Attn: Darius Kharabi, President & CEO
1490 O'Brien Drive, Suite C, Menlo Park, CA 94025
[**]

All financial invoices to Combangio (i.e., accounting contact) are e-mailed to:

[**]

All progress report invoices to Combangio (i.e., technical contact) are e-mailed to:

[**]
with a copy to:
Darius Kharabi
[**]

All general notices to Stanford are e-mailed or mailed to:

Office of Licensing
3000 El Camino Real
Building 5, Suite 300
Palo Alto, CA 94306-2100
[**]

All payments to Stanford are mailed to:

Stanford University
Office of Licensing
Department #44439
P.O. Box 44000
San Francisco, CA 94144-4439

All progress reports to Stanford are e-mailed or mailed to:

Office of Licensing
3000 El Camino Real
Building 5, Suite 300
Palo Alto, CA 94306-2100
[**]

Any notice related to Section 7.2 or Section 7.3 (Stanford Purchase Rights) shall be copied concurrently to [**].

Either party may change its address with written notice to the other party.

19. MISCELLANEOUS

19.1 **Combangio Confidential Information**. The content of all reports, audit information and product development, technical, sales, strategy, business or other corporate information disclosed to Stanford OTL by Combangio, its Affiliates or Sublicensees under this Agreement shall be considered "Combangio Confidential Information"; provided, however, that "Combangio Confidential Information" shall not include information that: (i) was publicly known and made generally available in the public domain prior to the time of such disclosure; (ii) becomes publicly known and made generally available to Stanford after such disclosure through no action or inaction of Stanford; (iii) is already in the possession of Stanford at the time of disclosure by the

disclosing party as shown by Stanford's files and records immediately prior to the time of disclosure; (iv) is obtained by Stanford from a third party without a breach of such third party's obligations of confidentiality; or (v) is independently developed by Stanford without use of or reference to other Combangio Confidential Information, as shown by documents and other competent evidence in Stanford's possession. Stanford agrees not to disclose Combangio Confidential Information to third parties or use Combangio Confidential Information for any reason except to the extent required by Stanford's internal governance rules and regulations and to the extent reasonably necessary for Stanford to exercise its rights and obligations under this Agreement. Stanford may acknowledge the existence of this Agreement and the extent of the grant in Article 3 to third parties. Combangio hereby grants permission for Stanford to include Combangio's name and a link to Combangio's website in Stanford's annual reports and on Stanford's websites that showcase technology transfer related stories.

19.2 **Waiver.** No term of this Agreement can be waived except by the written consent of the party waiving compliance.

19.3 **Choice of Law.** This Agreement and any dispute arising under it is governed by the laws of the State of California, United States of America, applicable to agreements negotiated, executed, and performed within California.

19.4 **Entire Agreement**. The parties have read this Agreement and agree to be bound by its terms, and further agree that it constitutes the complete and entire agreement of the parties and supersedes all previous communications, oral or written, and all other communications between them relating to the license and to the subject hereof. The parties agree that this Agreement supersedes all previous and future purchase orders. This Agreement may not be amended except by writing executed by authorized representatives of both parties. No representations or statements of any kind made by either party, which are not expressly stated herein, will be binding on such party.

19.5 **Exclusive Forum.** The state and federal courts having jurisdiction over Stanford, California, United States of America, provide the exclusive forum for any court action between the parties relating to this Agreement. Combangio submits to the jurisdiction of such courts, and waives any claim that such a court lacks jurisdiction over Combangio or constitutes an inconvenient or improper forum.

19.6 **Electronic Copy.** The parties to this document agree that a copy of the original signature (including an electronic copy) may be used for any and all purposes for which the original signature may have been used. The parties further waive any right to challenge the admissibility or authenticity of this document in a court of law based solely on the absence of an original signature.

The parties execute this Agreement in duplicate originals by their duly authorized officers or representatives.

THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY

Signature:	/s/ Scott Elrod
Name:	Scott Elrod
Title:	Associate Director
Date:	Oct 11, 2019

COMBANGIO, INC.

Signature:	/s/ Darius Kharabi
Name:	Darius Kharabi
Title:	President & CEO
Date:	Oct 11, 2019

Appendix A – Milestones

1. Combangio has already provided Stanford a preliminary business plan.

2. By [**], Combangio will have $[**] of available non-contingent, operating capital to proceed with the exploration and development of Licensed Product. Capital will be from a third party who may or may not be an investor in Combangio.

3. By [**], Combangio will provide to Stanford a listing of the management team or a schedule for the recruitment of key management positions.

4. By [**], Combangio will [**].

5. By [**], Combangio will [**].

6. By [**], Combangio will [**].

7. By [**], Combangio will [**].

8. By [**], Combangio will [**].

9. By [**], Combangio will [**].

10. By [**], Combangio will [**].

It is understood that the above Diligence Milestone due dates assume no material delays in the [**]. In the event that there are material delays in the [**] or other factors beyond Combangio's reasonable control, so long as Licensee, its Affiliate or its Sublicensee is diligently pursuing such Diligence Milestone and such delay is not caused by the negligence of Licensee, Affiliate or Sublicensee, the due date for such Diligence Milestone shall be extended by the amount of delay caused.

For purposes of this Agreement, the following capitalized terms shall have the meanings indicated:

"BLA" shall mean a Biological License Application, filed with the United States FDA as more fully defined in 21 C.F.R. § 601.

"FDA" shall mean the United States Food and Drug Administration, any successor entity thereto.

"IND" shall mean an investigational new drug application filed with the FDA as more fully defined in 21 C.F.R. §312.3 or, with respect to a country other than the United States, an institutional review board or ethics committee submission required to initiate a human clinical study in accordance with the laws and regulations of such country.

"NDA" shall mean a New Drug Application, filed with the United States FDA as more fully defined in 21 C.F.R. § 314.

“Phase I Clinical Study” shall mean a study of a Licensed Product in human volunteers or patients with the endpoint of determining initial tolerance, safety and/or pharmacokinetic information in a single dose, single ascending dose, multiple dose and/or multiple ascending dose regimens.

“Phase II Clinical Study” shall mean a study of a Licensed Product conducted on a limited number of human patients for the primary purpose of assessing preliminary clinical efficacy (including effective dose regimen).

“Phase III Clinical Study” shall mean a pivotal study of a Licensed Product in human patients to ascertain efficacy and safety of such Licensed Product for the purpose of preparing and submitting to the FDA a BLA or NDA for a Licensed Product.

Appendix B – **Sample Reporting Form**

Appendix C – **Client and Billing Agreement**

AMENDMENT No. 1

TO THE

LICENSE AGREEMENT EFFECTIVE THE 11TH DAY OF OCTOBER, 2019

BETWEEN

STANFORD UNIVERSITY

AND

COMBANGIO, INC.

Effective the 14th day of February, 2020, THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY ("Stanford"), an institution of higher education having powers under the laws of the State of California, and Combangio, Inc. ("Combangio"), a corporation having a principal place of business at 1490 O'Brien Drive, Menlo Park, CA 94025, agree as follows:

1. BACKGROUND

Stanford and Combangio are parties to an Exclusive License Agreement effective the 11th day of October, 2019 ("Original Agreement") covering the invention entitled "Methods to promote eye wound healing" disclosed in Stanford Docket [**]. Stanford and Combangio wish to amend the Original Agreement to clarify that the patent rights to Stanford Dockets [**] are not under the license to Combangio and are therefore being removed from the list of Licensed Patents.

2. AMENDMENT

2.1 The table of Licensed Patents in Paragraph 2.8 of the Original Agreement is hereby deleted in its entirety and replaced with the following:

Stanford	Country	Patent Type	Patent Status	Serial Number	Date Filed	Expiration Date
[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]

3. OTHER TERMS

3.1 Except as provided above, all other terms of the Original Agreement remain in full force and effect.

3.2 The parties to this document agree that a copy of the original signature (including an electronic copy) may be used for any and all purposes for which the original signature may have been used. The parties farther waive any right to challenge the admissibility or authenticity of this document in a court of law based solely on the absence of an original signature.

The parties execute this Amendment No. 1 by their duly authorized officers or representatives.

THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY

Signature:	/s/ Scott Elrod
Name:	Scott Elrod
Title:	Associate Director
Date:	Feb 14, 2020

COMBANGIO, INC.

Signature:	/s/ Darius Kharabi
Name:	Darius Kharabi
Title:	CEO
Date:	Feb 14, 2020

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

AMENDMENT #4

to

COMMERCIAL SUPPLY AGREEMENT BETWEEN
KALA PHARMACEUTICALS, INC. AND CATALENT PHARMA SOLUTIONS, LLC
(Dry Eye Product and Surgical Product in Multi-Dose Bottles)

This **FOURTH AMENDMENT** ("**Fourth Amendment**") is made and entered into effective as of February 9, 2022 ("**Fourth Amendment Effective Date**"), by and between and between Kala Pharmaceuticals, Inc., a Delaware corporation, with a place of business at 1167 Massachusetts Avenue, Arlington, MA 02476, USA ("**Client**"), and Woodstock Sterile Solutions, Inc., an Illinois corporation, having a place of business at 2210 Lake Shore Drive, Woodstock, IL 60098 ("**Woodstock**"). Each of Client and Woodstock may be referred to as a Party, and collectively as the Parties.

RECITALS:

A. Client and Catalent Pharma Solutions, LLC entered into a Commercial Supply Agreement effective as of June 27, 2016, and amended by the First Amendment thereto dated February 16, 2018, the Second Amendment thereto dated March 27, 2020, and the Third Amendment thereto dated December 11, 2020 (collectively as amended, the "**Agreement**").

B. Effective April 1, 2021, Woodstock became successor in interest to Catalent Pharma Solutions, LLC.

C. Pursuant to Section 18.1 of the Agreement, Client and Woodstock now desire to further amend the Agreement to revise its terms regarding annual price increases.

NOW, THEREFORE, in consideration of the mutual covenants, promises, rights and obligations contained herein, the Parties agree as follows:

1. **Price Increases**. Section 7.2, entitled "Unit Pricing Increase," of the Agreement is hereby deleted in its entirety and replaced with the following:

"**7.2** **Unit Pricing Increase**. Upon at least [**] days prior written notice, the Unit Pricing may be increased [**] by a percentage amount not to exceed [**]; provided that in no case shall such Unit Pricing increase greater than [**] percent ([**]%) above the Unit Pricing in effect during the immediately preceding twelve month period. For the remainder of [**], the Unit Pricing may be increased upon notification to Kala by a percentage amount not to exceed [**]; provided that in no case shall (a) the unit prices that form the bases for Kala purchase orders [**] (copies of which are attached hereto) be subject to any increase and (b) such Unit Pricing increase greater than [**] percent ([**]%) above the Unit Pricing in effect during the immediately preceding twelve month period. Further, any substantial increase in Catalent's cost of Raw Materials shall be passed through to Client, at the sole discretion of Catalent, promptly following Catalent's delivery of notice of such change in

cost, subject to the following: (a) for purposes of this Section 7.2, "substantial" shall mean an increase of [**]% or more in a Raw Material cost; (b) Catalent shall provide to Client written documentation of the change in Catalent's costs for such Raw Material justifying such price change; and (c) any such price change shall be in proportion to the substantial change in Catalent's cost of such Raw Material. If Catalent has passed through a price increase in a Raw Material to Client pursuant to this Section 7 .2, thereafter in the event there is any substantial price decrease in such Raw Material, Catalent shall pass through to Client such substantial price decrease promptly following Catalent's delivery of notice of such change in cost."

2. **Client Notice Address**. Client's address for notices set forth in Article 17 is hereby amended to read as follows:

Kala Pharmaceuticals, Inc.
1167 Massachusetts Avenue
Arlington, MA 02476
ATTN: [**]
[**]
Phone: [**]
Email: [**]

With a copy to

Kala Pharmaceuticals, Inc.
1167 Massachusetts Avenue
Arlington, MA 02476
ATTN: General Counsel

Catalent agrees that it shall not send notices to Client via facsimile.

3. **Other Terms**. Except as expressly amended herein, all other terms and conditions of the Agreement will remain in full force and effect. Any capitalized term used herein and not otherwise defined will have the same meaning as set forth in the Agreement. In the event of any conflict between this Fourth Amendment and the Agreement, the terms of this Fourth Amendment will control.

IN WITNESS WHEREOF, the parties have caused their respective Representatives to execute this Fourth Amendment effective as of the Fourth Amendment Effective Date.

KALA PHARMACEUTICALS, INC.	**CATALENT PHARMA SOLUTIONS, LLC**
By: /s/ Vincent Kosewski	By: /s/ Paul Josephs
Name: Vincent Kosewski	Name: Paul Josephs
Title: Sr. VP Mfg. & Supply	Title: President & CEO

Exhibit 10.35

FIRST AMENDMENT TO LEASE TERMINATION AGREEMENT

THIS **FIRST AMENDMENT TO LEASE TERMINATION AGREEMENT** (this "**First Amendment**"), dated as of December 22, 2021 (the "**Effective Date**"), is entered into by and between **COLUMBIA MASSACHUSETTS ARSENAL OFFICE PROPERTIES, LLC**, a Delaware limited liability company ("**Landlord**"), and **KALA PHARMACEUTICALS, INC.,** a Delaware corporation ("**Tenant**").

RECITALS

A. Landlord, as successor-in-interest to 480 Arsenal Group LLC, a Massachusetts limited liability company, as landlord, and Tenant, as tenant, are parties to that certain Lease dated February 28, 2018 (the "**Lease**"), with respect to the premises consisting of approximately 66,052 rentable square feet on the first (1st) and second (2nd) floors of the East Wing (collectively, the "**Premises**"), located in the building commonly known as 490 Arsenal Way, Watertown, Massachusetts 02472 (the "**Building**").

B. The term of the Lease is scheduled to expire on October 31, 2026, subject to Tenant's right to extend the term in accordance with the terms of the Lease.

C. Landlord and Tenant are parties to that certain Lease Termination Agreement dated November 12, 2021 (the "**Lease Termination Agreement**"), whereby Landlord and Tenant mutually agreed to terminate the Lease upon the terms and conditions set forth in the Lease Termination Agreement.

D. Landlord and Tenant desire to amend certain terms of the Lease Termination Agreement.

NOW THEREFORE, in consideration of the mutual promises and covenants contained herein, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto hereby agree as follows:

AGREEMENT

1. **Definitions**. All capitalized terms contained in this First Amendment shall, for the purposes hereof, have the same meanings ascribed to them in the Lease or the Lease Termination Agreement, as applicable, unless otherwise defined herein.

2. **Termination Date**. As of the Effective Date, subject to all of the terms and conditions of the Lease Termination Agreement, the "**Termination Date**", as such term is defined in the Lease Termination Agreement, shall be amended to be the date that is the earlier of: (i) the date that Tenant decommissions the Premises in accordance with the terms and conditions set forth in Section 10.07 of the Lease, and delivers a copy of the Laboratory Decommissioning Report to Landlord, which Laboratory Decommissioning Report shall not reveal any defects or issues that are unacceptable to Landlord, in Landlord's commercially reasonable discretion, or (ii) January 15, 2022. Following the Termination Date, Landlord and Tenant agree to execute a written certificate to confirm the Termination Date. Except as may be

expressly provided in the Lease Termination Agreement or this Amendment, the obligations of Landlord and Tenant to comply with all covenants and agreements under the Lease shall continue through and including the Termination Date.

3. **Continuing Validity**. Except as specifically amended hereby, all terms, covenants and conditions of the Lease and the Lease Termination Agreement shall remain in full force and effect and are hereby ratified, approved and affirmed. This First Amendment sets forth the entire agreement and between the parties with respect to the matters set forth herein. In the case of any inconsistency between the provisions of the Lease Termination Agreement and this First Amendment, the provisions of this First Amendment shall govern and control.

4. **Severability; Governing Law**. If any clause or provision of this First Amendment is illegal, invalid, or unenforceable under present or future laws, then the remainder of this First Amendment shall not be affected thereby and in lieu of such clause or provision, there shall be added as a part of this First Amendment a clause or provision as similar in terms to such illegal, invalid, or unenforceable clause or provision as may be possible and be legal, valid, and enforceable. This First Amendment shall be governed by and construed in accordance with the laws of the state in which the Premises is located. If Tenant consists of more than one party, each such party shall be jointly and severally liable for Tenant's obligations under this First Amendment.

5. **Time of Essence**. Time is of the essence in the performance of the parties' respective obligations set forth in this First Amendment.

6. **No Further Modification**. The Lease Termination Agreement and this First Amendment shall not be further modified or amended, except in writing signed by both Landlord and Tenant.

7. **Brokers**. Each party hereto represents and warrants to the other that it has dealt with no brokers or finders in connection with this First Amendment. Landlord hereby agrees to indemnify, protect and defend and hold Tenant harmless from and against all losses, claims, costs, expenses, damages (including, but not limited to, attorneys' fees of counsel selected by the indemnified party) resulting from the claims of any broker, finder, or other such party, claiming by, through or under the acts or agreements of Landlord. Tenant hereby agrees to indemnify, protect and defend and hold Landlord harmless from and against all losses, claims, costs, expenses, damages (including, but not limited to, attorneys' fees of counsel selected by the indemnified party) resulting from the claims of any broker, finder, or other such party, claiming by, through or under the acts or agreements of Tenant. The obligations of the parties pursuant to this Section 9 shall survive any termination of this First Amendment.

8. **Counterparts**. This First Amendment may be executed in counterparts each of which shall be deemed an original but all of which taken together shall constitute one and the same instrument. The signature of any party hereto sent to the other via facsimile, PDF or DocuSign shall constitute the valid execution and delivery of this First Amendment by such party.

9. **Benefit**. This First Amendment is for the benefit only of the parties hereto and no other person or entity shall be entitled to rely hereon, receive any benefit herefrom or enforce against any party hereto any provision hereof.

[signatures on following page]

IN WITNESS WHEREOF, the parties hereto have executed this First Amendment to Lease Termination Agreement on the date first above written.

LANDLORD:

Columbia Massachusetts Arsenal Office Properties, LLC
a Delaware limited liability company

By: Columbia Office Properties, LLC
a Delaware limited liability company
Its Sole Member

By: Clarion Partners, LLC
a New York limited liability company
Its Manager

By: /s/ Brian Collins
Name: Brian Collins
Its: Authorized Signatory

TENANT:

KALA PHARMACEUTICALS, INC.
a Delaware corporation

By: /s/ Mary Reumuth
Name: Mary Reumuth
Its: Chief Financial Officer

Exhibit 21.1

Subsidiaries of the Registrant

Name	Jurisdiction of Organization
Kala Pharmaceuticals Security Corporation	Massachusetts
Combangio, Inc.	Delaware

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, 333-239426 and 333-253503 on Form S-8 of our report dated March 29, 2022, relating to the consolidated financial statements of Kala Pharmaceuticals, Inc. and its subsidiaries appearing in the Annual Report on Form 10-K of Kala Pharmaceuticals, Inc. for the year ended December 31, 2021.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 29, 2022

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: March 29, 2022

/s/ Mark Iwicki
Mark Iwicki
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: March 29, 2022

/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, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Mark Iwicki, 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: March 29, 2022

/s/ Mark Iwicki
Mark Iwicki
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, 2021, 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: March 29, 2022

/s/ Mary Reumuth
Mary Reumuth
Chief Financial Officer
(principal financial and accounting officer)