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, 2022
OR

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

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

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**	**02476**
(Address of principal executive offices)	(Zip Code)

(781) 996-5252
(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, $0.001 par value per share	**KALA**	**The Nasdaq Capital Market**

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 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. ☐

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

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

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

As of June 30, 2022, 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 $20.2 million, based on the closing price of the registrant's common stock on June 30, 2022.

There were 2,025,495 shares of Common Stock ($0.001 par value) outstanding as of March 2, 2023.

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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

On October 20, 2022, we effected a 1-for-50 reverse stock split of our common stock either issued and outstanding or held as treasury stock. As a result of the reverse stock split, every 50 shares of issued and outstanding common stock were automatically combined into one issued and outstanding share of common stock, without any change in the par value per share. No fractional shares were issued as a result of the reverse stock split. Any fractional shares that would otherwise have resulted from the reverse stock split were rounded up to the next whole number. Unless otherwise indicated, all historical share and per share amounts in this Annual Report on Form 10-K have been adjusted to reflect the reverse stock split. Proportionate adjustments were made to the per share exercise price and the number of shares of common stock that may be purchased upon exercise of outstanding stock options and warrants, and the number of shares of common stock reserved for future issuance under our 2017 Equity Incentive Plan, as amended, and Employee Stock Purchase Plan.

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," "should," "target," "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 impacts the sale of our commercial business to Alcon Pharmaceuticals Ltd. and Alcon Vision, LLC, which we refer collectively as Alcon, will have on our business, results of operations and financial condition;
- our expectations with respect to, and the amount of, future milestone payments we may receive from Alcon in connection with the sale of our commercial business;
- our expectations with respect to our dependency on and potential advantages of KPI-012, our product candidate for the treatment of persistent corneal epithelial defects, or PCED;
- our expectations with respect to the potential financial impact, synergies, growth prospects and benefits of our acquisition of Combangio, Inc., or Combangio, or the Combangio Acquisition, including our expectations with respect to, and the amount of, future milestone payments we may pay in connection with the Combangio Acquisition;
- our development efforts for KPI-012 and our ability to discover and develop new programs and product candidates;
- the timing, progress and results of clinical trials for KPI-012, 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 any biologics license applications for KPI-012 and any other product candidate we may develop in the future;
- our ability to obtain regulatory approvals for KPI-012;
- our commercialization, marketing and manufacturing capabilities and strategy for KPI-012, if approved;
- our estimates regarding potential future revenue from sales of KPI-012, if approved;
- 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 KPI-012, if approved;
- the rate and degree of market acceptance and clinical utility of KPI-012 and our estimates regarding the market opportunity for KPI-012, if approved;
- plans to pursue the development of KPI-012 for indications in addition to PCED;
- our expectations with respect to our determination to cease the development of our preclinical pipeline programs that are unrelated to our mesenchymal stem cell secretome, or MSC-S, platform, including the development of KPI-287, our receptor tyrosine kinase inhibitor, and our selective glucocorticoid receptor modulators;
- the timing, progress and results of preclinical studies for our KPI-014 program;

- our expectations regarding our ability to fund our operating expenses, debt service obligations, and capital expenditure requirements with our cash on hand;
- our expectations regarding our ability to comply with the covenants under our loan agreement;
- our intellectual property position, including intellectual property acquired in the Combangio 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;
- our anticipated annualized reduction in operating expenses associated with our workforce reduction announced in July 2022; and
- the impact of COVID-19 on our business and operations.

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 filing 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 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. Our estimates of the potential market opportunity for 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.

Risk 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, 2022, we had an accumulated deficit of $587.2 million.
- Our limited operating history and our limited experience 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 will 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 efforts.
- Our substantial indebtedness may limit cash flow available to invest in the ongoing needs of our business, and a failure to comply with the covenants under our loan agreement, such as the requirement that our common stock continue to be listed on The Nasdaq Stock Market, could result in an event of default and acceleration of amounts due.
- The milestone consideration we are eligible to receive in connection with the sale of our commercial business to Alcon is subject to various risks and uncertainties.
- If we are unable to successfully complete the clinical development of, and obtain marketing approval for, KPI-012 or any other product candidate we may develop in the future, or experience significant delays in doing so, or if, after obtaining marketing approvals, we fail to successfully commercialize such product candidates, our business will be materially harmed.
- If clinical trials of KPI-012 or any other product candidate that we develop fail to demonstrate potency, safety and purity to the satisfaction of the U.S. Food and Drug Administration, or 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 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.
- 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 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.
- KPI-012 has been evaluated in a clinical trial outside of the United States, and we may in the future conduct clinical trials for product candidates at sites outside the United States. The FDA may not accept data from trials conducted in such locations.
- The ongoing coronavirus pandemic and the efforts to prevent its spread have adversely impacted our operations, 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.
- Even if KPI-012 or any other product candidates that we may develop in the future receives marketing approval, such products 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.

- If we are unable to establish and maintain sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, if and when necessary, we may not be successful in commercializing 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. KPI-012 and any other product candidate we may develop, if approved, may also compete with existing branded, generic and off-label products.

- We have relied, 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 contract with third parties for the manufacture of 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 product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

- 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.
- We may be unable to obtain and maintain patent protection for our technology or 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 product candidates may be impaired.

- KPI-012 is protected by patent rights 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 products, if and when approved, will be harmed.

Part I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company dedicated to the research, development and commercialization of innovative therapies for rare and severe diseases of the eye. Our product candidate, KPI-012, which we acquired from Combangio, Inc., or Combangio, on November 15, 2021, is a mesenchymal stem cell secretome, or MSC-S, and is currently in clinical development for the treatment of persistent corneal epithelial defects, or PCED, a rare disease of impaired corneal healing. Based on the positive results of a Phase 1b clinical safety and efficacy trial of KPI-012 in patients with PCED, along with favorable preclinical safety and efficacy results, we submitted an investigational new drug application, or IND, to the U.S. Food and Drug Administration, or FDA, which was accepted in December 2022. In February 2023, we dosed our first patient in our CHASE (**C**orneal **H**ealing **A**fter **SE**cretome therapy) Phase 2b clinical trial of KPI-012 for PCED in the United States, and we are targeting reporting top-line safety and efficacy data from this trial in the first quarter of 2024. If the results of the CHASE Phase 2b clinical trial are positive, and subject to discussion with regulatory authorities, we believe this trial could serve as the first of two pivotal trials required to support the submission of a Biologics License Application, or BLA, to the FDA.

We believe the multifactorial mechanism of action of KPI-012 also makes MSC-S a platform technology. We are evaluating the potential development of KPI-012 for additional rare front-of-the-eye diseases, such as for the treatment of Limbal Stem Cell Deficiency and ocular manifestations of moderate-to-severe Sjögren's. In addition, we have initiated preclinical studies under our KPI-014 program to evaluate the utility of our MSC-S platform for inherited retinal degenerative diseases, such as Retinitis Pigmentosa and Stargardt Disease. In connection with the determination to focus our research and development efforts on KPI-012, in 2022, we determined to cease the development of our preclinical pipeline programs that are unrelated to our MSC-S platform. We expect to commercialize in the United States any of our product candidates that receive marketing approval.

We previously developed and commercialized two marketed products, 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 applied a proprietary mucus-penetrating particle drug delivery technology, which we referred to as the AMPPLIFY® Drug Delivery Technology.

On July 8, 2022, we closed the transaction, or the Alcon Transaction, contemplated by the asset purchase agreement, dated as of May 21, 2022, or the Asset Purchase Agreement, by and between us, Alcon Pharmaceuticals Ltd. and Alcon Vision, LLC, which we refer to collectively as Alcon, pursuant to which Alcon purchased the rights to manufacture, sell, distribute, market and commercialize EYSUVIS and INVELTYS and to develop, manufacture, market and otherwise exploit the AMPPLIFY Drug Delivery Technology, which we collectively refer to as the Commercial Business. Alcon also assumed certain liabilities with respect to the Commercial Business at the closing of the Alcon Transaction.

Alcon paid us an upfront cash payment of $60.0 million upon the closing of the Alcon Transaction. Pursuant to the Asset Purchase Agreement, we are also eligible to receive from Alcon up to four commercial-based sales milestone payments as follows: (1) $25.0 million upon the achievement of $50.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2028, (2) $65.0 million upon the achievement of $100.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2028, (3) $75.0 million upon the achievement of $175.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2029 and (4) $160.0 million upon the achievement of $250.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2029. Each milestone payment will only become payable once, if at all, upon the first time such milestone is achieved, and only one milestone payment will be paid with respect to a calendar year. In the event that more than one milestone is achieved in a calendar year, the higher milestone payment will become payable and the lower milestone payment will become payable only if the corresponding milestone is achieved again in a subsequent calendar year. To date, we have not received any milestone payments pursuant to the Asset Purchase Agreement.

On July 8, 2022, we announced that we had committed to a course of action to terminate 113 employees, consisting of our entire commercial sales force and certain employees in our commercial, scientific, manufacturing, finance and administrative functions. The determination to proceed with the workforce reduction was made in the context of the closing of the Alcon Transaction and the changes to the scope of our research and development activities of KPI-012 as more fully described above. The workforce reduction was completed by the end of 2022.

The following table describes the stage of each of our development programs:

Product Candidate	Indication	Route of Administration	Pre-Clinical	Phase 1	Phase 2	Phase 3
KPI-012 for Rare Ocular Surface Disease	Persistent Corneal Epithelial Defect (PCED)	Topical	→	→	→	
	Partial Limbal Stem Cell Deficiency (LSCD)	Topical	→	→		
	Ocular Manifestations of Moderate-to Severe Sjögren's	Topical	→	→		
KPI-014 Program for Rare Inherited Retinal Disease		Intravitreal Injection	→			

We have retained worldwide commercial rights for our MSC-S platform, including KPI-012 and KPI-014. We own and/or exclusively license patents relating to this platform, including U.S. and foreign issued patents and pending patent applications. The expiration dates of the issued U.S. patents that we control covering KPI-012 are scheduled to expire no earlier than 2040, and a portfolio of additional U.S. and ex-U.S. patent applications covering the MSC-S platform is currently in prosecution.

Strategy

Our goal is to become a leading biopharmaceutical company dedicated to the research, development and commercialization of innovative therapies for rare and severe diseases of the front and back of the eye. Key elements of our strategy include:

- ***Advance the clinical development of, and seek regulatory approval for, KPI-012 for the treatment of PCED***. KPI-012 is a novel, human bone-marrow derived MSC-S 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 safety and efficacy trial of KPI-012 in patients with PCED, along with favorable preclinical safety and efficacy results, we submitted an IND to the FDA, which was accepted in December 2022. In February 2023, we dosed our first patient in the CHASE Phase 2b clinical trial of KPI-012 for PCED in the United States. If the results of the CHASE Phase 2b clinical trial are positive, and subject to discussions with regulatory authorities, we believe this trial could serve as the first of two pivotal trials required to support the submission of a 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, co-promotion and other marketing arrangements with one or more third parties.

- ***Advance KPI-012 for additional rare ocular surface disease indications and KPI-014 for rare inherited retinal diseases.*** We are also evaluating the potential of KPI-012 to treat other rare front-of-the-eye diseases, such as Limbal Stem Cell Deficiency and ocular manifestations of moderate-to-severe Sjögren's. In addition, we have initiated preclinical studies of KPI-014, our preclinical program evaluating the utility of our MSC-S platform for inherited retinal degenerative diseases, such as Retinitis Pigmentosa and Stargardt Disease.

- ***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 opportunistically in-licensing or acquiring the rights to complementary products, product candidates and technologies, particularly for the treatment of rare ophthalmic diseases. We also plan to explore a variety of transactions to maximize the value of our assets, including out-licensing transactions, collaborations, distributions and other development and marketing arrangements with one or more third parties for our product candidates.

Our Clinical-Stage Product Candidate

KPI-012 for Persistent Corneal Epithelial Defects

Persistent Corneal Epithelial Defects Overview

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 Oxervate®, 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 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, we believe 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 (Fibronectin)	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 completed Phase 1b clinical trial. KPI-012 has received orphan drug designation from the FDA for the treatment of PCED.

Clinical Development Plan of 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, Mexico. Based on the results of this Phase 1b clinical trial, we initiated a full preclinical development program and submitted an IND application to the FDA for KPI-012, which was accepted in December 2022.

In February 2023, we dosed our first patient in the CHASE Phase 2b clinical trial of KPI-012. The trial includes two patient cohorts, with the initial cohort involving an open label evaluation in two PCED patients to establish safety of the high dose KPI-012 (3 U/ml given QID) to be administered in the study. If no dose-limiting toxicity is observed after one week of dosing in these two patients, then the second cohort of approximately 90 patients will be initiated as a multicenter, randomized, double-masked, vehicle-controlled, parallel-group trial in PCED patients with varying underlying etiologies to evaluate the safety and efficacy of two doses of KPI-012 ophthalmic solution (1 U/ml and 3 U/ml) compared to vehicle when dosed topically four times per day for 56 days. The trial will have an 8-week treatment period with evaluations at frequent times during the dosing period and at 10 weeks and 26 weeks.

The trial is expected to enroll approximately 90 adult patients with PCED, and the primary endpoint of the trial will be complete healing of the PCED at Week 8 as measured by corneal fluorescein staining using a central-reading center assessment of corneal fluorescing staining photographs. We are targeting reporting top-line safety and efficacy data from the CHASE Phase 2b clinical trial in the first quarter of 2024. If the results are positive, and subject to discussions with regulatory authorities, we believe this trial can serve as the first of two pivotal trials required to support the submission of a BLA to the FDA.

Phase 1b Clinical Trial Results of KPI-012

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

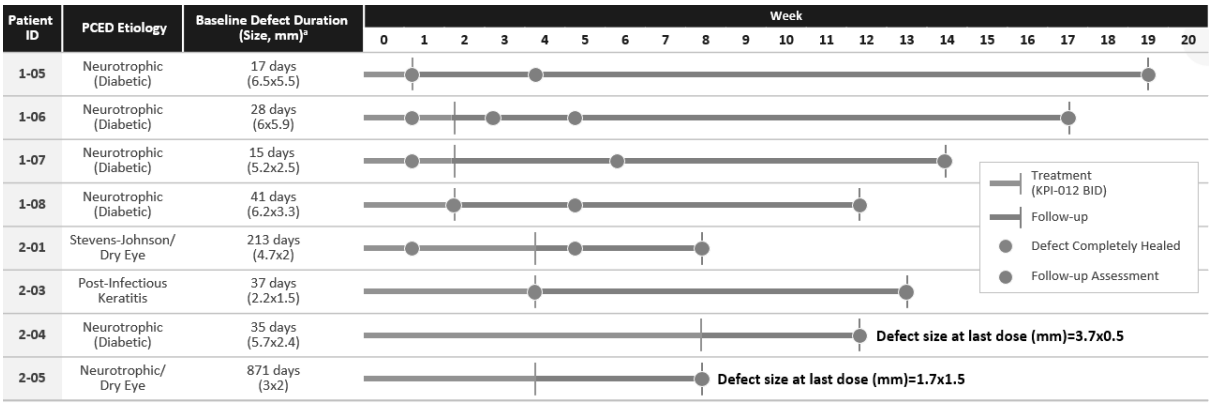
- Subjects with PCED of at least 10 days without improvement from one or more conventional non-surgical treatments in study eye due to any of the following:
  - NK, provided there was no active herpetic infection of the eye in the prior three months
  - Corneal Burns (alkali, acid and thermal)

- Post-photorefractive Keratectomy
- Post-corneal Transplant Surgery
- Corneal epithelial debridement resulting from Diabetic Vitrectomy Surgery
- Trauma
- Keratoconjunctivtis sicca
- Sjögren's
- 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 in the Phase 1b trial 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 adverse events (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 the two other patients 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 both patients, but the corneal staining images did not show complete healing of the defect.



	Mean	Median
PCED Size at Baseline (mm x mm)	5.1 x 3.5	5.6 x 2.9
PCED Duration at Baseline (Days)	58	32
PCED Healing Time (Days) KPI-012, 2x/day	12	7

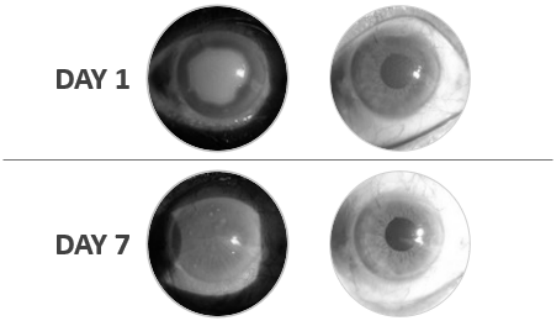


Figure 1. Summary of Phase 1b clinical trial of KPI-012 for PCED, including representative images for a healed patient study eye. The Day 1 images were taken on the first day of treatment, prior to first KPI-012 administration, with the fluorescein (green) stain demarking the corneal wound boundary of 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.

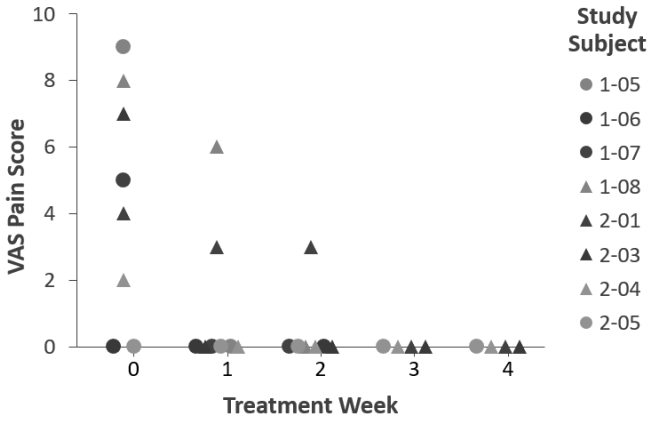


Figure 2. PCED cohort patient-reported score of pain level due to defect using a visual analogue scale, or VAS, which is a subjective rating of pain levels on a scale of 0 to 10 where a score of 0 represents no pain at all and a score of 10 represents the worst possible pain.

KPI-012 Preclinical Studies and Results

KPI-012 was 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.

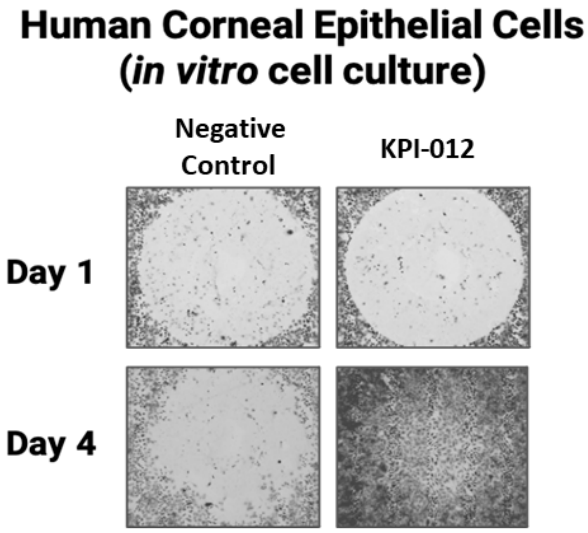


Figure 3. Representative images from an in vitro human corneal epithelial wound closure assay. A mechanical wound instilled to a corneal epithelial cell monolayer on Day 1 healed after treatment with KPI-012 (Day 4 of treatment), but not negative control (vehicle). Depicted images are wounded cell monolayers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

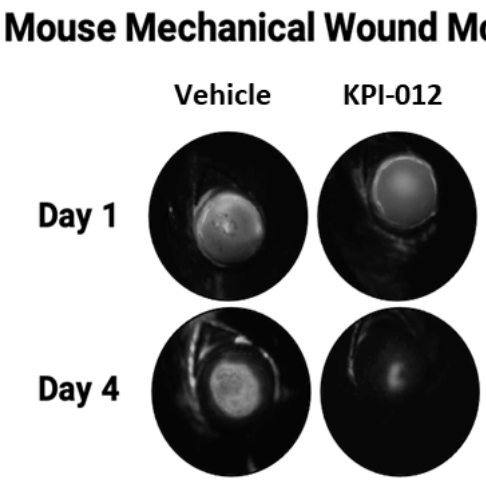


Figure 4. Representative images of wounded mouse corneas after mechanical injury (Day 1). Depicted is the fluorescein (green) stain, which demarks the corneal wound boundary. Treatment with KPI-012 rapidly healed the wound size (as indicated by the disappearance of the green stain by Day 4) relative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

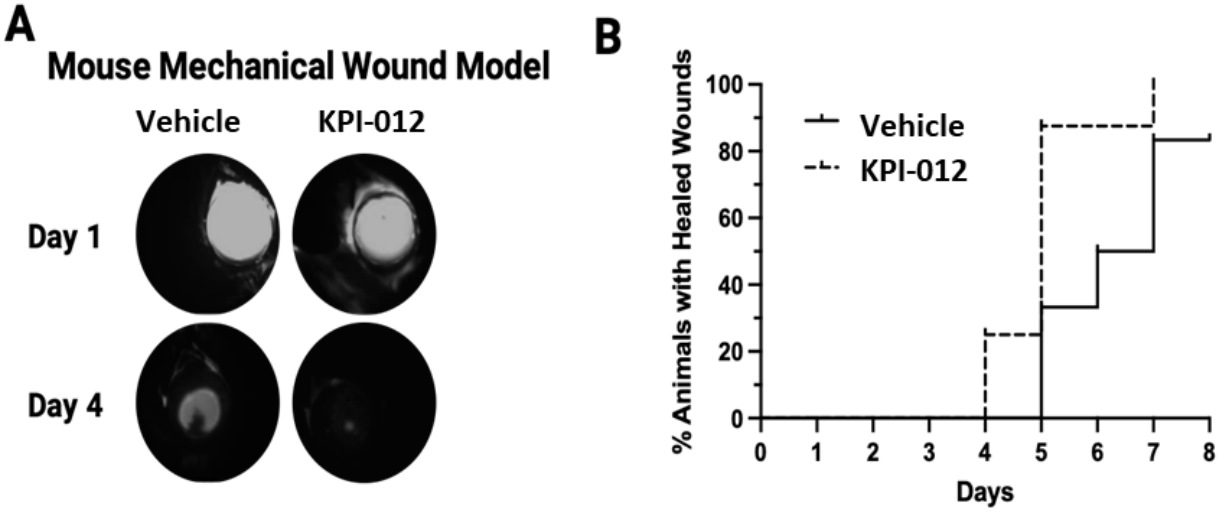


Figure 5. Summary of second mouse corneal mechanical study. (A) Representative images of wounded mouse corneas after mechanical injury (Day 1) and after four days of treatment with KPI-012 or vehicle (Day 4). Depicted is the fluorescein (green) stain, which demarks the corneal wound boundary. Treatment 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).

Other Potential Indications for KPI-012 and for KPI-014

We believe the multifactorial mechanism of action of KPI-012 also makes it a platform technology, and we are evaluating the potential development of KPI-012 for additional rare front of the eye diseases, such as for the treatment of Limbal Stem Cell Deficiency and ocular manifestations of moderate-to-severe Sjögren's. In addition, we have initiated preclinical studies under our KPI-014 program to evaluate the utility of our MSC-S platform for inherited retinal degenerative diseases, such as Retinitis Pigmentosa and Stargardt Disease.

Limbal stem cell deficiency, or LSCD, is an ocular surface disease characterized by the loss or deficiency of stem cells in the junction of the cornea and limbus, where they play an essential role in the generation and repopulation of corneal epithelial cells. When the limbal stem cell population is reduced or depleted, the ability of the corneal epithelium to repair and renew itself is compromised, which can result in recurrent epithelial breakdown, neovascularization, conjunctival overgrowth and other sequalae that can lead to loss of corneal clarity and vision impairment, as well as significant pain and diminished quality of life. There are currently no approved pharmaceutical products for the treatment of LSCD. Approximately 70% of LSCD patients – or about 70,000 patients in the United States – have partial LSCD, meaning they have some level of remaining limbal stem cells but still suffer significant pathology and symptomology. We believe these patients may be appropriate candidates for KPI-012 to maintain the integrity of the ocular surface and to avoid the vision impairment and pain associated with the disease. In addition to the effects of KPI-012 on corneal healing observed in both animal models and in PCED patients, there is data in the literature that suggest that MSC-S can restore the limbal stem cell niche, which would be of significant benefit in both partial or complete LSCD.

Sjögren's is a chronic multisystem autoimmune disease characterized by insufficient fluid production in certain glands of the body leading to substantial dryness, primarily of the eyes and the mouth. Approximately 90% of Sjögren's patients suffer from ocular manifestations and experience significant ocular symptoms, which often impact a patient's daily life and productivity, and as a result, the quality of life in Sjögren's patients can be significantly diminished. Despite current treatment options, many Sjögren's patients do not achieve significant improvement in their ocular symptoms. We believe there is a significant unmet need for new therapies that can provide meaningful improvement in the ocular symptoms, visual impairment and quality of life to the approximately 50% of Sjögren's patients, or roughly 95,000 people in the United States, who suffer with moderate-to-severe disease.

We are also looking to leverage the manufacturing and delivery expertise gained from KPI-012 development to develop a unique secretome formulation – designated as KPI-014 – specific for retinal disease. The initial focus for the program is to target inherited retinal diseases, such as Retinitis Pigmentosa and Stargardt Disease. MSC-S therapies have shown great promise to treat inherited retinal diseases, or IRDs, with the recognition that they function through their secretome (i.e., the secretion of paracrine factors that enhance retinal cell function and survival). We believe an MSC-S engineered for intravitreal delivery may provide an improved treatment option for IRDs as compared to the traditional MSC-based approach.

IRDs are associated with mutations in over 280 different genes, where each IRD has one or more mutations that cause disease onset and results in vision loss. It is projected that over 200,000 individuals in the United States alone suffer from IRDs. While significant progress has been made with gene therapies, these are typically limited to a single gene or mutation. With over 280 different IRD-associated genes, a therapy broadly effective for most IRDs does not currently exist, leaving patients with little-to-no options to slow disease progression and vision loss. We are developing KPI-014 with the goal of providing a broad, genotype-agnostic, therapeutic benefit to reduce vision loss and improve quality of life for patients suffering from IRDs.

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. 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 KPI-012 and any other product candidates that we develop are the 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 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 are currently only two product candidates in active clinical development for the treatment of a broad PCED population. KIO-201, a chemically modified form of the natural polymer hyaluronic acid administered as an eye drop, is currently being studied in a Phase 2 clinical trial in patients with PCED by Kiora Pharmaceuticals, Inc. Nexagon, an antisense oligonucleotide that inhibits connexin43, is currently being studied in a Phase 2 clinical trial in patients with PCED resulting from severe ocular chemical and/or thermal injuries, by Amber Ophthalmics.

A number of companies are pursuing development of product candidates for the treatment of NK, including ReGenTree, LLC (Timbetasin), Recordati S.p.A. (Udonitrectag) and Claris Biotherapeutics, Inc. (CSB-001).

Competition in Limbal Stem Cell Deficiency and Sjögren's

Competitive products and product candidates in LSCD include two stem cell-based approaches. ABCB5+ limbal stem cells, which are being studied in Phase 1/2 clinical trials and are being developed by RHEACELL GmbH & Co. KG, utilize allogeneic limbal stem cells derived from human corneal rims, which are expanded ex-vivo and manufactured as an advanced-therapy medicinal product. Holoclar utilizes autologous limbal stem cells derived from the healthy portion of the patient's eye. Holoclar is approved in the European Union for treatment of LSCD caused by ocular burns and is developed by Chiesi. To our knowledge, there are no products in development focused on Partial Limbal Stem Cell Deficiency.

Competitive pharmaceutical products in moderate-to-severe Sjögren's include cyclosporine, lifitegrast, ophthalmic cortisone and systemic immunosuppressants. To our knowledge, there are only two topical ophthalmic product candidates in active clinical development for ocular manifestations of moderate-to-severe Sjögren's. Lacripep™, a synthetic peptide fragment of lacritin being developed by Tear Solutions, recently completed a Phase 2 clinical trial in patients with primary Sjögren's-associated ocular surface disease. Oxervate® (cenegermin-bkbj) is currently being evaluated in Phase 3 clinical trials in patients with severe Sjögren's dry eye disease. Several systemic pharmaceutical product candidates are also in clinical development for the treatment of Sjögren's, including Dazodalibep (Horizon Therapeutics), SAR-441344 (Sanofi), Ianalumab (Novartis), Branebrutinib (Novartis), Iscalimab (Novartis) and OSE-127 (OSE Immuno Therapeutics).

Sales and Marketing

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 KPI-012, if approved, in certain markets outside the United States utilizing a variety of collaboration, distribution, co-promotion, distribution and other marketing arrangements with one or more third parties.

Manufacturing and Supply

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 utilize our substantial in-house expertise and know-how to develop and scale-up our manufacturing processes before these processes are transferred to third-party contract manufacturers, and to understand and establish controls of critical process parameters. We also have personnel with deep product development experience who actively manage the third-party contract manufacturers producing KPI-012 and plan to use such personnel to manage third-party contract manufacturers for any products that we may develop in the future.

We also rely, and expect to continue to rely, on third parties for packaging, labeling, sterilization, storage, distribution and other production logistics for KPI-012. We have only limited supply 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 MSC-S 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 MSCs 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 trial was cultivated using a planar culture model, we implemented a bioreactor cultivation model for our ongoing CHASE Phase 2b clinical trial of KPI-012. We also plan to utilize 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 are 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 knowhow, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We seek to protect our proprietary position by, among other methods, filing U.S. and certain foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business, where patent protection is available. We also rely on trade secrets, know--how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

As of February 15, 2023, we owned 49 U.S. issued patents and 9 U.S. patent applications, as well as 55 foreign issued patents and 41 foreign patent applications (including Patent Cooperation Treaty, or PCT, applications). We exclusively licensed one U.S. patent application, as well as two 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:

- Three U.S. patents and two U.S. patent applications relating to pharmaceutical compositions including KPI-012 for treating ocular conditions, and 18 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 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;

- 43 U.S. patents and 7 U.S. patent applications, relating to TKI compounds, including KPI-287, and their uses, and 50 related foreign patents, and 23 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; and

Three U.S. patents relating to antibiotic compounds and their uses, and five related foreign patents, 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.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.

Licensing and Other Arrangements

Stanford University License Agreement

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 required to pay Stanford a low double-digit percentage of certain consideration we receive as a result of granting sublicenses to the licensed patents. In connection with our acquisition of Combangio, we paid Stanford 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.

Combangio Merger Agreement

In connection with the acquisition of Combangio on November 15, 2021, we entered into an Agreement and Plan of Merger, or the Merger Agreement, with Combangio. In connection with 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 155,664 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 136,314 shares of common stock which were issued on January 3, 2022 and (ii) an aggregate of 19,350 shares of common stock that were initially held back as partial security for the satisfaction of indemnification obligations and other payment obligations of the Combangio Equityholders and that will be issued in March 2023 upon escrow release.

In addition, pursuant to the Merger Agreement, the Combangio Equityholders are entitled to receive from us up to $105.0 million in payments that are contingent upon the achievement of specified development, regulatory and commercialization milestones, or the Contingent Consideration, and are payable in cash and shares of our common stock, subject to the Share Cap (as defined below), of which $4.9 million will be paid in March 2023. If the issuance of the Deferred Purchase Consideration or any contingent consideration payable in shares of our common stock, or the 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 such consideration in excess of the Share Cap in cash. The portion of any payment of Contingent Consideration payable in cash is referred to as "Contingent Cash Consideration".

Upon dosing of the first patient in our CHASE Phase 2b clinical trial of KPI-012 for PCED in the United States in February 2023, or the Dosing Milestone, in March 2023 we will pay to the former Combangio Equityholders an aggregate of $2.5 million in cash and $2.4 million in shares of our common stock (representing an aggregate of 105,039 shares of our common stock). The remaining amount of $0.1 million will be paid in January 2024. Upon payment of the Dosing Milestone, we reached the Share Cap and any Contingent Consideration payable under the Merger Agreement in the future will be paid only in cash.

Subject to the terms and conditions of the Merger Agreement, the former Combangio Equityholders are entitled to receive from us the following remaining Contingent Consideration in cash:

- (i) $5.0 million payable 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 pivotal clinical trial, (ii) $12.5 million payable upon regulatory approval by the FDA of marketing and sale of a Product Candidate in the United States, subject to certain specified reductions; (iii) $17.5 million payable upon the first commercial sale of a Product Candidate in the United States, subject to certain specified reductions and (iv) an aggregate of up to $65.0 million payable 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 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.

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.

Securities Purchase Agreement for Private Placement

On November 28, 2022, we entered into a Securities Purchase Agreement, or the Securities Purchase Agreement, with certain institutional investors named therein, or the Purchasers, pursuant to which we agreed to issue and sell, in a private placement priced at-the-market under Nasdaq rules, shares of our common stock and shares of our Series E Convertible Non-Redeemable Preferred Stock, or Series E Preferred Stock, in two tranches for aggregate gross proceeds of up to $31.0 million, which we refer to collectively as the Private Placement.

Pursuant to the Securities Purchase Agreement, if at any time during the four-year period following the date of the first tranche closing, or the Participation Period, we propose to offer and sell new equity securities in an offering that is conducted pursuant to an exemption from registration under the Securities Act of 1933, as amended, or the Securities Act, or in an offering that is registered under the Securities Act that is not conducted as a firm-commitment underwritten offering, then, subject to compliance with securities laws and regulations, we have agreed to offer each Purchaser the right to purchase its pro rata share of the total amount of the new equity securities, subject to certain conditions and limitations. In addition, if during the Participation Period, we propose to offer and sell new equity securities in a firm-commitment underwritten offering registered under the Securities Act, then subject to compliance with securities laws and regulations, we have agreed to use our commercially reasonable efforts to cause the managing underwriters of such offering to contact the Purchasers about potentially participating in such offering and to provide to each Purchaser the opportunity to purchase its pro rata share of such new equity securities, subject to certain conditions and limitations. The participation rights will terminate if the Purchasers are offered the opportunity to participate in an offering pursuant to the participation rights and do not purchase at least 50% of their aggregate pro rata share of the new equity securities offered for sale in such offering.

Pursuant to the Securities Purchase Agreement, the Purchasers have the right to have up to two non-voting observers attend and participate in all Board and committee meetings and, subject to the Purchasers owning directly specified minimum amounts of our common stock, the right to have the Board nominate and recommend for election by the stockholders up to three Purchaser designees to the Board (one designee at 9.9%, two designees at 15.0% and three designees at 25.0%) designated by the Purchasers, provided that at such time as the Purchasers have designated three Board designees, at least one such designee must qualify as an "independent" director under Nasdaq rules and be acceptable to the members of the Board who are not Purchaser designees.

The Purchasers' participation rights, observer rights and Board designation rights also will terminate at such time as the Purchasers and their affiliates cease to own, in the aggregate, specified minimum amounts of the shares purchased in the Private Placement.

Pursuant to the Securities Purchase Agreement, we agreed that we will not without the prior approval of the requisite Purchasers (i) issue or authorize the issuance of any equity security that is senior or *pari passu* to the Series E Preferred Stock with respect to liquidation preference, (ii) incur any additional indebtedness for borrowed money in excess of $1,000,000, in the aggregate, outside the ordinary course of business, subject to specified exceptions, including the refinancing of our existing indebtedness or (iii) pay or declare any dividend or make any distribution on, any shares of our capital stock, subject to specified exceptions. In connection with the Private Placement, we have also entered into a registration rights agreement with the Purchasers, pursuant to which the Purchasers are entitled to certain resale registration rights with respect to the shares of common stock acquired in the Private Placement and the shares of common stock issuable upon conversion of the shares of Series E Preferred Stock acquired in the Private Placement.

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, biological products, or biologics, are licensed for marketing by the FDA under the Public Health Service Act, or the PHSA, and regulated by the FDA under the Food, Drug and Cosmetic Act, or FDCA. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor. A sponsor seeking approval to market and distribute a new 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 a BLA requesting marketing approval for one or more proposed indications, including payment of application user fees;
- review of the 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 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 BLA; and
- FDA review and approval of the 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 a sponsor 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. These studies are typically referred to as IND-enabling studies. 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 BLA. In support of a request for an IND, sponsors 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 has issued several Notices of Noncompliance to manufacturers since 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 a 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 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 a 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 December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans.

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 a BLA is submitted (Pre-BLA meeting). Meetings at other times may also be requested. There are four 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-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. Finally, a type D meeting is focused on a narrow set of issues (should be limited to no more than two focused topics) and should not require input from more than three disciplines or divisions.

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. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Manufacturing facilities 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, or PREA, 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 sponsor plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The sponsor, 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 sponsor may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the sponsor, 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. The law now requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. It further requires the FDA to publicly post the PREA Non-Compliance letter and sponsor's response. 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. None of these expedited programs, however, changes the standards for approval but they may help expedite the development or approval process of product candidates.

- *Fast Track designation*: Product candidates 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.
- *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. With passage of the Food and Drug Omnibus Reform Act, or FDORA, in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to: require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require a sponsor of a product granted accelerated approval to submit progress reports on its

post-approval studies to FDA every six months (until the study is completed; and use expedited procedures to withdraw accelerated approval of a BLA after the confirmatory trial fails to verify the product's clinical benefit. Further, FDORA requires the agency to publish on its website "the rationale for why a post-approval study is not appropriate or necessary" whenever it decides not to require such a study upon granting accelerated approval.

- *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.

Acceptance and Review of 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 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, 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 2023 this application fee is approximately $3.25 million), and the sponsor of an approved application is also subject to an annual program fee, currently more than $394,000 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 sponsor 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 sponsor. 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 sponsor 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 sponsor 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. With passage of FDORA, Congress clarified FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to FDA as well as other persons holding study records or involved in the study process. To ensure cGMP and GCP compliance by its employees and third-party contractors, a sponsor 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 sponsor 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 BLAs

The FDA reviews a BLA 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 investigational product 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 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 sponsor 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 sponsor 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 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.

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 , such as distributing scientific or medical journal information. Further, with passage of the Pre-Approval Information Exchange Act, or PIE Act, in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance but the new legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products.

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.

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 sponsor 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 sponsor 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. In December 2022, Congress clarified through FDORA that FDA may approve multiple first interchangeable biosimilar biological products so long as the products are all approved on the first day on which such a product is approved as interchangeable with the reference 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 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 sponsor agreeing to perform, and reporting on, the requested clinical trials within the statutory timeframe. This six-month

exclusivity may be granted if a 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." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, FDA announced that, in matters beyond the scope of that court order, FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

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 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 sponsor 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 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 were suspended and reduced through the end of June 2022, 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 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 has been delayed until January 1, 2026 by the Infrastructure Investment and Jobs Act.

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.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028 and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a

potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at 2,000 a year.

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.

In 2018, California passed into law the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation, or GDPR, in Europe, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or CPRA, which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities. In addition, other states, including Virginia, Colorado, Utah and Connecticut already have passed state privacy laws. Virginia's privacy law also

went into effect on January 1, 2023, and the laws in the other three states will go into effect later in the year. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

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, a sponsor 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 main characteristics of the new Clinical Trials Regulation include: a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

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 sponsor 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, a sponsor 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 sponsor 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 sponsors 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 sponsor 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, but sponsors can also request EMA to conduct an accelerated assessment, for instance, in cases of unmet medical needs.

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 sponsors 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 a sponsor 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 sponsor 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.

Additionally, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-US Privacy Shield. The European Commission initiated the process to adopt an adequacy decision for the EU-US Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court.

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, 2022, we had a total of 34 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 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 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 $44.8 million and $142.6 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $587.2 million. Prior to the sale of our commercial business to Alcon Pharmaceuticals Ltd. And Alcon Vision, LLC, or collectively Alcon, in July 2022, we generated only limited revenues from sales of EYSUVIS and INVELTYS. We have financed our operations primarily through proceeds from the sale of our commercial business to Alcon in July 2022, our initial public offering, follow-on public offerings of common stock and sales under our at-the-market offering facilities, private placements of common stock and 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 prior to the sale of our commercial business to Alcon in July 2022, engaging in activities to launch and commercialize EYSUVIS and INVELTYS. As of result of the acquisition of Combangio in November 2021, or the Combangio Acquisition, and the sale of our commercial business to Alcon, we are devoting, and intend to continue to devote, substantial financial resources to the research and development and potential commercialization of KPI-012, our product candidate in clinical development for the treatment of persistent corneal epithelial defects, or PCED, and any other indications we determine to pursue. We have no revenue-generating commercial products, our cash flows have diminished as a result of the sale of our commercial business to Alcon and, as a result of our acquisition of Combangio, we may be required to pay certain milestones and royalty payments to former equityholders of Combangio.Although we are eligible to receive up to $325.0 million in payments from Alcon based upon the achievement of specified commercial sales-based milestones with respect to EYSUVIS and INVELTYS, there can be no assurance as to when we may receive such milestone payments or of the amount of milestone payments we may receive, if any. We expect to continue to incur significant expenses and operating losses for the foreseeable future, 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 in the future as we conduct any necessary preclinical studies and clinical trials and other development activities for any other product candidates we may develop in the future, including our ongoing preclinical studies under our KPI-014 program, which is a mesenchymal secretome formulation that is in preclinical development for the treatment of inherited retinal degenerative diseases, such as Retinitis Pigmentosa and Stargardt Disease. If we obtain marketing approval for KPI-012 or any product candidates we may develop, we expect that our selling, general and administrative expenses will increase substantially if and as we incur commercialization expenses related to product marketing, sales and distribution.

Our expenses will also increase if and as we:

- 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;
- grow our sales, marketing and distribution capabilities in connection with the commercialization of any product candidates for which we may submit for and obtain marketing approval;
- initiate and progress any preclinical development programs under our mesenchymal stem cell secretome, or MSC-S platform, including from our KPI-014 program;
- conduct clinical trials and other development activities and/or seek marketing approval for any product candidates we may develop in the future;
- in-license or acquire the rights to other products, product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control, scientific, manufacturing, commercial and management personnel to support our operations;
- expand our operational, financial and management systems; and
- increase our product liability insurance coverage if we initiate commercialization efforts for our product candidates.

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 U.S. Food and Drug Administration, or 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. We do not expect to generate revenue from KPI-012 or any other product candidate we may develop for the foreseeable future, if at all. Achieving and maintaining profitability will require us to be successful in a range of challenging activities, including:

- completing the clinical development of KPI-012 for PCED and any other indications we determine to pursue;
- subject to obtaining favorable results from our ongoing and planned clinical trials of KPI-012, applying for and obtaining marketing approval of KPI-012;

- successfully commercializing KPI-012, if approved;
- discovering, developing and successfully seeking marketing approval and commercialization of any additional product candidates we may develop in the future, including under our KPI-014 program;
- hiring and building a full commercial organization required for marketing, selling and distributing those products for which we obtain marketing approval;
- manufacturing at commercial scale, marketing, selling and distributing those products for which we obtain marketing approval;
- achieving an adequate level of market acceptance, and obtaining and maintaining coverage and adequate reimbursement from third-party payors for any products we commercialize;
- obtaining, maintaining and protecting our intellectual property rights; and
- adapting our business in response to the pandemic health event resulting from COVID-19 and its collateral consequences.

As a company, we have limited experience commercializing products, and we may not be able to commercialize a product successfully in the future. 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.

We may never succeed in the foregoing activities and we 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 and our limited experience in developing biologics may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Our operations to date have been limited to organizing and staffing our company, acquiring rights to intellectual property, business planning, raising capital, conducting research and development activities, and prior to the sale of our commercial business to Alcon in July 2022, developing and commercially launching EYSUVIS and INVELTYS. While we have had experience with obtaining marketing approval for and commercially launching two commercial products, we no longer have any commercial products following the sale of our commercial business to Alcon, we have only one product candidate in clinical development and we cannot be certain that we will be able to develop, obtain marketing approval for and commercialize a product in the future. If we are successful in developing and obtaining marketing approval for KPI-012 or any product candidate we may develop in the future, we will again have to transition from a company with a research and development focus to company capable of supporting commercial activity. We may not be successful in such a transition. In addition, prior to our acquisition of KPI-012 in November 2021, we had no prior experience developing biological product candidates. As such, we may encounter delays or difficulties in our efforts to develop and commercialize KPI-012.

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 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 will 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 efforts.

We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we conduct research and development activities, and initiate clinical trials of, and seek regulatory approval for, KPI-012 and any other product candidate that we develop in the future. If we do obtain regulatory approval for KPI-012 or any other product candidate that we develop, we expect to incur commercialization expenses related to product sales, marketing, distribution and manufacturing capabilities. Accordingly, we will 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 future commercialization efforts.

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

- the timing and amount of milestone payments we ultimately receive from Alcon under the asset purchase agreement;
- the timing and amount of our future milestone payments to Combangio equityholders under the merger agreement;
- the progress, costs and results of our ongoing and 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 costs and timing of commercialization activities for KPI-012, if approved, including establishing product sales, marketing, medical affairs, distribution and outsourced manufacturing capabilities;
- our ability to successfully commercialize KPI-012, if approved, in the United States and other jurisdictions and the amount of revenue received from commercial sales;
- 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, including under our KPI-014 program;
- 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 $70.5 million as of December 31, 2022, will enable us to fund our operations, debt service obligations, and capital expenditure requirements into the first quarter of 2025. We expect that our existing cash resources will be sufficient to enable us to obtain safety and efficacy data from our ongoing CHASE Phase 2b clinical trial of KPI-012 in PCED. However, we do not expect that our existing cash resources will be sufficient to enable us to complete the clinical development of KPI-012 for PCED or any other indication. We have based our estimates 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.

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 we develop. 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 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 any 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 rights and 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 and covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

For example, 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 addition, under our securities purchase agreement for our December 2022 private placement, we have agreed that we will not, without the prior approval of the requisite investors in the private placement (1) issue or authorize the issuance of any equity security that is senior or *pari passu* to the Series E Convertible Non-Redeemable Preferred Stock with respect to liquidation preference, (2) incur any additional indebtedness for borrowed money in excess of $1,000,000, in the aggregate, outside the ordinary course of business, subject to specified exceptions, including the refinancing of its existing indebtedness or (3) pay or declare any dividend or make any distribution on, any of our shares of capital stock, subject to specified exceptions.

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 and a failure to comply with the covenants under our Loan Agreement, such as the requirement that our common stock continue to be listed on the Nasdaq Stock Market, could result in an event of default and acceleration of amounts due.

We have a substantial amount of indebtedness. As of December 31, 2022, we had $43.3 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%. On December 27, 2022, we entered into an amendment to the Loan Agreement, pursuant to which the lender and agent agreed to amend certain provisions of the Loan Agreement to permit the transfer of the listing of our common stock from The Nasdaq Global Select Market to The Nasdaq Capital Market in consideration for our agreement to prepay certain amounts outstanding under the Loan Agreement. In January 2023, in

satisfaction of our obligations under the amendment, we paid down $9.3 million of principal under the Loan Agreement, plus final payment fees and accrued and unpaid interest thereon. Following such prepayment, the aggregate principal amount outstanding under the Loan Agreement was $34.0 million.

In addition, under the loan amendment, the start date for amortization payments under the Loan Agreement was changed from January 1, 2026 to January 1, 2025, at which time the aggregate principal balance of the term loan then outstanding under the Loan Agreement is required to be repaid in five monthly installments. Pursuant to the Loan Agreement, we may also make partial prepayments of the term loan to the lender, subject to specified conditions, including the payment of applicable fees and accrued and unpaid interest on the principal amount of the term loan being repaid. Our obligations under the Loan Agreement are secured by substantially all of our assets.

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, particularly if we are in default under our Loan Agreement and all of our indebtedness under the Loan Agreement is due, and funds from external sources may not be available on a timely basis or 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. In particular, the delisting of our common stock from The Nasdaq Capital Market or the transfer of the listing of our common stock to another nationally recognized stock exchange having listing standards that are less restrictive than The Nasdaq Capital Market, in each case after a specified cure period, are events of default under our Loan Agreement.

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 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.

The milestone consideration we are eligible to receive in connection with the sale of our commercial business to Alcon is subject to various risks and uncertainties.

The milestone consideration we are eligible to receive for the sale of our commercial business to Alcon is subject to various risks and uncertainties. In addition to the upfront payment of $60.0 million we received from Alcon at closing, we are eligible to receive up to four commercial-based sales milestone payments as follows: (1) $25.0 million upon the achievement of $50.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2028, (2) $65.0 million upon the achievement of $100.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2028, (3) $75.0 million upon the achievement of $175.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2029 and (4) $160.0 million upon the achievement of $250.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2029.

We cannot predict what success, if any, Alcon and its affiliates may have with respect to sales of EYSUVIS and INVELTYS and, therefore, it is uncertain as to when we may receive the milestone payments, which milestone payments we may receive and if we will receive any milestone payments at all. If we do not receive some or all of the milestone payments, our business will be harmed.

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 fair value of warrants, contingent consideration, 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. In particular, to report historical product revenue, we estimated the amount of our products that may be returned and presented this amount as a reduction of revenue in the period the related product revenue was recognized, in addition to establishing a liability. If our product return estimates are lower than the actual amount of product returns we experience, our existing reserves will be insufficient to cover future returns. 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.

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 results of operations.

Risks Related to Product Development

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

As a result of the sale of our commercial business to Alcon in July 2022, including our commercial products, EYSUVIS and INVELTYS, and our decision to cease the development of our preclinical pipeline programs that are unrelated to our MSC-S platform, we are substantially dependent on the success of KPI-012 and any other product candidate we may develop in the future. As a result, we intend to devote a substantial portion of our research and development resources and business efforts to the development of KPI-012.

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

- completing and obtaining favorable results from our ongoing and planned clinical trials of KPI-012 and any other product candidate we develop;
- clearance of any investigational new drug application, or IND, submission for any other product candidates 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;
- if approved, successfully launching and commercializing 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;
- if approved, obtaining 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 any such approved 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 potency, purity and 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 we may develop in the future, which would materially harm our business. We may never generate the necessary data or results required to

obtain regulatory approval of KPI-012 or any other product candidate we develop and the commercialization of KPI-012 or any other product candidate we develop may never occur.

If clinical trials of KPI-012 or any other biological product candidate that we develop fail to demonstrate potency, safety and purity 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 potency, purity and safety for a biologic product 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 trial of KPI-012 in 12 patients with PCED may not be indicative of future results in later stage clinical trials, including in our ongoing CHASE Phase 2b clinical trial of KPI-012 in patients with PCED. 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 potency, safety and purity in any clinical trial could negatively impact the perception of our other product candidates and/or cause the FDA or other regulatory authorities to require additional testing before approving any of our product candidates. For example, in our STRIDE 2 Phase 3 clinical trial evaluating the safety and efficacy of EYSUVIS versus placebo in patients with dry eye disease, we did not achieve statistical significance for the primary symptom endpoint of ocular discomfort severity, and subsequently we received a complete response letter from the FDA indicating that positive efficacy data from an additional clinical trial was needed to support a new drug application for EYSUVIS.

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 may 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.

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 ongoing and 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 product candidates, we may need to abandon or limit our development and/or commercialization efforts for such product candidates.

If 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 any of our 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. 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 eye 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 a product by patients could result in additional unexpected side effects or adverse events. There can be no assurance that any product we may develop will

be used correctly, and if used incorrectly, such misuse could hamper commercial adoption or market acceptance of such 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. In July 2022, we sold our commercial business, including EYSUVIS and INVELTYS, to Alcon and we made a strategic determination to cease the development of our preclinical pipeline programs that are unrelated to our MSC-S platform and to focus our research and development efforts on KPI-012.

We may never realize the anticipated benefits of these decisions and, as a result, 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 KPI-012 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 been evaluated in clinical trials outside of the United States, and we may in the future conduct clinical trials for product candidates at sites outside the United States. 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 a Phase 1b clinical trial of KPI-012 for PCED in 12 patients in Mexico. Based on the results of the Phase 1b clinical trial conducted in Mexico, we initiated a full preclinical development program and submitted an IND application to the FDA for KPI-012 which was approved in December 2022, and in February 2023, we dosed our first patient in the CHASE Phase 2b clinical trial of KPI-012 for PCED in the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

The ongoing coronavirus pandemic and the efforts to prevent its spread have adversely impacted our operations, 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.

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 KPI-012 and any other product candidates we develop, 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, including our ongoing CHASE Phase 2b clinical trial, or any other product candidates that we develop.

Additionally, while we currently are not experiencing interruptions in our manufacturing of 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. 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 the market for INVELTYS, which is indicated for the treatment of inflammation and pain following ocular surgery. The COVID-19 pandemic had negatively impacted our revenues from INVELTYS. In addition, the COVID-19 pandemic has generally had an adverse impact on the launch of pharmaceutical products, and we believe the pandemic impacted our launch of EYSUVIS. We cannot predict whether the COVID-19 pandemic will impact Alcon's ability to commercialize EYSUVIS and INVELTYS, and as a result, we cannot be certain whether the COVID-19 pandemic might adversely affect when we may receive milestone payments from Alcon, which milestone payments we may receive and if we will receive any milestone payments at all.

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 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 treatments, and the impact of the foregoing on our 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.

Risks Related to the Commercialization of our Product Candidates

Even if KPI-012 or any other product candidates that we may develop in the future receives marketing approval, such products 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.

If KPI-012 or any other product candidate that we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by clinicians, patients, third-party payors and others in the medical community. 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.

Biosimilar and generic versions of any products that compete with KPI-012 or any other product candidates we may develop would likely be offered at a substantially lower price than we expect to offer for our product candidates, if approved. As a result, clinicians, patients and third-party payors may choose to rely on such products rather than our product candidates.

Our assessment of the potential market opportunity for KPI-012 is based on industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. 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 PCED is difficult to precisely estimate. Our estimates of the potential market opportunities for 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 KPI-012 for PCED may be smaller than we expect, and as a result our future 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 KPI-012.

If KPI-012 or any other product candidate for which we may obtain marketing approval does 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 KPI-012 or any other product candidate for which we may obtain marketing approval, will depend on a number of factors, including:

- the efficacy and potential advantages of 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;
- the clinical indications for which the product is licensed or 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 KPI-012 or any other product candidate that we may develop, if and when they are approved, 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 KPI-012 or any other product candidate that we may develop if and when they are approved 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 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 KPI-012 or any other product candidate that we may 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 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 KPI-012 or any other product candidate if and when they are approved.

There may be significant delays in obtaining coverage and reimbursement for newly approved products and coverage may be more limited than the indications for which the product is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for coverage and reimbursement does not imply that a product 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 products, 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 product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products 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 products 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 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 product 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.

Even if a product candidate we develop is approved for sale in the United States or in other countries, there can be no assurance that such product candidate 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 such product candidate profitably.

If we are unable to establish and maintain sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, if and when necessary, we may not be successful in commercializing KPI-012 or any other product candidate that we may develop if and when they are approved.

We established a sales, marketing and distribution infrastructure for the commercial launch of INVELTYS and EYSUVIS, and, as a company, we have limited experience in the sales, marketing and distribution of therapeutic products. Following the sale of our commercial business to Alcon in July 2022 and our determination to focus our research and development efforts on KPI-012, we committed to a course of action to terminate 113 employees, consisting of our entire commercial sales force and certain employees in our commercial, scientific, manufacturing, finance and administrative functions. To achieve commercial success for any product for which we obtain marketing approval in the future, we will again need to establish sales, marketing and distribution capabilities, either ourselves or through collaborations or other arrangements with third parties.

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. Establishing and maintaining a sales force would require us to continue to implement and improve our managerial, operational and financial systems, which we may not do effectively. Any inability to manage growth, when necessary, 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.

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 a larger sales force and at a higher cost than previously anticipated. If the commercial launch of any product candidate for which we establish a commercial infrastructure is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition any such sales, marketing and distribution personnel.

Factors that may inhibit our efforts to commercialize on our own KPI-012 or any other product candidate we develop, if and when approved, 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 establishing, 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 KPI-012 in certain markets outside the United States utilizing a variety of collaboration, distribution, co-promotion 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 KPI-012 ourselves. We may also consider seeking marketing approval outside the United States for other product candidates we may develop 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 KPI-012 or any other product candidate we may develop 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 any product candidate for which we obtain marketing approval. If we do not establish and maintain our sales, marketing and distribution capabilities successfully, when needed, either on our own or in collaboration with third parties, we will not be successful in commercializing any 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. KPI-012 and any other product candidate we may develop, if approved, 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 our product candidate, KPI-012, and we will face competition with respect to 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.

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 are currently only two product candidates in active clinical development for the treatment of a broad PCED population. To our knowledge, there are currently only two product candidates in active clinical development for the treatment of a broad PCED population. KIO-201, a chemically modified form of the natural polymer hyaluronic acid administered as an eye drop, is currently being studied in a Phase 2 clinical trial in patients with PCED by Kiora Pharmaceuticals, Inc. Nexagon, an antisense oligonucleotide that inhibits connexin43, is currently being studied in a Phase 2 clinical trial in patients with PCED resulting from severe ocular chemical and/or thermal injuries, by Amber Ophthalmics. A number of companies are pursuing development of product candidates for the treatment of NK, including ReGenTree, LLC (Timbetasin), Recordati S.p.A. (Udonitrectag) and Claris Biotherapeutics, Inc. (CSB-001).

We are also aware of potential competitors for KPI-014 for limbal stem cell deficiency, or LSCD, and Sjögren's. Competitive products and product candidates in LSCD include two stem cell-based approaches. ABCB5+ limbal stem cells, which are being studied in Phase 1/2 clinical trials and are being developed by RHEACELL GmbH & Co. KG, utilize allogeneic limbal stem cells derived from human corneal rims, which are expanded ex-vivo and manufactured as an advanced-therapy medicinal product. Holoclar utilizes autologous limbal stem cells derived from the healthy portion of the patient's eye. Holoclar is approved in the European Union for treatment of LSCD caused by ocular burns and is developed by Chiesi. To our knowledge, there are no products in development focused on Partial Limbal Stem Cell Deficiency.

Competitive pharmaceutical products in moderate-to-severe Sjögren's include cyclosporine, lifitegrast, ophthalmic cortisone and systemic immunosuppressants. To our knowledge, there are only two topical ophthalmic product candidates in active clinical development for ocular manifestations of moderate-to-severe Sjögren's. Lacripep™, a synthetic peptide fragment of lacritin being developed by Tear Solutions, recently completed a Phase 2 clinical trial in patients with primary Sjögren's-associated ocular surface disease. Oxervate® (cenegermin-bkbj) is currently being evaluated in Phase 3 clinical trials in patients with severe Sjögren's dry eye disease. Several systemic pharmaceutical product candidates are also in clinical development for the treatment of Sjögren's, including Dazodalibep (Horizon Therapeutics), SAR-441344 (Sanofi), Ianalumab (Novartis), Branebrutinib (Novartis), Iscalimab (Novartis) and OSE-127 (OSE Immuno Therapeutics).

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. Our competitors may develop products that are available on a generic basis, and 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 biosimilar and generic products.

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.

Product liability lawsuits against us could divert our resources and could cause us to incur substantial liabilities and limit commercialization of any 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 if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for 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 any products that we may develop.

We currently hold $15 million in product liability insurance coverage in the aggregate, with a per incident limit of $15 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage if we expand our ongoing and planned clinical trials for KPI-012. We will need to further 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 Our Dependence on Third Parties

We have relied, 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 have relied 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 have relied, and expect to continue to 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 products, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of 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 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 preclinical and clinical quantities of any product candidates. 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 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 for KPI-012. 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 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 enter into agreements for commercial supply of KPI-012 on acceptable terms or at all. We also expect to rely on third-party manufacturers to manufacture preclinical, clinical and commercial supplies of any other product candidates we develop, as well as for packaging, serialization, storage, distribution and other production logistics.

We are subject to risks related to our reliance on third-party manufacturers for the manufacture of the drug substance and 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 MSC-S 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 trial was cultivated using a planar culture model, we implemented a bioreactor cultivation model for our ongoing CHASE Phase 2b clinical trial of KPI-012. We also plan to utilize 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.

Our third party manufacturers may encounter shortages in the raw materials necessary to produce our product candidates in the quantities needed for our clinical trials, 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, including shortages caused by the purchase of such raw materials 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 necessary to manufacture sufficient quantities of KPI-012 or any other product candidates we may develop, may have a material adverse effect on our business.

The FDA maintains strict requirements governing the manufacturing process and third-party manufacturers are subject to inspection and approval by the FDA before a company can commence the manufacture and sale of any of its products or product candidates, and thereafter subject to FDA inspection from time to time. Failure by third-party manufacturers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to 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 product candidates and harm our business and results of operations.

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 ongoing and planned clinical trials or development timeline.

Our current and anticipated future dependence upon others for the manufacture of 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.

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 cGMPs, lot consistency and timely availability of raw materials. Even if we obtain regulatory

approval for KPI-012 or any product candidates we may develop in the future, 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 product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to develop and commercialize 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 if we do not establish our own sales, marketing and distribution capabilities in the United States for our product candidates 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 product candidates we may develop. 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 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 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 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 product candidates or products 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.

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 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 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 potential commercialization of 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 or 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 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 and product candidates, including KPI-012. We have sought to protect our proprietary position by filing in the United States and in certain foreign jurisdictions patent applications related to our proprietary technologies 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 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 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 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.

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 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 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. 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 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.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property rights, 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 rights. 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 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 and may have negative impacts on our business, operating results and financial condition.

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 KPI-012 and any other product candidate we may develop in the future and to 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 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 if our product candidates commence commercialization. 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 product candidates and their uses. Thus, we do not know with certainty that 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 any products, if and when approved, 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 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 may 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.

KPI-012 is protected by patent rights 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 products, if any when approved, 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 KPI-012. 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 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 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 were developed using United States government funds. As a result, the United States government may have certain rights to intellectual property embodied in KPI-012 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 Stanford University License Agreement, under which we license certain patent rights related to KPI-012, imposes royalty and other financial obligations on us and other substantial performance obligations. We also may enter into additional licensing and funding arrangements with third parties that may impose diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under current or future license and collaboration agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product or product candidate that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could diminish the value of any product or product candidate. 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 Stanford may conclude that we have materially breached the Stanford University License Agreement and might therefore terminate the agreement, thereby removing our ability to market products covered by our license agreement with Stanford. If the Stanford University 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 Stanford University License Agreement is terminated, Stanford 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 Stanford University License Agreement will revert to Stanford at no cost to Stanford. This could have a material adverse effect on our competitive business position, our financial condition, our results of operations and our business prospects.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize any affected product or product candidate, 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 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 and our 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. The marketing approval process is expensive, time-consuming and uncertain. As a result, we cannot predict when or if we, or any collaborators we may have in the future, will obtain marketing approval to commercialize KPI-012 or any product candidates we may develop in the future.

KPI-012 and any other future product candidate and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, potency, purity, 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, which we sold to Alcon in July 2022, 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 KPI-012 or any other product candidate we may develop 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 a biologic product candidate's purity, safety and potency. 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 KPI-012 or any other product candidate that we develop does not satisfy these standards 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 biologics 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 biologics 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 biologics 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. 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 KPI-012 or any other product candidate we may develop 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. Clinical trials of any product candidate in the United States 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 any product candidate for which we obtain marketing approval. Promotional communications with respect to biologic 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, if any of our product candidates receives marketing approval, 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 products to ensure they 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 products 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 manufacturers or quality assurance standards applicable to medical device manufacturers, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any contract manufacturers we may engage in the future, our future collaborators and their contract manufacturers will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to clinicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a risk evaluation and mitigation strategy.

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

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 European Medicines Agency 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." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved. 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 an application for marketing approval 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 will play a primary role in the recommendation and prescription and use of any product candidates for which we obtain marketing approval. Our future 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 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 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 affect our ability to commercialize our products, if and when approved, and increase the difficulty and cost for us to obtain reimbursement for our products, if and when approved.

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 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 products 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 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 and reduced through the end of June 2022, with the full 2% cut resuming thereafter. 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 any of our product candidates for which we may obtain regulatory approval or the frequency with which 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 any product which receives regulatory approval 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.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028 and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at 2,000 a year.

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

If we or any third-party manufacturers we engage or may engage in the future 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 in the future 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.

In 2018, California passed into law the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation, or GDPR, described below, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or the CPRA, which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities. In addition, other states, including Virginia, Colorado, Utah, and Connecticut already have passed state privacy laws. Virginia's privacy law also went into effect on January 1, 2023, and the laws in the other three states will go into effect later in the year. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

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 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 our 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.

The GDPR places restrictions on the cross-border transfer of personal data from the EU to countries that have not been found to offer adequate data protection legislation, such as the United States. There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the European Union, or CJEU, invalidated the EU-U.S. Privacy Shield, 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. While we were not self-certified under the Privacy Shield, this CJEU decision may lead to increased scrutiny on data transfers from the EEA to the United States generally and increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners. Additionally, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-US Privacy Shield. The European Commission initiated the process to adopt an adequacy decision for the EU-US Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court.

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, 2022, we had federal net operating loss, or NOL, carryforwards of $349.4 million, which may be available to offset future federal tax liabilities and expire at various dates beginning in 2030. As of December 31, 2022, we also had state NOL carryforwards of $390.6 million, which may be available to offset future state income tax liabilities and expire at various dates beginning in 2023. As of December 31, 2022, we had no federal and state research and development credit carryforwards. 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. During December 2022, an additional ownership change occurred as a result of our entry into the securities purchase agreement for the private placement transaction. As a result of the most recent ownership change, the utilization of our net operating loss carryforwards is subject to an annual limitation of $0.2 million. We may be further limited by any changes that may have occurred or may occur subsequent to December 31, 2022. 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

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 L. Trachtenberg, our General Counsel, Chief Compliance Officer and Corporate Secretary, as well as the other principal members of our management, scientific and clinical 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 Combangio Acquisition and their expertise developing biologics.

Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and other 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. Our decision to sell our commercial business to Alcon, our determination to cease the development of our preclinical pipeline programs unrelated to our MSC-S platform and to focus our research and development efforts on KPI-012 and our workforce reduction in July 2022 could harm our ability to attract and retain qualified personnel who are critical to our business. 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 successfully develop and commercialize KPI-012 and any other product candidate we may develop in the future will be harmed.

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.

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 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. 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

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 is 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.

Our October 2022 reverse stock split may decrease the liquidity of the shares of our common stock.

The liquidity of the shares of our common stock may be affected adversely by the 1-for-50 reverse stock split we effected in October 2022 given the reduced number of shares that are outstanding following the reverse stock split, which may lead to reduced trading and a smaller number of market makers for our common stock, particularly if the price per share of our common stock is not sustained. In addition, the reverse stock split has increased the number of stockholders who own "odd lots" of less than 100 shares of our common stock, A purchase or sale of less than 100 shares of common stock may result in incrementally higher trading costs through certain brokers, particularly "full service" brokers. Therefore, those stockholders who own fewer than 100 shares of our common stock following the reverse stock split may be required to pay higher transaction costs if they sell their common stock.

The price of our common stock is volatile and fluctuates substantially, which could result in substantial losses for purchasers of our common stock.

Our stock price is volatile and fluctuates substantially. 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:

- the recent sale of our commercial business to Alcon;

- our strategic decision to focus our research and development efforts on our MSC-S platform, including KPI-012;

- results of preclinical studies and clinical trials of KPI-012 or any other product candidates we may develop;

- our ability to receive marketing approval for and to successfully commercialize KPI-012 or any other product candidate we may develop;

- 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, including as a result of our workforce reduction in July 2022;
- the level of expenses related to the 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 cannot obtain regulatory approval for or fail to successfully commercialize 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 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, 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 2, 2023, we had outstanding 2,025,495 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. If our stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. In addition, 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 December 2022, we sold to certain institutional investors shares of our common stock and shares of our Series E Convertible Non-Redeemable Preferred Stock in a private placement priced at the market under Nasdaq rules for gross proceeds of approximately $31.0 million. While the securities issued in the private placement and 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.

Moreover, we have entered into a registration rights agreement with the purchasers in the private placement entitling them to certain resale registration rights with respect to the 76,813 shares of common stock issued in the private placement and the 5,314,400 shares of common stock issuable upon conversion of the Series E Convertible Non-Redeemable Preferred Stock.

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.

Our existing stockholders will experience dilution upon any future conversion of the outstanding shares of our Series E Convertible Non-Redeemable Preferred Stock into shares of our common stock.

Each outstanding share of Series E Convertible Non-Redeemable Preferred Stock is initially convertible into 100 shares of our common stock at any time at the option of the holder, subject to certain beneficial ownership limitations. Our existing stockholders will experience dilution upon any future conversion of the outstanding shares of our Series E Convertible Non-Redeemable Preferred Stock into shares of our common stock.

Investors in our December 2022 private placement may have the ability to exercise significant influence over certain of our business decisions.

Pursuant to the terms of the securities purchase agreement for the private placement transaction, investors in the private placement transaction have consent rights over certain significant matters of the Company's business. Specifically, we have agreed that we will not, without the prior approval of the requisite investors (1) issue or authorize the issuance of any equity security that is senior or *pari passu* to the Series E Convertible Non-Redeemable Preferred Stock with respect to liquidation preference, (2) incur any additional indebtedness for borrowed money in excess of $1,000,000, in the aggregate, outside the ordinary course of business, subject to specified exceptions, including the refinancing of our existing indebtedness or (3) pay or declare any dividend or make any distribution on, any of our shares of capital stock, subject to specified exceptions. We have also granted the investors in our private placement the right to have our board of directors nominate and recommend for election by the stockholders up to three investor designees to our board of directors, subject to certain requirements and exceptions. In addition, such investors have certain rights to participate in our future equity offerings, which rights are more fully described in Item 1, "Business" of this Annual Report on Form 10-K. As a result, these stockholders, may have the ability to exercise significant influence over certain matters affecting our business.

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. If our common stock is delisted from Nasdaq, we will be in default under our Loan Agreement.

Our common stock is currently listed on The Nasdaq Capital Market. We must satisfy Nasdaq's continued listing requirements, including, among other things, a minimum closing bid price of $1.00 per share and a minimum market value of listed securities, 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 and employees and fewer business development opportunities. In addition, 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.

During 2022, we received multiple deficiency letters from Nasdaq notifying us of our noncompliance with various listing standards for continued inclusion on The Nasdaq Global Select Market. On each of March 2, 2022 and May 24, 2022, we received a deficiency letter from Nasdaq notifying us that, for 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 The Nasdaq Global Select Market pursuant to Nasdaq Listing Rule 5450(a)(1), or the Bid Price Requirement. We were provided a period of 180 calendar days to regain compliance with the Bid Price Requirement, and in each case, we

regained compliance within the cure period, including in the second instance by implementing a reverse stock split of our common stock.

On July 6, 2022, we received another deficiency letter from Nasdaq notifying us that we were not in compliance with Nasdaq Listing Rule 5450(b)(2)(A), or the Minimum MVLS Requirement, for continued listing on the Nasdaq Global Select Market, as the market value of our common stock was less than $50,000,000 for the previous 30 consecutive business days. Nasdaq also noted that we were not in compliance with Nasdaq Listing Rule 5450(b)(1)(A), as our stockholders' equity was less than $10,000,000 and Nasdaq Listing Rule 5450(b)(3)(A), as our total assets and total revenue for the most recently completed fiscal year or for two of the three most recently completed fiscal years were less than $50,000,000. A company that has its primary equity security listed on The Nasdaq Global Select Market must satisfy at least one of the standards in Nasdaq Listing Rule 5450(b).

On December 5, 2022, we received another deficiency letter from Nasdaq notifying us that we were not in compliance with Nasdaq Listing Rule 5450(b)(2)(C), or the Minimum MVPHS Requirement, for continued listing on the Nasdaq Global Select Market, as the market value of our publicly held shares was less than $15,000,000 for each of the previous 30 consecutive business days.

In accordance with Nasdaq Listing Rule 5810(c)(3), we were provided until January 2, 2023 to regain compliance with the Minimum MVLS Requirement and until June 5, 2023 to regain compliance with the Minimum MVPHS Requirement. Alternatively, if we did not regain compliance with the Minimum MVLS Requirement or the Minimum MVPHS Requirement by the applicable compliance date, we were eligible to transfer the listing of our common stock to the Nasdaq Capital Market, provided that we met the applicable requirements for continued listing on the Nasdaq Capital Market.

Following the receipt of the gross proceeds from the second tranche of a private placement in December 2022 and after amending our Loan Agreement to permit a transfer, we applied to transfer the listing of our common stock to the Nasdaq Capital Market. The transfer was approved effective January 11, 2023 following Nasdaq's determination that we met the applicable requirements for continued listing on the Nasdaq Capital Market, including Nasdaq Listing Rule 5550(b)(1), the minimum stockholders equity requirement for continued listing on The Nasdaq Capital Market. In addition, Nasdaq advised us that, upon the transfer of our listing to the Nasdaq Capital Market, we would be in compliance with Nasdaq Listing Rule 5550(a)(5), the market value of publicly held shares requirement for continued listing on The Nasdaq Capital Market.

There are many factors that may adversely affect our ability comply with the requirements for continued listing on the Nasdaq Capital Market, including those described throughout this "Risk Factors" section. Many of these factors are outside of our control. As a result, we cannot assure you that we will continue to comply with the requirements for continued listing on the Nasdaq Capital Market. Any potential delisting of our common stock from the Nasdaq Capital Market would likely harm our ability to raise capital and may result in the potential loss of confidence by investors and employees and fewer business development opportunities.

In addition, a delisting of our common stock from The Nasdaq Capital Market or the transfer of the listing of our common stock to another nationally recognized stock exchange having listing standards that are less restrictive than The Nasdaq Capital Market, in each case after a specified cure period, are events of default under our Loan Agreement. If such an event of default were to occur and we fail to secure a waiver or forbearance from the third-party lender, the lender would be entitled to accelerate the amounts due under our Loan Agreement. In such event, we may not be able to make accelerated payments, and the lender could seek to enforce security interests in the collateral securing such indebtedness. Acceleration of the repayment of the outstanding indebtedness would raise substantial doubt about our ability to continue as a going concern, shorten the period for which we will be able to fund our operations and capital expenditure requirements and would adversely effect our financial condition and ability to pursue our business strategy.

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

We are 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 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:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- reduced disclosure obligations regarding executive compensation;
- 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; 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 since we ceased being an "emerging growth company" as of December 31, 2022, we 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 Capital 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 a smaller reporting company, we may take advantage of certain exemptions from various reporting requirements 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 a non-accelerated filer and a smaller reporting 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 and our securities purchase agreement entered into with certain institutional investors for our December 2022 private placement restrict us from paying dividends. 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. The 2017 Tax Act, as amended by the CARES Act, 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% and the limitation of the deduction for NOLs to 80% of current year taxable income for losses arising in taxable years beginning after December 31, 2017 (though any such NOLs may be carried forward indefinitely). In addition, beginning in 2022, the 2017 Tax Act eliminates the option to deduct research and development expenditures currently and requires corporations to capitalize and amortize them over five years.

In addition to the CARES Act, as part of Congress's response to the COVID-19 pandemic, economic relief legislation was enacted in 2020 and 2021 containing tax provisions. The Inflation Reduction Act, or IRA, was also signed into law in August 2022. The IRA introduced new tax provisions, including a one percent excise tax imposed on certain stock repurchases by publicly traded companies. The one percent excise tax generally applies to any acquisition of stock by the publicly traded company (or certain of its affiliates) from a stockholder of the company in exchange for money or other property (other than stock of the company itself), subject to a de minimis exception. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases.

Regulatory guidance under the 2017 Tax Act, the IRA, and such additional legislation is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to the 2017 Tax Act, the IRA and such additional legislation.

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

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 Combangio 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 Stock Market under the symbol "KALA" since July 20, 2017 in connection with our initial public offering, or IPO. From July 20, 2017 through January 10, 2023 our common stock traded on The Nasdaq Global Select Market. On January 11, 2023, our common stock began trading on The Nasdaq Capital Market. Prior to our IPO, there was no public market for our common stock.

Holders

As of March 2, 2023, there were approximately 26 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 our Securities Purchase Agreement, dated November 28, 2022, with certain institutional investors named therein relating to our December 2022 private placement (which is more fully described in Item 1., Business and Item 7., Management's Discussion and Analysis of Financial Condition and Results of Operations). Future debt financing arrangements also 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 is set forth in "Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" and is incorporated herein by reference.

Recent Sales of Unregistered Securities

We did not sell any shares of our common stock, shares of our preferred stock or warrants to purchase shares of our stock, or grant any stock options, restricted stock units or restricted stock awards, during the twelve months ended December 31, 2022 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.

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.

Unless otherwise indicated, all information in this Annual Report on Form 10-K gives effect to a 1-for-50 reverse stock split of our common stock that became effective on October 20, 2022, and all references to historical share and per share amounts give effect to the reverse stock split.

Overview

We are a clinical-stage biopharmaceutical company dedicated to the research, development and commercialization of innovative therapies for rare and severe diseases of the eye. Our product candidate, KPI-012, which we acquired from Combangio, Inc., or Combangio, on November 15, 2021, is a mesenchymal stem cell secretome, or MSC-S, and is currently in clinical development for the treatment of persistent corneal epithelial defects, or PCED, a rare disease of impaired corneal healing. Based on the positive results of a Phase 1b clinical safety and efficacy trial of KPI-012 in patients with PCED, along with favorable preclinical safety and efficacy results, we submitted an investigational new drug application, or IND, to the U.S. Food and Drug Administration, or FDA, which was accepted in December 2022. In February 2023, we dosed our first patient in our CHASE (**C**orneal **H**ealing **A**fter **SE**cretome therapy) Phase 2b clinical trial of KPI-012 for PCED in the United States, and we are targeting reporting top-line safety and efficacy data from this trial in the first quarter of 2024. If the results of the CHASE Phase 2b clinical trial are positive, and subject to discussion with regulatory authorities, we believe this trial could serve as the first of two pivotal trials required to support the submission of a Biologics License Application, or BLA, to the FDA.

We believe the multifactorial mechanism of action of KPI-012 also makes MSC-S a platform technology. We are evaluating the potential development of KPI-012 for additional rare front-of-the-eye diseases, such as for the treatment of Limbal Stem Cell Deficiency and ocular manifestations of moderate-to-severe Sjögren's. In addition, we have initiated preclinical studies under our KPI-014 program to evaluate the utility of our MSC-S platform for inherited retinal degenerative diseases, such as Retinitis Pigmentosa and Stargardt Disease. In connection with the determination to focus our research and development efforts on KPI-012, in 2022, we determined to cease the development of our preclinical pipeline programs that are unrelated to our MSC-S platform. We expect to commercialize in the United States any of our product candidates that receive marketing approval. For a further description of our acquisition of Combangio, or Combangio Acquisition, see Item 1, "Business," "Liquidity and Capital Resources" below and Note 3, "Acquisitions and Divestitures" of our consolidated financial statements.

We previously developed and commercialized two marketed products, 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 applied a proprietary mucus-penetrating particle drug delivery technology, which we referred to as the AMPPLIFY® Drug Delivery Technology.

On July 8, 2022, we closed the transaction, or the Alcon Transaction, contemplated by the asset purchase agreement, dated as of May 21, 2022, or the Asset Purchase Agreement, by and between us, Alcon Pharmaceuticals Ltd. and Alcon Vision, LLC, which we refer to collectively as Alcon, pursuant to which Alcon purchased the rights to manufacture, sell, distribute, market and commercialize EYSUVIS and INVELTYS and to develop, manufacture, market and otherwise exploit the AMPPLIFY Drug Delivery Technology, which we collectively refer to as the Commercial Business. Alcon also assumed certain liabilities with respect to the Commercial Business at the closing of the Alcon

Transaction. For a further description of the Alcon Transaction, see Item 1, "Business," "Liquidity and Capital Resources" below and Note 3, "Acquisitions and Divestitures" of our consolidated financial statements.

On July 8, 2022, we announced that we had committed to a course of action to terminate 113 employees, consisting of our entire commercial sales force and certain employees in our commercial, scientific, manufacturing, finance and administrative functions. The determination to proceed with the workforce reduction was made in the context of the closing of the Alcon Transaction and the changes to the scope of our research and development activities of KPI-012 as more fully described above. We completed the workforce reduction by the end of 2022.

Since inception, we have incurred significant losses from operations and negative cash flows from operations. Our net losses were $44.8 million for the year ended December 31, 2022 and $142.6 million for the year ended December 31, 2021. As of December 31, 2022, we had an accumulated deficit of $587.2 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 had generated only limited revenues from product sales prior to the sale of the Commercial Business to Alcon in July 2022. We have financed our operations primarily through proceeds from the sale of our Commercial Business to Alcon in July 2022, 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 common stock and preferred stock (including our private placement of common stock and preferred stock for gross proceeds of approximately $31.0 million in December 2022, or our Private Placement), borrowings under credit facilities and our Loan Agreement with 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, prior to the sale of our Commercial Business to Alcon in July 2022, engaging in activities to launch and commercialize EYSUVIS and INVELTYS. As a result of our acquisition of Combangio and the sale of our Commercial Business to Alcon, we are devoting, and intend to continue to devote, substantial financial resources to the research and development and potential commercialization of KPI-012. We have no revenue-generating commercial products and, as a result of our acquisition of Combangio, we may be required to pay certain milestones and royalty payments to former equityholders of Combangio, which are more fully described in the "Liquidity and Capital Resources" section. Although we are eligible to receive up to $325.0 million in payments from Alcon based upon the achievement of specified commercial sales-based milestones with respect to EYSUVIS and INVELTYS, there can be no assurance when we may receive such milestone payments or of the amount of milestone payments we may receive, if any. We expect to continue to incur significant expenses and operating losses for the foreseeable future, 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.

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 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. In addition, government restrictions have at times led to moratoria on elective ocular surgeries in many jurisdictions, which had significantly reduced the demand for INVELTYS, which is indicated for the treatment of inflammation and pain following ocular surgery. The COVID-19 pandemic had negatively impacted our revenues from INVELTYS. In addition, the COVID-19 pandemic has generally had an adverse impact on the launch of pharmaceutical products, and we believe the pandemic impacted the launch of EYSUVIS. We cannot predict whether the COVID-19 pandemic will impact Alcon's ability to commercialize EYSUVIS and INVELTYS, and as a result, it cannot be certain whether the COVID-19 pandemic might adversely affect when we may receive milestone payments from Alcon, which milestone payments we may receive and if we will receive any milestone payments at all. Any impact of the COVID-19 pandemic on our development of KPI-012 and any other product candidate we may develop in the future, Alcon's commercialization efforts of EYSUVIS and INVELTYS, and our operational and financial performance will depend on certain developments, including the length and severity of this pandemic, 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 treatments, and the full extent of the impact on 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, vendors, 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 coronavirus pandemic and the efforts to prevent its spread have adversely impacted our operations, 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. On July 8, 2022, we sold our Commercial Business, including EYSUVIS and INVELTYS, to Alcon and ceased recording gross revenue on sales of EYSUVIS and INVELTYS. Our product revenues for the periods presented herein 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.

We currently have no commercial products in our portfolio. Moreover, we only recently commenced the CHASE Phase 2b clinical trial of KPI-012 for PCED in the United States and, accordingly, we do not expect to generate revenue from KPI-012 or any other product candidate we may develop for the foreseeable future, if at all. See the section titled "Business Impact of COVID-19 Pandemic" above for information about the impact of COVID-19 on sales and commercialization of EYSUVIS and INVELTYS.

Cost of Product Revenues

Cost of product revenues consisted 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. The determination of whether inventory costs will be realizable requires estimates by management. Prior to the sale of our Commercial Business in July 2022, write-downs of inventory were recorded as a cost of product revenues in the consolidated statements of operations and comprehensive loss. Following the sale of our Commercial Business, any adjustments to the remaining EYSUVIS and INVELTYS inventory, or Remaining Inventory, are recorded within other expense in the consolidated statements of operations and comprehensive loss. Following the sale of the Commercial Business, the only customer for our current inventory is Alcon. If Alcon does not purchase any additional inventory, the Remaining Inventory balance, net of the deferred gain on sale of the Commercial Business, will be recorded to other expense in the consolidated statements of operations and comprehensive loss. As a result of the sale of our Commercial Business to Alcon, which occurred on July 8, 2022, we do not expect to generate cost of product revenues until such time as we commercialize another product candidate.

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 related to EYSUVIS and INVELTYS prior to the sale of the Commercial Business to Alcon, 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 2023 as compared to such expenses for the year ended December 31, 2022 as a result of the workforce reduction announced on July 8, 2022 and the sale of our Commercial Business to Alcon in July 2022. We anticipate that our selling, general and administrative expenses will remain largely consistent with the expenses anticipated for 2023 for the foreseeable future as we continue to support our development efforts for KPI-012 and seek marketing approval for KPI-012 and any other product candidate we may develop in the future. If we obtain marketing approval for KPI-012 or any product candidates we may develop, we expect that our selling, general and administrative expenses will increase substantially if and as we incur commercialization expenses related to product marketing, sales and distribution.

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 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 2023 as compared to such expenses for the year ended December 31, 2022 as we advance the clinical development of KPI-012 and as we conduct any necessary preclinical studies and clinical trials and other development activities for any other product candidate we may develop in the future, including our ongoing and planned preclinical studies under our KPI-014 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 are unable to predict the impact it may have on our research and development activities.

KPI-012 is in Phase 2b 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 will need to raise additional capital and may seek collaborations in the future to advance KPI-012 and any product candidate we may develop. 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.

Loss (Gain) on Fair Value Remeasurement of Deferred Purchase Consideration

In connection with the closing of the Combangio Acquisition on November 15, 2021, we agreed to issue an aggregate of 155,664 shares, or the Deferred Purchase Consideration, of our common stock to former Combangio stockholders and other equityholders, or the Combangio Equityholders, consisting of (i) an aggregate of 136,314 shares of common stock which were issued on January 3, 2022 and (ii) an aggregate of 19,350 shares of common stock that were held back by us and will be issued on the escrow release date in March 2023. We recorded an obligation for such Deferred Purchase Consideration at fair value on the acquisition date. We then revalued 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 or loss on fair value remeasurement of Deferred Purchase Consideration in our consolidated statements of operations and comprehensive loss.

Gain on Fair Value Remeasurement of Contingent Consideration

In addition to the Deferred Purchase Consideration, consideration payable to the Combangio Equityholders includes potential payments of up to $105.0 million, of which $4.9 million will be paid in March 2023, payable in cash and shares of our common stock that are contingent upon the achievement of specified development, regulatory and commercialization milestones which potential payments and milestones are more fully described in Item 1, "Business" and in "Liquidity and Capital Resources" below and Note 3, "Acquisitions and Divestitures" of our consolidated financial statements. We recorded an obligation for such contingent consideration at fair value on the acquisition date. We then revalue our contingent consideration obligations each reporting period. Changes in the fair value of our contingent consideration obligations, other than changes due to issuance, are recognized as a gain or loss on fair value remeasurement of contingent 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 final payment fees paid upon extinguishment of a debt agreement. For the year ended December 31, 2022, the loss on extinguishment of debt related to the partial extinguishment of debt under the Loan Agreement with Oxford Finance on July 8, 2022 in connection with the closing of the Alcon Transaction. For the year ended December 31, 2021, the loss on extinguishment of debt related to the extinguishment of the credit agreement, or the Athyrium Credit Facility, with Athyrium Opportunities III Acquisition LP, or Athyrium.

Gain on Sale of Commercial Business

Gain on sale of Commercial Business represents the gain recognized as a result of the sale of our Commercial Business to Alcon on July 8, 2022.

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 termination 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 and that involve a significant level of estimation uncertainty.

Revenue

Following the sale of our Commercial Business to Alcon in July 2022, we no longer have any commercial products in our portfolio. We accounted for revenue in accordance with Accounting Standards Codification, or 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 performed 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 recognized revenue when it was probable that we would collect the consideration to which we were entitled in exchange for the goods or services that would be transferred to the customer.

Product revenues, net

We sold EYSUVIS and INVELTYS primarily to wholesalers in the United States, or Customers. These Customers subsequently resold our products to specialty and other retail pharmacies. In addition to agreements with Customers, we entered 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 represented a single performance obligation. We recognized revenue from product sales at the point the Customer obtained control of the product, which occurred upon delivery. The transaction price ("net sales price") that was recognized as revenue for product sales included the selling price to the Customer and an estimate of variable consideration. Components of variable consideration included 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 was not received. Variable consideration was 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 considered all relevant information when estimating variable consideration such as assessment of our then 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 were reasonably available. We included estimated amounts for variable consideration in the net sales price to the extent it was determined probable that a significant reversal of cumulative revenue recognized would not occur when the uncertainty associated with the variable consideration was resolved.

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

Reserves for Variable Consideration:

Trade Discounts and Allowances

We provided 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 were based on contractually-determined percentages and were recorded as a reduction of revenue and accounts receivable in the period in which the related product revenue was 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 purchased the product from us. Customers charged us for the difference between what they paid for the product and the ultimate selling price to the qualified healthcare providers. These components of variable consideration were established in the same period that the related revenue was recognized, resulting in a reduction of product revenue

and accounts receivable. Reserves for chargebacks consisted of credits we expected to issue for units that remained in the distribution channel at the end of each reporting period and that we expected would be sold to qualified healthcare providers, as well as chargebacks that Customers had claimed, but for which we had not yet issued a credit.

Product Returns

Consistent with industry practice, we had 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 estimated the amount of our products that may be returned and presented this amount as a reduction of revenue in the period the related product revenue was recognized, in addition to establishing a liability. Our estimates for product returns were 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 developed over time.

Commercial Payor and Medicare Part D Rebates

We contracted 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 were based on contractual percentages applied to the amount of product prescribed to patients who were covered by the PBMs or the Plans with which it contracted. We estimated the 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 would be made for product that had been recognized as revenue but remained in the distribution channel at the end of each reporting period. We also estimated the number of patients in the prescription drug coverage gap for whom we would owe an additional liability under the Medicare Part D program. Such estimates were recorded in the same period the related revenue was recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Government Rebates

We were subject to discount obligations under Medicaid and other government programs. For Medicaid, reserves were 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 consisted of estimates of claims for the current period and estimated future claims that would be made for product that had been recognized as revenue but remained in the distribution channel at the end of each reporting period. These reserves were recorded in the same period the related revenue was recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Co-pay Assistance Programs

We offered co-pay assistance programs (the "co-pay programs"), which were intended to provide financial assistance to patients who may or may not be covered by commercial insurance or, with respect to INVELTYS, who opt out of Medicare Part D programs. The calculation of accruals for the co-pay programs were based on actual claims processed during the period as well as an estimate of the number and cost per claim that we expected to receive associated with product that had been recognized as revenue but remained 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 was 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. The determination of whether inventory costs will be realizable requires estimates by management. Prior to the sale of our Commercial Business in July 2022, such impairment charges were recorded within cost of product revenues, unless associated with our samples inventory, in which case the charges were recorded to selling, general and administrative expense. Following the sale of our Commercial Business, any adjustments to the Remaining Inventory are recorded within other expense in the consolidated statements of operations and comprehensive loss. Following the sale of the Commercial Business, the only customer for our current inventory is Alcon. If Alcon does not purchase any additional inventory, the Remaining Inventory balance, net of the deferred gain on sale of the Commercial Business, will be recorded to other expense 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 and estimates 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 5, “Fair Value of Financial Instruments”, of our consolidated financial statements.

Results of Operations

Comparison of the Years ended December 31, 2022 and 2021

The following table summarizes the results of our operations for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		
	2022	2021	Change
	(in thousands)		
Product revenues, net	$ 3,892	$ 11,240	$ (7,348)
Costs and expenses:			
Cost of product revenues	2,560	4,097	(1,537)
Selling, general and administrative	65,035	105,061	(40,026)
Research and development	17,653	11,515	6,138
Acquired in-process research and development	—	26,617	(26,617)
Loss (gain) on fair value remeasurement of Deferred Purchase Consideration	638	(5,805)	6,443
Gain on fair value remeasurement of contingent consideration	(288)	—	(288)
Total operating expenses	85,598	141,485	(55,887)
Loss from operations	(81,706)	(130,245)	48,539
Other income (expense)			
Interest income	664	104	560
Interest expense	(7,266)	(8,380)	1,114
Loss on extinguishment of debt	(2,583)	(5,395)	2,812
Gain on sale of Commercial Business	46,995	—	46,995
Gain on lease modification	—	1,311	(1,311)
Other income (expense), net	(926)	—	(926)
Net loss	$ (44,822)	$ (142,605)	$ 97,783

Product revenues, net

Product revenues, net was $3.9 million for the year ended December 31, 2022, consisting of $2.3 million from EYSUVIS sales and $1.6 million from INVELTYS sales, compared to $11.2 million for the year ended December 31, 2021, which consisted of $6.3 million from EYSUVIS sales and $4.9 million from INVELTYS sales. The decrease in product revenues, net of $7.3 million was largely due to the sale of our Commercial Business to Alcon in July 2022 resulting in a decrease in the total units sold of both products in the year ended December 31, 2022 as well as higher estimated allowances per unit sold on both products during the year ended December 31, 2022 as compared to those allowances per unit sold during the year ended December 31, 2021, partially offset by a higher per unit gross selling price of both products during the year ended December 31, 2022 as compared to the per unit gross selling price of both products sold during the year ended December 31, 2021. As a result of the sale of our Commercial Business, we no longer have any commercial products in our portfolio.

Cost of product revenues

Cost of product revenues was $2.6 million for the year ended December 31, 2022, compared to $4.1 million for the year ended December 31, 2021, a decrease of $1.5 million due to the sale of our Commercial Business to Alcon in July 2022.

Selling, general and administrative expenses

Selling, general and administrative expenses were $65.0 million for the year ended December 31, 2022, compared to $105.1 million for the year ended December 31, 2021, which was a decrease of $40.1 million. The decrease in selling, general and administrative expenses for the year ended December 31, 2022 was primarily due to the sale of our Commercial Business to Alcon and our related workforce reduction and includes a $20.8 million decrease in employee-related expenses, a $9.7 million decrease in external sales and marketing costs, a $6.8 million decrease in stock-based compensation costs and a decrease in certain medical affairs costs attributable to our former commercial

products. Also contributing to the decrease as compared to the year ended December 31, 2021, was a $6.2 million decrease in facility related costs. These decreases, as compared to the year ended December 31, 2021, were partially offset by $1.6 million recorded to selling, general and administrative expenses related to the workforce reduction, a $1.0 million increase in administrative and professional service fees and $0.8 million of transaction costs related to the Alcon Transaction which were not incurred in the year ended December 31, 2021.

Research and development expenses

The following table summarizes the research and development expenses incurred during the years ended December 31, 2022 and 2021:

	Year Ended December 31,		
	2022	2021	Change
	(in thousands)		
KPI-012 development costs	$ 5,803	$ —	$ 5,803
Employee-related costs	9,256	7,417	1,839
Other research and development costs	2,594	4,098	(1,504)
Total research and development	$ 17,653	$ 11,515	$ 6,138

Research and development expenses were $17.7 million for the year ended December 31, 2022 compared to $11.5 million for the year ended December 31, 2021, an increase of $6.2 million. The increase was primarily the result of $5.8 million in KPI-012 development costs and a $1.9 million increase in employee-related costs, partially offset by a $1.5 million decrease in other research and development costs, which primarily included preclinical studies related to our former pipeline programs and other facility related costs.

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 of Combangio. There were no acquired IPR&D expenses for the year ended December 31, 2022.

Loss (gain) on fair value remeasurement of Deferred Purchase Consideration

The loss on fair value remeasurement of Deferred Purchase Consideration for the year ended December 31, 2022 was $0.6 million and the gain on fair value remeasurement of Deferred Purchase Consideration for the year ended December 31, 2021 was $5.8 million. The amounts were primarily due to a change in the fair value of our underlying stock price.

Gain on fair value remeasurement of contingent consideration

Gain on fair value remeasurement of contingent consideration for the year ended December 31, 2022 was $0.3 million and was primarily due to changes in discount rates, partially offset by the passage of time. The change in fair value remeasurement of contingent consideration for the year ended December 31, 2021 was *de minimis*.

Interest income

Interest income was $0.7 million for the year ended December 31, 2022, compared to $0.1 million for the year ended December 31, 2021, an increase of $0.6 million. Interest income consists of interest earned on our cash, cash equivalents and short-term investments, if any. The increase was attributable to higher interest rates, partially offset by lower cash, cash equivalents and short-term investments balances during the year ended December 31, 2022.

Interest expense

Interest expense was $7.3 million for the year ended December 31, 2022, compared to $8.4 million for the year ended December 31, 2021, a decrease of $1.1 million. Interest expense for the year ended December 31, 2022 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. 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 and our Athyrium Credit Facility. During the year ended December 31, 2022, $80.0 million of indebtedness was outstanding under our Loan Agreement until $36.7 million was repaid on July 8, 2022 resulting in an outstanding indebtedness of $43.3 million as of December 31, 2022. 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.

Loss on extinguishment of debt

The loss on extinguishment of debt was $2.6 million for the year ended December 31, 2022, compared to $5.4 million for the year ended December 31, 2021. Upon the partial repayment of $36.7 million of indebtedness under our Loan Agreement in July 2022, the prepayment premium, unaccreted amount of the final payment fee due and a pro-rata portion of the debt discount were recorded as loss on extinguishment of debt for the year ended December 31, 2022. Upon the repayment in full of all amounts owed under the Athyrium Credit Facility in May 2021, 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.

Gain on sale of Commercial Business

The gain on sale of Commercial Business was $47.0 million for the year ended December 31, 2022, which was comprised of the $65.0 million in cash consideration received from Alcon at the closing less $4.2 million of deferred gain on sale of Commercial Business, $11.7 million net book value of assets transferred and $2.1 million of transaction costs. There was no gain on sale of Commercial Business for the year ended December 31, 2021.

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, 2022.

Other income (expense), net

Other income and expense was a net expense of $0.9 million for the year ended December 31, 2022. There was no other income and expense for the year ended December 31, 2021. The other income and expense during the year ended December 31, 2022 primarily represents a $4.2 million expense recorded to assets held for sale for expiring inventory, partially offset by $3.6 million of reimbursable transition related services we provided to Alcon following the sale of the Commercial Business.

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 only generated limited revenues from product sales prior to the sale of our Commercial Business to Alcon in July 2022. We have financed our operations primarily through proceeds from the sale of our Commercial Business to Alcon in July 2022, our IPO, follow-on public common stock offerings and sales of our common stock under our ATM Offerings, private placements of common stock and preferred stock (including our Private Placement), borrowings under credit facilities and our Loan and Security Agreement, or the Loan Agreement, with Oxford Finance LLC, or Oxford Finance, convertible promissory notes and warrants.

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 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 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, or the Amended and Restated Sales Agreement, pursuant to which we could issue and sell, from time to time, up to an aggregate of $75.0 million of our common stock under our ATM Offering. Through December 31, 2021, we issued and sold an aggregate of 171,626 shares of our common stock under the ATM Offering pursuant to the terms of the Amended and Restated Sales Agreement, resulting in net proceeds of $61.8 million. In the year ended December 31, 2022, under the Amended and Restated Sales Agreement, we issued and sold an aggregate of 148,461 shares of our common stock, resulting in net proceeds of $1.0 million. As of December 31, 2022, there was $10.3 million of shares of common stock remaining and available for sale under the Amended and Restated Sales Agreement and, excluding the shares of common stock that may be offered under the Amended and Restated Sales Agreement, there was $275.0 million of securities available to be issued under the 2020 Shelf Registration. From January 1, 2023 through January 10, 2023, we issued and sold an additional 245,887 shares of our common stock under the Amended and Restated Sales Agreement, resulting in net proceeds of $10.0 million. On January 10, 2023, the Amended and Restated Sales Agreement terminated in accordance with its terms when we completed the sale of $75.0 million of our shares of common stock thereunder. As of the date of termination of the Amended and Restated Sales Agreement, we had sold an aggregate of 565,974 shares of our common stock under such agreement for aggregate gross proceeds of $75.0 million.

On January 19, 2023, we entered into a new sales agreement with Jefferies, or the Open Market Sale Agreement, pursuant to which we may issue and sell, from time to time, shares of our common stock through Jefferies under our ATM Offering. We filed a prospectus supplement relating to the Open Market Sale Agreement under our 2020 Shelf Registration, pursuant to which we may offer and sell shares of common stock having an aggregate offering price of up to $40.0 million under the Open Market Sale Agreement. Through the date of filing of this Annual Report on Form 10-K, we sold 69,974 shares of our common stock under the Open Market Sale Agreement resulting in net proceeds of $1.4 million. In the aggregate, subsequent to December 31, 2022 through the date of filing of this Annual Report on Form 10-K, we sold 315,861 shares of our common stock pursuant to our Amended and Restated Sales Agreement and our Open Market Sale Agreement for total net proceeds of $11.4 million.

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, or Agent, pursuant to which a term loan of up to an aggregate principal amount of $125.0 million became 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. In connection with our entry into the Asset Purchase Agreement, on May 21, 2022, we entered into an amendment to the Loan Agreement, or the Second Loan Amendment. Pursuant to the Second Loan Amendment, the Lender and Agent consented to the entry by us into the Asset Purchase Agreement and the sale of the Commercial Business to Alcon and agreed to release its liens on the Commercial Business in consideration for the payment by us at the closing of the Alcon Transaction of an aggregate amount of $40.0 million, or the Second Amendment Prepayment, to the Lender and Agent.

The Second Amendment Prepayment, which represented a partial prepayment of principal in the amount of $36.7 million of the $80.0 million principal amount outstanding under the term loan advanced by the Lender under the Loan Agreement, plus a prepayment fee of $0.7 million and a final payment fee of $2.6 million, was paid on July 8, 2022 in connection with the closing of the Alcon Transaction.

In July 2022, we sold our Commercial Business to Alcon. In addition to the upfront cash payment of $60.0 million we received from Alcon pursuant to the Asset Purchase Agreement, we are also eligible to receive from Alcon up to four commercial-based sales milestone payments as follows: (1) $25.0 million upon the achievement of $50.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2028, (2) $65.0 million upon the achievement of $100.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2028, (3) $75.0 million upon the achievement of $175.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2029 and (4) $160.0 million upon the achievement of $250.0 million or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2029. Each milestone payment will only become payable once, if at all, upon the first time such milestone is achieved, and only one milestone payment will be paid with respect to a calendar year. In the event that more than one milestone is achieved in a calendar year, the higher milestone payment will become payable and the lower milestone payment will become payable only if the corresponding milestone is achieved again in a subsequent calendar year. To date, we have not received any milestone payments pursuant to the Asset Purchase Agreement. We now have no revenue-generating commercial products, and although we are eligible to receive up to $325.0 million in milestone-based payments from Alcon, there can be no assurance as to when we may receive such milestone payments or the amount of milestone payments we may receive, if any.

On December 27, 2022, we entered into an amendment to the Loan Agreement with Combangio and Oxford Finance, or the Third Loan Amendment. Pursuant to the Third Loan Amendment, the Lender and Agent agreed to amend certain provisions of the Loan Agreement to permit the transfer of the listing of our common stock from The Nasdaq Global Select Market to The Nasdaq Capital Market. Pursuant to the Third Loan Amendment, we agreed (A) to make partial prepayments of the principal amount of the term loan outstanding under the Loan Agreement as follows, or the Third Amendment Prepayments: (1) a payment of $5.0 million on or before June 30, 2023, representing a partial prepayment of principal in the amount of $4.7 million, plus a final payment fee of $0.3 million and (2) a payment of $5.0 million on or before January 31, 2024, representing a partial prepayment of principal in the amount of $4.7 million, plus a final payment fee of $0.3 million and (B) the start date for us to make amortization payments under the Loan Agreement was changed from January 1, 2026 to January 1, 2025, or the Amortization Date.

Pursuant to the Third Loan Amendment, in addition to the Third Amendment Prepayments, if we make an additional prepayment under the Loan Agreement equal to $5.0 million (inclusive of the final payment fee) on or prior to December 31, 2024, or the First Extension Prepayment, the Amortization Date will be automatically changed to July 1, 2025, and the maturity date of the Loan Agreement will be automatically changed from May 1, 2026 to November 1, 2026. If, in addition to the Third Amendment Prepayments and the First Extension Prepayment, we make an additional prepayment under the Loan Agreement equal to $2.5 million (inclusive of the final payment fee) on or prior to June 30, 2025, or the Second Extension Prepayment, the Amortization Date will be automatically changed to January 1, 2026, and the maturity date of the Loan Agreement will be automatically changed to May 1, 2027.

Under the Third Loan Amendment, the Lender and Agent also agreed to waive the prepayment fees for the Third Amendment Prepayments, the First Extension Prepayment, the Second Extension Prepayment and any other prepayments under the Loan Agreement. Pursuant to the Loan Agreement, we also will be required to pay all accrued and unpaid interest on the principal amounts of the term loan being repaid at the time of repayment. On January 25, 2023, we paid the Third Amendment Prepayments and the principal loan balance under the Loan Agreement following the Prepayments was $34.0 million.

We paid a facility fee of $0.4 million on the closing date of the Loan Agreement. 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 make partial repayments of the term loan to the Lender, subject to specified conditions, including the payment of applicable fees and accrued and unpaid interest on the principal amount of the term loan being repaid. For further information about the Loan Agreement, see Note 11, “Debt”, of our consolidated financial statements.

On November 28, 2022, in connection with the Private Placement, we entered into a Securities Purchase Agreement, or the Securities Purchase Agreement, with certain institutional investors names therein, or the Purchasers, pursuant to which we agreed to issue and sell, in a private placement priced at-the-market under Nasdaq rules, shares of our common stock and shares of our Series E Convertible Non-Redeemable Preferred Stock, or the Series E Preferred Stock, in two tranches for aggregate gross proceeds of up to $31.0 million, which we refer collectively as the Private Placement. Pursuant to the Securities Purchase Agreement, at the first closing of the Private Placement on December 1, 2022, we issued and sold to the Purchasers (i) 76,813 shares of common stock, at a price per share equal to $5.75 and (ii) 9,666 shares of Series E Preferred Stock, at a price per share equal to $575.00, for aggregate gross proceeds of approximately $6.0 million. On December 27, 2022, following the certification by our Chief Executive Officer that the FDA accepted our IND application for KPI-012, we issued and sold to the Purchasers at a second closing of the Private Placement a total of 43,478 shares of Series E Preferred Stock, at a price per share equal to $575.00, for aggregate gross proceeds of approximately $25.0 million. For further information about the Private Placement and the Securities Purchase Agreement, see Item 1, "Business."

As a result of the acquisition of Combangio, 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 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 which are in the mid-to-high single digits. The total potential maximum payout for the milestone payments which are contingent upon the achievement of specified development, regulatory and commercialization milestones is $40.0 million and the total potential maximum payout for future sales-based milestone payments is an additional $65.0 million. To date, of the $40.0 million of contingent consideration payable upon achievement of specified development, regulatory and commercialization milestones, we are obligated to pay to the former Combangio Equityholders an aggregate of $2.5 million in cash and $2.4 million in shares of our common stock (representing an aggregate of 105,039 shares of our common stock) upon dosing of the first patient in our Phase 2b clinical trial of KPI-012 for PCED in the United States in February 2023. We anticipate making this payment and issuing these shares of our common stock in March 2023. The remaining amount of $0.1 million for this milestone will be paid in January 2024. For a full description of the consideration payable as a result of the Combangio Acquisition, see Note 3 of our consolidated financial statements.

Our other material cash requirements from known contractual and other obligations as of December 31, 2022 primarily related to our licensing agreement with Stanford University. For information related to our future commitments relating to our licensing agreement, see Note 17, "Commitments and Contingences" of our consolidated financial statements.

Cash Flows

As of December 31, 2022 and 2021, we had $70.5 million and $92.1 million in cash and cash equivalents, respectively. As of December 31, 2022 and 2021, we had $43.3 million and $80.0 million in indebtedness, respectively, which represented the aggregate principal amount that was outstanding under the Loan Agreement with Oxford Finance.

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

	Year Ended December 31,		
	2022	2021	Change
	(in thousands)		
Net cash used in operating activities	$ (78,908)	$ (108,235)	$ 29,327
Net cash provided by investing activities	62,717	70,803	(8,086)
Net cash (used in) provided by financing activities	(7,942)	42,554	(50,496)
(Decrease) increase in cash and restricted cash	$ (24,133)	$ 5,122	$ (29,255)

Operating Activities

Net cash used in operating activities for the year ended December 31, 2022 was $78.9 million compared to $108.2 million for the year ended December 31, 2021, a decrease of $29.3 million, primarily due to a $18.2 million

decrease in the net loss adjusted for non-cash charges and the timing of working capital fluctuations which accounted for $11.1 million of the decrease. Notable working capital fluctuations include a decrease to accounts receivable in the year ended December 31, 2022 of $15.1 million as a result of the sale of our Commercial Business on July 8, 2022, whereas accounts receivable had increased by $5.8 million in the year ended December 31, 2021 driven by an increase in sales largely due to the launch of EYSUVIS. Inventory increased 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 $14.0 million.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2022 was $62.7 million compared to net cash provided of $70.8 million for the year ended December 31, 2021, a decrease of $8.1 million. Net cash provided by investing activities for the year ended December 31, 2022 related to proceeds from the disposition of the Commercial Business, net of transaction costs, of $62.9 million, proceeds from the sales or maturities of short-term investments of $5.0 million and proceeds from the sale of property and equipment of $0.1 million, partially offset by the purchases of short-term investments of $5.0 million and purchases of property and equipment and other assets of $0.3 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.

Financing Activities

Net cash used in financing activities for the year ended December 31, 2022 was $7.9 million, a decrease of $50.5 million compared to net cash provided by financing activities of $42.6 million in the year ended December 31, 2021. Net cash used in financing activities for the year ended December 31, 2022 largely consisted of $40.0 million of repayment of principal, prepayment premium and final payment fee on our Loan Agreement, partially offset by net proceeds of $30.8 million from the issuance of common stock and Series E Preferred Stock in our Private Placement, $1.0 million of net proceeds from the sale of shares of our common stock under the Amended and Restated Sales Agreement, and $0.3 million of proceeds from the exercise of stock options and the issuance of common stock under our employee stock purchase plan. 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 Amended and Restated Sales Agreement 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.

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 in the future as we conduct any necessary preclinical studies and clinical trials and other development activities for any other product candidates we may develop in the future, including our ongoing preclinical studies under our KPI-014 program. If we obtain marketing approval for KPI-012 or any product candidates we may develop, we expect that our selling, general and administrative expenses will increase substantially if and as we incur commercialization expenses related to product marketing, sales and distribution.

Our expenses will also increase if and as we:

- 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;
- grow our sales, marketing and distribution capabilities in connection with the commercialization of any product candidates for which we may submit for and obtain marketing approval;
- initiate and progress any preclinical development programs under our MSC-S platform, including from our KPI-014 program;
- conduct clinical trials and other development activities and/or seek marketing approval for any product candidates we may develop in the future;
- in-license or acquire the rights to other products, product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control, scientific, manufacturing, commercial and management personnel to support our operations;
- expand our operational, financial and management systems; and
- increase our product liability insurance coverage if we initiate commercialization efforts for our product candidates.

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, 2022, will enable us to fund our operations, debt service obligations, and capital expenditure requirements into the first quarter of 2025. We expect that our existing cash resources will be sufficient to enable us to obtain safety and efficacy data from our ongoing CHASE Phase 2b clinical trial of KPI-012 in PCED. However, we do not expect that our existing cash resources will be sufficient to enable us to complete the clinical development of KPI-012 for PCED or any other indication. We have based our estimates 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. We do not expect to generate revenue from KPI-012 or any other product candidate we may develop for the foreseeable future, if at all. Achieving and maintaining profitability will require us to be successful in a range of challenging activities, including:

- completing the clinical development of KPI-012 for PCED and any other indications we determine to pursue;
- subject to obtaining favorable results from our ongoing and planned clinical trials of KPI-012, applying for and obtaining marketing approval of KPI-012;
- successfully commercializing KPI-012, if approved;
- discovering, developing and successfully seeking marketing approval and commercialization of any additional product candidates we may develop in the future, including under our KPI-014 program;
- hiring and building a full commercial organization required for marketing, selling and distributing those products for which we obtain marketing approval;
- manufacturing at commercial scale, marketing, selling and distributing those products for which we obtain marketing approval;
- achieving an adequate level of market acceptance, and obtaining and maintaining coverage and adequate reimbursement from third-party payors for any products we commercialize;
- obtaining, maintaining and protecting our intellectual property rights; and
- adapting our business in response to the pandemic health event resulting from COVID-19 and its collateral consequences.

As a company, we have limited experience commercializing products, and we may not be able to commercialize a product successfully in the future. 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. We may never succeed in the foregoing activities and we 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. In addition, under the Securities Purchase Agreement, we also agreed that we will not, without the prior approval of the requisite Purchasers, (i) issue or authorize the issuance of any equity security that is senior or *pari passu* to the Series E Preferred Stock with respect to liquidation preference, (ii) incur any additional indebtedness for borrowed money in excess of $1.0 million, in the aggregate, outside the ordinary course of business, subject to specified exceptions, including the refinancing of our existing indebtedness or (iii) pay or declare any dividend or make any distribution on, any shares of our capital stock, subject to specified exceptions.

We will 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, Summary of Significant Accounting Policies, to the consolidated 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, 2022 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, 2022 and 2021, the aggregate principal amount outstanding under the Loan Agreement was $43.3 million and $80.0 million, respectively, 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. In January 2023, we paid down $9.3 million of principal under the Loan Agreement, and following such payment, the aggregate principal amount outstanding under the Loan Agreement was $34.0 million.

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-43 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, 2022. 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, 2022, 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, 2022. 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, 2022, our internal control over financial reporting was effective.

As a non-accelerated filer and a "smaller reporting company", as defined in Rule 12-b-2 under the Exchange 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, 2022 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

Executive Officers and Directors

Set forth below are the names of, and certain information for, each executive officer and member of our board of directors as of March 1, 2023. There are no family relationships among any of our directors or executive officers.

Name	Age	Position
Executive Officers		
Mark Iwicki	56	Chief Executive Officer and Chairman of the Board
Todd Bazemore	52	President and Chief Operating Officer
Kim Brazzell, Ph.D.	70	Head of Research and Development and Chief Medical Officer
Darius Kharabi	44	Chief Business Officer
Mary Reumuth, C.P.A.	47	Chief Financial Officer and Treasurer
Eric L. Trachtenberg	49	General Counsel, Chief Compliance Officer and Corporate Secretary
Non-Employee Directors		
Mark S. Blumenkranz, M.D.(2)	72	Director
Marjan Farid, M.D.(3)	49	Director
Andrew I. Koven(2)(3)	65	Director
C. Daniel Myers(2)(3)	68	Director
Robert Paull(1)(3)	46	Director
Gregory D. Perry(1)	62	Director
Howard B. Rosen(1)(2)	65	Director

(1) Member of the Audit Committee.

(2) Member of the Compensation Committee.

(3) Member of the Nominating and Corporate Governance Committee.

Executive Officers

Mark Iwicki has served as our Chief Executive Officer and Chairman of our board of directors since September 2015. Mr. Iwicki previously served as our President from August 2017 to December 2021 and as Executive Chairman of our board of directors from April 2015 to September 2015. Prior to joining us, Mr. Iwicki served as President and Chief Executive Officer of Civitas Therapeutics, Inc., or Civitas, a biopharmaceutical company, from January 2014 to November 2014. Prior to Civitas, Mr. Iwicki served as President and Chief Executive Officer at Blend Therapeutics, Inc., or Blend, a biopharmaceutical company, from December 2012 to January 2014. Prior to Blend, Mr. Iwicki was President and Chief Executive Officer of Sunovion Pharmaceuticals Inc. (formerly Sepracor Inc.), or Sunovion, a pharmaceutical company. Mr. Iwicki was at Sepracor/Sunovion from October 2007 to June 2012. Prior to joining Sepracor Inc., Mr. Iwicki was Vice President and Business Unit Head at Novartis Pharmaceuticals Corporation, a biopharmaceutical company. He was at Novartis from March 1998 to October 2007. Prior to that, Mr. Iwicki held management positions at Astra Merck Inc. and Merck & Co., Inc. In addition to serving on our board of directors, Mr. Iwicki also currently serves on the boards of Aerovate Therapeutics, Inc., Merus N.V., Akero Therapeutics, Inc. and Third Harmonic Bio, Inc. and formerly served on the board of Aimmune Therapeutics, Inc. and Pulmatrix Inc., all

publicly-traded companies. Mr. Iwicki holds a B.S. in Business Administration from Ball State University and an M.B.A. from Loyola University.

Todd Bazemore has served as our President since December 2021 and as our Chief Operating Officer since November 2017. Previously, he served as Executive Vice President and Chief Operating Officer of Santhera Pharmaceuticals (USA) Inc., or Santhera, a pharmaceutical company and subsidiary of Santhera Pharmaceuticals Holdings AG, from September 2016 until November 2017. Prior to joining Santhera, Mr. Bazemore served as Executive Vice President and Chief Commercial Officer of Dyax Corp., or Dyax, a biopharmaceutical company focused on orphan diseases, between April 2014 and January 2016, when Dyax was acquired by Shire plc. At Dyax, Mr. Bazemore oversaw all aspects of Dyax's commercial department including sales, marketing, commercial analytics, market access and patient services. Between April 2012 and September 2013, he served as Vice President, Managed Markets at Sunovion Pharmaceuticals, Inc., or Sunovion (a subsidiary of Dainippon Sumitomo Pharma Co. Ltd.), a global biopharmaceutical company focused on serious medical conditions. Prior to that, Mr. Bazemore held several roles of increasing responsibility at Sunovion, including Vice President of Sales and Vice President of Respiratory Business Unit. Since October 2020, Mr. Bazemore has served on the board of directors of Pulmatrix Inc., a clinical stage publicly traded biopharmaceutical company. He received his Bachelor of Science from the University of Massachusetts, Lowell.

Kim Brazzell, Ph.D. has served as our Chief Medical Officer since February 2013 and as our Head of Research and Development since December 2021. Dr. Brazzell served as Chief Medical Officer of Mimetogen Pharmaceuticals, Inc., a clinical stage biotechnology company, from January 2012 until December 2015. Dr. Brazzell also held several executive positions at Inspire Pharmaceuticals, Inc., or Inspire, a specialty pharmaceutical company focusing on ophthalmic and respiratory products, including Executive Vice President of Medical and Scientific Affairs from 2010 to 2011, Executive Vice President and Head of Ophthalmology Business from 2009 to 2010, and Senior Vice President of Ophthalmic Research and Development from 2004 to 2008. Prior to joining Inspire, Dr. Brazzell served as Global Head of Clinical R&D and Senior Vice President, U.S. R&D, of Novartis Ophthalmics AG from 2000 to 2004. Dr. Brazzell also served as Vice President, R&D at Ciba Vision Ophthalmics, Inc. and as Associate Director, R&D, at Alcon Laboratories, Inc. Dr. Brazzell received a B.S. in Pharmacy and a Ph.D. in Pharmaceutical Sciences from the University of Kentucky.

Darius Kharabi has served as our Chief Business Officer since November 2021. From August 2018 to November 2021, Mr. Kharabi was co-founder and CEO of Combangio Inc., a clinical stage ophthalmology mesenchymal stem cell secretome company acquired by Kala Pharmaceuticals in November 2021. He is the co-founder of Lagunita Biosciences LLC, an early-stage medical investment company, and from October 2015 to August 2018 he helped create and manage multiple Lagunita portfolio life-science companies, including xCella Biosciences, acquired by Ligand, Kedalion Therapeutics, acquired by Novartis AG, and Combangio. From October 2015 through August 2019 he served as the Chief Operating Officer of xCella Biosciences and from October 2015 through November 2017 he served as the President of Kedalion. Prior to Lagunita, he served as Vice President, Corporate Development and International Sales at OrthAlign, a commercial stage orthopedic surgery navigation company, where his responsibilities included the launch of the KneeAlign® total knee arthroplasty navigation product line in the US and global markets. Mr. Kharabi started his career as a biotechnology licensing attorney at Wilson, Sonsini, Goodrich & Rosati, PC. He received his B.S. in Biochemistry from Georgetown University and his J.D. and M.B.A. degrees from Stanford University.

Mary Reumuth, C.P.A. has served as our Chief Financial Officer since July 2017, Senior Vice President, Finance from February 2017 to July 2017, our Vice President, Finance from December 2014 to February 2017, our Senior Director, Finance from February 2014 to December 2014, our Corporate Controller from February 2014 to July 2017 and as our Treasurer since February 2014. Prior to joining us, Ms. Reumuth acted as an independent financial consultant from November 2012 to January 2014 and, prior to that, served as Corporate Controller for Enobia Pharma Corp., or Enobia, a global biopharmaceutical company acquired by Alexion Pharmaceuticals, Inc., from May 2011 to June 2012. Prior to Enobia, Ms. Reumuth served as Director of Finance at Verenium Corporation, or Verenium, a biotechnology company, from December 2007 to March 2011. From 2001 to 2007, Ms. Reumuth held a variety of finance and accounting positions at Genzyme Corporation, or Genzyme, (now a Sanofi Company), and ILEX Oncology, Inc., or ILEX (acquired by Genzyme). Prior to ILEX, Ms. Reumuth was an auditor at Ernst & Young LLP. Since April 2022, Ms. Reumuth has served on the board of directors of Olink Holding AB, a publicly traded company. Ms. Reumuth earned her Bachelor's degree in Business Administration from Texas A&M University-Corpus Christi, and is a Certified Public Accountant.

Eric L. Trachtenberg has served as our General Counsel and Corporate Secretary since April 2018 and as our Chief Compliance Officer since June 2018. Previously, he served as General Counsel, Chief Compliance Officer and Corporate Secretary of Aralez Pharmaceuticals Inc., or Aralez, a pharmaceutical company, from February 2016 to March 2018. Prior to that, he served in similar capacities for Pozen Inc., Aralez's predecessor, from June 2015 to February 2016. Mr. Trachtenberg also formerly served as Deputy General Counsel at Auxilium Pharmaceuticals, Inc., a specialty biopharmaceutical company, from May 2012 through its acquisition by Endo Pharmaceuticals in February 2015. Prior to Auxilium, he was Vice President, General Counsel and Corporate Secretary of Enobia Pharma, Inc. from April 2011 through its acquisition by Alexion Pharmaceuticals in April 2012. Prior to that, Mr. Trachtenberg served as Vice President and Associate General Counsel of Sepracor Inc. (now known as Sunovion Pharmaceuticals Inc.) commencing in May 2007 and remained in that position following the acquisition of Sepracor Inc. by Dainippon Sumiztomo Pharma through April 2011. Mr. Trachtenberg also held a Senior Counsel position at Kos Pharmaceuticals, Inc. from July 2005 to April 2007 before its acquisition by Abbott. Mr. Trachtenberg began his career at Blank Rome LLP. He holds a Juris Doctorate and Master of Business Administration from Temple University and a Bachelor of Science in Management from Tulane University.

Non- Employee Directors

Mark S. Blumenkranz, M.D., MMS, has served as a member of our board of directors since November 2021. Dr. Blumenkranz has served as the HJ Smead Professor Emeritus in the Department of Ophthalmology at Stanford University since March 2019, the Co-Director of its Ophthalmic Innovation Program since 2016, and he previously served as Department Chair from 1997 until 2015. Dr. Blumenkranz played a leading role in the planning, fundraising and construction of the Byers Eye Institute at Stanford University and served as its Director from its opening in September 2010 through June 2015. Dr. Blumenkranz previously served on the board of directors of Oculex Pharmaceuticals, Inc., which was acquired by Allergan, Inc. in 2003, Macusight, an ophthalmic pharmaceutical company, acquired by Santen in 2010, Peak Surgical, Inc., an innovator in pulsed plasma mediated electro-surgery that was acquired by Medtronic, Inc. in 2011, and OptiMedica Corp. which was acquired by Abbott Medical Optics in 2013. In 2006, he co-founded Adverum Biotechnologies, Inc., and served as chairman of its board of directors through 2016. In 2011, he co-founded Oculeve, Inc., and served on its board directors through its acquisition by Allergan in August 2015. He was a founder and served on the board of directors of Verana Health, Inc., a digital medicine and health analytics company, from 2009 until 2020. He was the founding Chairman of Kedalion Therapeutics, an ophthalmic drug delivery company and served as its chief executive officer from September 2019 until June 2022, when it was acquired by Novartis AG. He also served on the board of directors of One Medical from 2019 until its acquisition by Amazon in February 2023. He currently serves as director at BVI Visitec, a global ophthalmic surgical company, and Iveric Bio, Inc., a publicly traded ophthalmic biopharmaceutical company. Since October 2015, Dr. Blumenkranz has served as Managing Partner of Lagunita Biosciences LLC, an early-stage medical investment company, that is our current 5% beneficial stockholder. Since May 2015, Mr. Blumenkranz has also served as the Managing Partner of Garland Investments, Inc. Dr. Blumenkranz holds an A.B. in Biology, Master's Degree in Biochemical Pharmacology, and M.D. from Brown University. He completed his internship and ophthalmic residency at Stanford and subsequently the Executive Program at Stanford's Graduate School of Business. We believe that Dr. Blumenkranz's experience in the ophthalmology field qualifies him to serve as a member of our board of directors.

Marjan Farid, M.D. has served as a member of our board of directors since October 2022. Since 2007, Dr. Farid has served as Professor of Clinical Ophthalmology, Director of Cornea, Refractive & Cataract Surgery, and Vice Chair of Ophthalmic Faculty at the Gavin Herbert Eye Institute, University of California Irvine. Her clinical practice is divided between patient care, teaching, and research. Dr. Farid's research interests focus on corneal surgery, specifically the use of the femtosecond laser for corneal transplantation. Dr. Farid is also the founder of the Severe Ocular Surface Disease Center at the University of California Irvine, where she performs limbal stem cell transplants, as well as artificial corneal transplantation, for the treatment of patients with severe ocular surface disease. Dr. Farid also serves as the Chair of the Corneal Clinic Committee of the American Society of Cataract and Refractive Surgery. Dr. Farid received a B.S. in Biology from the University of California - Los Angeles and M.D. from the University of California - San Diego. We believe that Dr. Farid's experience in the ophthalmology field qualifies her to serve as a member of our board of directors.

Andrew I. Koven has served as a member of our board of directors since September 2017 and as our Lead Independent Director since December 2018. Mr. Koven was, until his retirement in January 2019, the President and Chief Business Officer of Aralez Pharmaceuticals Inc., or Aralez, a public specialty pharmaceutical company, and served in that role with the company's predecessor, Pozen Inc., or Pozen, commencing in June 2015. Prior to joining

Pozen, Mr. Koven served as Executive Vice President, Chief Administrative Officer and General Counsel of Auxilium Pharmaceuticals Inc., a public specialty biopharmaceutical company, from February 2012 until January 2015, when it was acquired by Endo International plc. Mr. Koven served as President and Chief Administrative Officer and a member of the board of directors of Neurologix, Inc., a company focused on the development of multiple innovative gene therapy development programs, from September 2011 to November 2011. Before Neurologix, Mr. Koven served as Executive Vice President and Chief Administrative and Legal Officer of Inspire Pharmaceuticals, Inc., a public specialty pharmaceutical company, from July 2010 until May 2011 when it was acquired by Merck & Co., Inc. Previously, Mr. Koven served as Executive Vice President, General Counsel and Corporate Secretary of Sepracor Inc. (now Sunovion), a public specialty pharmaceutical company, from March 2007 until February 2010 when it was acquired by Dainippon Sumitomo Pharma Co., Ltd. Prior to joining Sepracor, Mr. Koven served as Executive Vice President, General Counsel and Corporate Secretary of Kos Pharmaceuticals, Inc., a public specialty pharmaceutical company, from August 2003 until its acquisition by Abbott Laboratories (now AbbVie) in December 2006. Mr. Koven began his career in the pharmaceutical industry first as an Assistant General Counsel and then as Associate General Counsel at Warner-Lambert Company from 1993 to 2000, followed by his role as Senior Vice President and General Counsel at Lavipharm Corporation from 2000 to 2003. Mr. Koven also currently serves on the board of NeuroBo Pharmaceuticals, Inc., a publicly-traded company, and has served as its chairperson since January 2022. From 1986 to 1992 he was a corporate associate at Cahill, Gordon & Reindel in New York. From 1992 to 1993 he served as Counsel, Corporate and Investment Division, at The Equitable Life Assurance Society of the U.S. Mr. Koven holds a Master of Laws (LL.M.) Degree from Columbia University School of Law and a Bachelor of Laws (LL.B.) Degree and Bachelor of Arts Degree in Political Science from Dalhousie University. We believe that Mr. Koven's extensive experience in the pharmaceutical industry qualifies him to serve as a member of our board of directors.

C. Daniel Myers has served as a member of our board of directors since October 2021. Mr. Myers served as the Chief Executive Officer of MediPrint Ophthalmics, Inc. (formerly Leo Lens Pharma), a private eye-care company, from April 2020 to April 2022. Previously, Mr. Myers co-founded Alimera Sciences, Inc., or Alimera, a publicly traded pharmaceutical company, and served as its Chief Executive Officer from 2003 until January 2019. Before co-founding Alimera, Mr. Myers was an initial employee of Novartis Ophthalmics (formerly CIBA Vision Ophthalmics), a pharmaceutical company, and served as its Vice President of sales and marketing from 1991 to 1997 and as President from 1997 to 2003. Mr. Myers has served as a director of Alimera since 2003 and has served as chairman of its board of directors since January 2019. In addition, Mr. Myers served on the board of directors of Ocular Therapeutix, Inc., a publicly traded biopharmaceutical company, from 2009 to 2012. Mr. Myers holds a B.S. in Industrial Management from the Georgia Institute of Technology. We believe that Mr. Myers' experience in the biopharmaceutical industry, including his specific experience with ophthalmology pharmaceutical companies, qualifies him to serve as a member of our board of directors.

Robert Paull has served as a member of our board of directors since July 2009. Mr. Paull was a co-founder of, and since 2014 has been a Venture Partner at, Lux Capital Management, or Lux Capital, where he focuses on healthcare ventures. Mr. Paull has served as an Advisor to Zelda Ventures, an investment advisor firm, since January 2023, to Broken String Biosciences, a biosciences company, since April 2022 and to Outsized Ventures, an early-stage venture capital fund, since December 2021. In addition, Mr. Paull served as our founding Chief Executive Officer, President and Treasurer from July 2009 to June 2012. Mr. Paull also served as founding Chief Executive Officer of Genocea Biosciences Inc., a vaccine discovery and development company, from August 2006 to February 2009, and was the co-founder of Lux Research, Inc., an emerging technology market research and consulting firm, which was founded in January 2004. From January 2018 to December 2020, Mr. Paull was the founding Chief Executive Officer of Mahana Therapeutics, Inc., a digital therapeutics company. Mr. Paull holds a B.S. in Architecture from the University of Virginia. We believe that Mr. Paull's extensive experience guiding and investing in healthcare ventures qualifies him to serve as a member of our board of directors.

Gregory D. Perry has served as a member of our board of directors since February 2018. Mr. Perry served as Chief Financial Officer for Finch Therapeutics Group, Inc., a public therapeutics company focused on the microbiome, from June 2018 to April 30, 2022. Previously, he served as Chief Financial and Administrative Officer of Novelion Therapeutics Inc., or Novelion, a public biopharmaceutical company, from November 2016 to December 2017. Prior to this, Mr. Perry was Chief Financial Officer of Aegerion Pharmaceuticals, Inc., a public biopharmaceutical company, from July 2015 until its merger with Novelion in November 2016. Prior to that, he served as Chief Financial and Business Officer of Eleven Biotherapeutics, Inc., a public company, from January 2014 to June 2015. Before joining Eleven Biotherapeutics, Mr. Perry served as the Interim Chief Financial Officer of InVivo Therapeutics, a public biotechnology company, from September 2013 to December 2013, and prior to that he served as the Senior Vice

President and Chief Financial Officer of ImmunoGen, Inc., a public biotechnology company, from 2009 until he was promoted in 2011 to Executive Vice President and Chief Financial Officer, a role he held until 2013. Before that, he was the Chief Financial Officer of Elixir Pharmaceuticals. Mr. Perry previously was Senior Vice President and Chief Financial Officer of Transkaryotic Therapies. He has also held various financial leadership roles within PerkinElmer Inc., Domantis Ltd., Honeywell and General Electric. Since May 2016, Mr. Perry has served on the board of directors of Merus N.V., a public clinical-stage immuno-oncology company, including as Chair of its Audit Committee. From December 2011 to February 2016, Mr. Perry served on the board of directors of Ocata Therapeutics, a public biotechnology company, including as Chair of its Audit Committee and a member of its Compensation Committee, until it was acquired by Astellas Pharma Inc. Mr. Perry received a B.A. in Economics and Political Science from Amherst College. We believe that Mr. Perry's experience in the biopharmaceutical industry, including his specific experience in financial leadership roles in biopharmaceutical companies, qualifies him to serve as a member of our board of directors.

Howard B. Rosen has served as a member of our board of directors since January 2014. Since 2008, Mr. Rosen has served as a consultant to several companies in the biotechnology industry. He has served at Stanford University as an adjunct professor in Chemical Engineering since 2021 and as a lecturer in Management since 2011, and he previously served as a lecturer in Chemical Engineering from 2009 until 2021. Mr. Rosen served as Chief Executive Officer of AcelRx Pharmaceuticals, Inc., or AcelRx, a public specialty pharmaceutical company developing products for pain relief, from April 2016 to March 2017, and Interim Chief Executive Officer from April 2015 to March 2016. Mr. Rosen also served as Interim President and Chief Executive Officer of Pearl Therapeutics, Inc. from June 2010 to March 2011. From 2004 to 2008, Mr. Rosen was Vice President of Commercial Strategy at Gilead Sciences, Inc., a biopharmaceutical company. From 2003 until 2004, Mr. Rosen was President of ALZA Corporation, a pharmaceutical and medical systems company that merged in 2001 with Johnson & Johnson, a global healthcare company. Prior to that, from 1994 until 2003, Mr. Rosen held various positions at ALZA Corporation. Mr. Rosen is a member of the board of directors of AcelRx and also served on the board of directors of Alcobra, Ltd., a public pharmaceutical company, until November 2017. Mr. Rosen is also currently a member of the board of directors of private companies, including Firecycte Therapeutics, Inc., Hammerton, Inc., Hopewell Therapeutics, Inc. and Entrega, Inc., and was a member of the board of directors of Metera Pharmaceuticals, Inc. from 2018 to 2020 and Aria Pharmaceuticals, Inc. from 2020 to 2023. Mr. Rosen holds a B.S. in Chemical Engineering from Stanford University, an M.S. in Chemical Engineering from the Massachusetts Institute of Technology and an M.B.A. from the Stanford Graduate School of Business where he was an Arjay Miller Scholar and a Henry Ford II Scholar. We believe that Mr. Rosen's experience in the biopharmaceutical industry, including his specific experience with the development and commercialization of pharmaceutical products, qualifies him to serve as a member of our board of directors.

Bankruptcies

From February 2016 to March 2018, Eric L. Trachtenberg, our General Counsel and Chief Compliance Officer, served as General Counsel, Chief Compliance Officer and Corporate Secretary of Aralez. Prior to that, Mr. Trachtenberg served in similar capacities for Pozen, Aralez's predecessor, from June 2015 to February 2016. In addition, Mr. Koven was, until his retirement on January 30, 2019, the President and Chief Business Officer of Aralez and served in that role with the company's predecessor, Pozen, commencing on June 1, 2015. On August 10, 2018, Aralez and its affiliates each filed a voluntary petition for relief under Chapter 11 of the United States Bankruptcy Code.

Composition of the Board of Directors

Our board of directors is authorized to have, and currently consists of, eight members divided into three classes, with members of each class holding office for staggered three-year terms. There are currently three Class I directors (Marjan Farid, M.D., Andrew I. Koven and Gregory D. Perry), whose terms expire at the 2024 annual meeting of stockholders; two Class II directors (Mark Iwicki and Mark S. Blumenkranz, M.D.), whose terms expire at the 2025 annual meeting of stockholders; and three Class III directors (Robert Paull, C. Daniel Myers and Howard B. Rosen) whose terms expire at the 2023 annual meeting of stockholders (in all cases subject to the election and qualification of their successors or to their earlier death, resignation or removal).

Audit Committee and Audit Committee Financial Expert

The members of our audit committee are Howard B. Rosen, Robert Paull and Gregory D. Perry. Mr. Perry is the chair of the audit committee. Our board of directors has determined that Mr. Perry is an "audit committee financial expert" as defined in applicable SEC rules. Our board of directors has determined that Mr. Perry is an "independent

director" as defined under applicable Nasdaq rules and satisfies the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer and principal accounting officer. A copy of the code is available on the "Investors—Corporate Governance" section of our website, which is located at www.kalarx.com. Our board of directors is responsible for overseeing the code of business conduct and ethics and must approve any waivers of the code for directors, officers and employees. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

The information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report or in any other report or document we file with the SEC, and any reference to our website address is intended to be an inactive textual reference only.

Item 11. Executive Compensation

Executive and Director Compensation Processes

Our executive compensation program is administered by the compensation committee of our board of directors, subject to the oversight and approval of our board of directors. Our compensation committee reviews our executive compensation practices on an annual basis and based on this review approves, or, as appropriate, makes recommendations to our board of directors for approval of our executive compensation program. In designing our executive compensation program, our compensation committee considers publicly available compensation data for national and regional companies in the biotechnology/pharmaceutical industry to help guide its executive compensation decisions at the time of hiring and for subsequent adjustments in compensation. Our director compensation program is administered by our board of directors with the assistance of the compensation committee. The compensation committee conducts an annual review of director compensation and makes recommendations to the board of directors with respect thereto.

Since 2018, our compensation committee has retained Aon's Human Capital Solutions practice, a division of Aon plc (formerly Radford), as its independent compensation consultant, to provide comparative data on executive compensation practices in our industry and to advise on our executive and director compensation programs generally. In January 2023, our compensation committee retained Pearl Meyer, as an additional independent compensation consultant, to advise on a proposed option exchange program. Although our compensation committee considers the advice and guidelines of Aon as to our executive and director compensation programs, and considered the advice of Pearl Meyer as to the proposed option exchange program, our compensation committee ultimately makes its own decisions about these matters and recommendations to our board about these matters. During the fiscal year ended December 31, 2022, the compensation committee directly engaged Aon to develop recommendations covering equity compensation for executives and an equity compensation strategy for non-officer employees; and review and make recommendations with respect to our director compensation program. Aon ultimately developed recommendations that were reviewed by the compensation committee.

In the future, we expect that our compensation committee will continue to engage independent compensation consultants to provide additional guidance on our executive compensation programs, our director compensation programs and to conduct further competitive industry benchmarking against a peer group of publicly traded companies.

The compensation committee reviewed information regarding the independence and potential conflicts of interest of Aon and Pearl Meyer, taking into account, among other things, the factors set forth in the Nasdaq listing standards. Based on such review, the compensation committee concluded that the engagements of Aon and Pearl Meyer did not raise any conflict of interest.

Under its charter, the compensation committee may form, and delegate authority to, subcommittees, consisting of independent directors, as it deems appropriate. During fiscal year 2022, the compensation committee did not form or delegate authority to such subcommittees. In addition, under its charter, the compensation committee may delegate to

one or more executive officers the power to grant options, restricted stock units or other stock awards pursuant to its 2017 Equity Incentive Plan, as amended, to employees who are not directors or executive officers of the Company. During fiscal year 2022, the compensation committee delegated authority to our Chief Executive Officer to grant certain stock options and restricted stock units to non-executive employees with respect to annual equity awards.

Executive Compensation

The following discussion relates to the compensation of our Chief Executive Officer, Mark Iwicki, our President and Chief Operating Officer, Todd Bazemore, and our Head of Research and Development and Chief Medical Officer, Kim Brazzell, Ph.D. for the periods presented. These three individuals are collectively referred to in this Annual Report on Form 10-K as our named executive officers. Each year, our compensation committee and board of directors review and determine the compensation of our named executive officers.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to each of our named executive officers for the periods presented.

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Stock Awards ($)(2)	Option Awards ($)(3)	All other Compensation ($)	Total ($)
Mark Iwicki	2022	682,110	409,266	—	770,803	6,120 (4)	1,868,299
Chief Executive Officer	2021	643,500	270,270	521,360	1,330,806	6,120 (4)	2,772,056
Todd Bazemore	2022	515,000	257,500	—	242,777	10,540 (5)	1,025,817
President and Chief Operating Officer	2021	489,878	171,457	188,650	483,131	10,240 (6)	1,343,356
Kim Brazzell, Ph.D.	2022	500,000	225,000	—	242,777	25,912 (7)	993,689
Head of Research and Development and Chief Medical Officer	2021	476,207	150,005	188,650	483,131	18,976 (8)	1,316,969

(1) The amounts reported in the "Bonus" column reflect discretionary annual cash bonuses earned by our named executive officers for their performance in the years ended December 31, 2022 and 2021.

(2) The amounts reported in the "Stock Awards" column reflect the aggregate grant date fair value of restricted stock unit awards granted during 2021 computed in accordance with the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718. For the assumptions underlying the valuation of such restricted stock unit awards, see Note 2 to our financial statements appearing in this Annual Report on Form 10-K.

(3) The amounts reported in the "Option Awards" column reflect the aggregate grant date fair value of stock options (which for 2022, have time- and/or performance-based vesting conditions) awarded during the periods presented, computed in accordance with the provisions of FASB ASC Topic 718 using a Black-Scholes option pricing model. For performance-based stock options included in the "Option Awards" column for the year ended December 31, 2022, the amounts in the table reflect the grant date fair value of such awards based on the probable outcome of the performance conditions at the end of the year which represent $82,138, $31,291 and $31,291 for Mr. Iwicki, Mr. Bazemore and Dr. Brazzell, respectively. Assuming that the highest level of performance conditions were achieved, the value of the performance-based options at grant date for Mr. Iwicki, Mr. Bazemore and Dr. Brazzell would have been $246,414, $93,872 and $93,872, respectively. 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. For the assumptions underlying the valuation of the stock option grants, see Note 14 to our financial statements appearing in this Annual Report on Form 10-K.

(4) Amount represents compensation of $6,120 from premiums we paid on behalf of Mr. Iwicki for life and disability insurance.

(5) Amount represents compensation of $6,100 from matching contributions made by us to Mr. Bazemore's tax-qualified 401(k) Savings Plan account and $4,440 from premiums we paid on behalf of Mr. Bazemore for life and disability insurance.

(6) Amount represents compensation of $5,800 from matching contributions made by us to Mr. Bazemore's tax-qualified 401(k) Savings Plan account and $4,440 from premiums we paid on behalf of Mr. Bazemore for life and disability insurance.

(7) Amount represents compensation of $6,100 from matching contributions made by us to Dr. Brazzell's tax-qualified 401(k) Savings Plan account and $19,812 from premiums we paid on behalf of Dr. Brazzell for life and disability insurance.

(8) Amount represents compensation of $5,800 from matching contributions made by us to Dr. Brazzell's tax-qualified 401(k) Savings Plan account and $13,176 from premiums we paid on behalf of Dr. Brazzell for life and disability insurance.

Narrative Disclosure to Summary Compensation Table

Base Salary. We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

Mr. Iwicki's, Mr. Bazemore's and Dr. Brazzell's annual base salaries were $682,110, $515,000 and $500,000, respectively, for 2022. In December 2022, our compensation committee increased Mr. Iwicki's, Mr. Bazemore's and Dr. Brazzell's annual base salaries to $709,394, $535,600 and $520,000, respectively, effective January 1, 2023.

Annual Bonus. Performance-based bonuses, which are calculated as a percentage of base salary, are designed to motivate our employees to achieve annual goals based on our strategic, financial and operating performance objectives. Historically, our board of directors or our compensation committee has approved discretionary annual cash bonuses to our named executive officers with respect to their prior year performance.

With respect to 2022 performance, our compensation committee awarded bonuses of $409,266, $257,500 and $225,000 to Mr. Iwicki, Mr. Bazemore and Dr. Brazzell, respectively, which represented payments at 100% of each individual's target bonus opportunity (which target bonus opportunities, expressed as a percentage of 2022 annual base salary, were 60%, 50% and 45%, respectively). Mr. Iwicki's individual performance-based target bonus amount for 2023, expressed as a percentage of his 2023 base salary, is 60%. Mr. Bazemore's individual performance-based target bonus amount for 2023, expressed as a percentage of his 2023 base salary, is 50%. Dr. Brazzell's individual performance-based target bonus amount for 2023, expressed as a percentage of his 2023 base salary, is 45%.

Equity Incentives. Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incentivizes our executive officers to remain in our employment during the vesting period. Accordingly, our compensation committee annually reviews the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options and/or restricted stock units with time-based and/or performance-based vesting conditions.

In January 2022, we granted to Mr. Iwicki options to purchase 15,499 shares of our common stock and to each of Mr. Bazemore and Dr. Brazzell options to purchase 4,759 shares of our common stock. Such options vest monthly as to 1/48th of the shares underlying the option.

In January 2022, we also granted performance-based stock options to Mr. Iwicki, Mr. Bazemore, and Dr. Brazzell. Specified portions of the options will vest based on the level of achievement of specified performance metrics relating to financial, operational and scientific matters. The level of achievement of the performance metrics will be determined by the compensation committee based on pre-specified criteria. The target number of options eligible to vest

under the performance-based options is set forth in the table below. A higher or lower number of options than the target (or no portion) may vest based on the level of achievement of each of the performance metrics, except that in no event will more than 150% of the target number of options vest.

	Number of Shares Based on Level of Achievement		
Name	**Threshold[(1)]**	**Target[(2)]**	**Maximum[(3)]**
Mark Iwicki	1,890	3,780	5,670
Todd Bazemore	720	1,440	2,160
Kim Brazzell	720	1,440	2,160

(1) Assumes all of the specified performance metrics are achieved at a threshold level of performance (50% of target).

(2) Assumes all of the specified performance metrics are achieved at a target level of performance (100% of target).

(3) Assumes all of the specified performance metrics are achieved at a maximum level of performance (150% of target).

Prior to our IPO, our executives were eligible to participate in our 2009 Plan. Following the closing of our IPO, our employees and executives are eligible to receive stock options and other stock-based awards pursuant to the 2017 Equity Incentive Plan and no further grants are made under the 2009 Plan. For a description of our 2009 Plan and our 2017 Equity Incentive Plan, as amended, see "-Stock Option and Other Compensation Plans".

Historically, we have used stock options to compensate our executive officers in the form of initial grants in connection with the commencement of employment and also at various times, often but not necessarily annually. The award of stock options to our executive officers, including our Chief Executive Officer, generally have been and going forward are expected to be made by our board of directors. We have granted stock options to our executive officers with both time-based and performance-based vesting conditions. Since our IPO and going forward, annual and other option grants made to existing executive officers and employees typically vest monthly as to 1/48th of the shares underlying the option. Vesting and exercise rights cease shortly after termination of employment except in the case of death or disability and, in certain circumstances, including, upon a change in control. Prior to the exercise of an option, the holder has no rights as a stockholder with respect to the shares subject to such option, including no voting rights and no right to receive dividends or dividend equivalents. In addition, prior to our IPO, we have granted stock options with exercise prices equal to the fair market value of our common stock on the date of grant as determined by our board of directors or compensation committee, based on a number of objective and subjective factors. The exercise price of all stock options granted after our IPO has been and will be equal to the fair market value of shares of our common stock on the date of grant, which will be determined by reference to the closing market price of our common stock on The Nasdaq Capital Market on the date of grant.

At times, we have also used restricted stock units to compensate our executive officers. The awards of restricted stock units to our executive officers, including our Chief Executive Officer, were made by our board of directors in 2021 and 2020. We have granted restricted stock units to our executive officers with time-based and/or performance-based vesting conditions. Time-based restricted stock unit awards vest over two or three years, as applicable. Restricted stock units with performance-based vesting conditions were all fully vested as of December 31, 2022. Prior to settlement of the restricted stock units, the holder has no rights as a stockholder with respect to the shares subject to such restricted stock unit, including no voting rights and no right to receive dividends or dividend equivalents. None of our executive officers is currently party to an employment agreement that provides for guaranteed equity awards.

Outstanding Equity Awards at December 31, 2022

The following table sets forth information regarding all outstanding equity awards held by each of our named executive officers as of December 31, 2022.

	Option Awards					Stock Awards			
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Number of Securities Underlying Unexercised Unearned Options (#)	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested ($) (1)	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested ($)
Mark Iwicki	5,449	—	—	167.00	6/3/2025	—	—	—	—
	7,576	—	—	260.50	9/11/2025	—	—	—	—
	12,195	—	—	167.00	6/17/2026	—	—	—	—
	1,572	—	—	750.00	7/18/2027	—	—	—	—
	4,599		—	643.00	2/6/2028	—	—	—	—
	9,008	191 (2)	—	259.50	1/1/2029	—	—	—	—
	5,320	1,979 (3)	—	192.00	1/1/2030	—	—	—	—
	2,898	3,161 (4)	—	343.00	1/3/2031	—	—	—	—
	3,549	11,950 (5)	—	68.50	1/3/2032	—	—	—	—
	—	—	1,890 (6)	68.50	1/3/2032	—	—	—	—
	—	—	—	—	—	1,014 (8)	38,684	—	—
Todd Bazemore	3,439	—	—	980.00	11/19/2027	—	—	—	—
	499		—	643.00	2/6/2028	—	—	—	—
	3,426	73 (2)	—	259.50	1/1/2029	—	—	—	—
	2,769	730 (7)	—	172.50	10/10/2029	—	—	—	—
	1,750	650 (3)	—	192.00	1/1/2030	—	—	—	—
	1,050	1,149 (4)	—	343.00	1/3/2031	—	—	—	—
	1,089	3,670 (5)	—	68.50	1/3/2032	—	—	—	—
	—	—	720 (6)	68.50	1/3/2032	—	—	—	—
	—	—	—	—	—	367 (8)	14,001	—	—
Kim Brazzell, Ph.D	308	—	—	260.50	10/2/2025	—	—	—	—
	2,047	—	—	167.00	6/17/2026	—	—	—	—
	942	—	—	750.00	7/18/2027	—	—	—	—
	1,399	—	—	643.00	2/6/2028	—	—	—	—
	2,936	63 (2)	—	259.50	1/1/2029	—	—	—	—
	1,745	654 (3)	—	192.00	1/1/2030	—	—	—	—
	1,050	1,149 (4)	—	343.00	1/3/2031	—	—	—	—
	1,089	3,670 (5)	—	68.50	1/3/2032	—	—	—	—
	—	—	720 (6)	68.50	1/3/2032	—	—	—	—
	—	—	—	—	—	367 (8)	14,001	—	—

(1) Amounts shown are based on a price of $38.15 per share, which was the closing price of our common stock as reported on The Nasdaq Global Select Market on December 30, 2022, the last trading day of the year.

(2) The option vests over four years, with 2.0833% of the shares underlying the option vested on February 2, 2019 and 2.0833% of the shares vesting monthly thereafter.

(3) The option vests over four years, with 2.0833% of the shares underlying the option vested on February 2, 2020 and 2.0833% of the shares vesting monthly thereafter.

(4) The option vests over four years, with 2.0833% of the shares underlying the option vested on February 4, 2021 and 2.0833% of the shares vesting monthly thereafter.

(5) The option vests over four years, with 2.0833% of the shares underlying the option vested on February 3, 2022 and 2.0833% of the shares vesting monthly thereafter.

(6) The option vests based on the level of achievement of specified performance metrics, as more fully described above under “-Narrative Disclosure to Summary Compensation Table”. Options are included in this table based on achieving a threshold level of performance. As of December 31, 2022, none of the performance metrics had been certified by the compensation committee as having been achieved.

(7) The option vests over four years, with 2.0833% of the shares underlying the option vested on November 15, 2019 and 2.0833% of the shares vesting monthly thereafter.

(8) The restricted stock units vest as to 1/2 of the shares on each of January 4, 2023 and 2024.

Employment Agreements with Named Executive Officers

Letter Agreement with Mr. Iwicki

Mr. Iwicki was appointed as our Chief Executive Officer and Chairman of our board of directors pursuant to a letter agreement with us dated September 10, 2015, which amended and restated a prior letter agreement. Mr. Iwicki is an at-will employee, and his employment with us can be terminated by him or us at any time and for any reason.

Mr. Iwicki's base salary is subject to annual review and adjustment by our compensation committee. Mr. Iwicki's annual base salary was $709,394, effective January 1, 2023. In addition, Mr. Iwicki is eligible to receive a discretionary bonus in a target amount of 60% of his annual base salary, as determined by our board of directors in its sole discretion.

On March 11, 2019, Mr. Iwicki's employment letter agreement was amended to revise the severance benefits he is entitled to receive upon termination in connection with the following events. Subject to his execution and nonrevocation of a release of claims in our favor, in the event of the termination of Mr. Iwicki's employment by us without cause or by him for good reason, each as defined in his employment letter agreement, and such termination is not within the twenty-four month period following a change of control, as defined in his employment letter agreement, Mr. Iwicki will be entitled to a lump sum payment in an amount equal to (i) twenty-four months of his then-current annual base salary, (ii) any bonus earned for the year prior to the year of termination that has not yet been paid, (iii) an amount equal to 200% of his target bonus attributable to the year of termination and (iv) a pro-rated portion of any bonus attributable to the year of termination based upon performance against company but not individual objectives. In addition, Mr. Iwicki will be entitled to twenty-four months of COBRA premiums for continued health benefit coverage on the same terms as were applicable to him prior to his termination and outplacement services for the twenty-four month period.

Further, in the event of the termination of Mr. Iwicki's employment by us without cause or by him for good reason within the twenty-four month period following a change of control, Mr. Iwicki will be entitled to a lump sum payment in an amount equal to (i) thirty months of his then-current annual base salary, (ii) any bonus earned for the year prior to the year of termination that has not yet been paid, (iii) a pro-rated portion of any bonus attributable to the year of termination based upon performance against company but not individual objectives and (iv) 250% of the greater of (A) the average bonus Mr. Iwicki received during the two years prior to termination or resignation, or (B) the target bonus for the year of termination or resignation. In addition, Mr. Iwicki will be entitled thirty months of COBRA premiums for continued health benefit coverage on the same terms as were applicable to him prior to his termination and outplacement services for thirty months.

In addition, in the event we terminate his employment or other service relationship with us without cause, he terminates his employment or other service relationship with us for good reason, or his employment or other service relationship with us terminates by reason of his death or disability, Mr. Iwicki is entitled to the automatic vesting and exercisability of any unvested options that would have vested if Mr. Iwicki's employment or other service relationship with us had continued for twenty-four months following such termination. In addition, provided Mr. Iwicki is an employee, member of our board of directors or is otherwise providing services to us at the time of a change of control, as defined in the letter agreement, or in the event of the termination of Mr. Iwicki's employment by us without cause or by him for good reason in contemplation of a change of control, as defined in the letter agreement, Mr. Iwicki's time-based equity awards will vest in full upon consummation of such change in control. Options granted to Mr. Iwicki will be exercisable for up to eighteen months following the termination of his employment or other relationship with us other than a termination for cause. Mr. Iwicki also is entitled to piggyback registration rights with respect to options granted pursuant to his employment letter agreement.

In addition, in the event we terminate his employment without cause or he terminates his employment for good reason within the twenty-four month period following a change of control, Mr. Iwicki is entitled to the automatic vesting

and exercisability of any options and other equity awards granted to him following a change of control that vest solely based on his continued employment and have not vested.

Letter Agreement with Mr. Bazemore

Mr. Bazemore was appointed as our Chief Operating Officer pursuant to a letter agreement with us dated November 6, 2017 and was appointed as our President commencing December 16, 2021. Mr. Bazemore is an at-will employee, and his employment with us can be terminated by him or us at any time and for any reason.

Mr. Bazemore's base salary is subject to annual review and adjustment by our compensation committee. Mr. Bazemore's annual base salary was $535,600, effective January 1, 2023. In addition, Mr. Bazemore is eligible to receive a discretionary bonus in a target amount of 50% of his annual base salary, as determined by our board of directors in its sole discretion.

On March 11, 2019, Mr. Bazemore's employment letter agreement was amended to revise the severance benefits he is entitled to receive upon termination in connection with the following events. Subject to his execution and nonrevocation of a release of claims in our favor, in the event of the termination of Mr. Bazemore's employment by us without cause or by him for good reason, each as defined in his employment letter agreement, and such termination is not within the twenty-four month period following a change of control, as defined in his employment letter agreement, Mr. Bazemore will be entitled to a lump sum payment in an amount equal to (i) twelve months of his then-current annual base salary, (ii) any bonus earned for the year prior to the year of termination that has not yet been paid, (iii) a pro-rated portion of any bonus attributable to the year of termination based upon performance against company but not individual objectives and (iv) an amount equal to 100% of his target bonus for the year of termination. In addition, Mr. Bazemore is entitled to twelve months of COBRA premiums for continued health benefit coverage on the same terms as were applicable to him prior to his termination and outplacement services for the twelve-month period.

Further, in the event of the termination of Mr. Bazemore's employment by us without cause or by him for good reason within the twenty-four month period following a change of control, Mr. Bazemore will be entitled to a lump sum payment in an amount equal to (i) eighteen months of his then-current annual base salary, (ii) any bonus earned for the year prior to the year of termination that has not yet been paid, (iii) a pro-rated portion of any bonus attributable to the year of termination based upon performance against company but not individual objectives and (iv) 150% of the greater of (A) the average bonus Mr. Bazemore received during the two years prior to termination or resignation, or (B) the target bonus for the year of termination or resignation. In addition, Mr. Bazemore is entitled to eighteen months of COBRA premiums for continued health benefit coverage on the same terms as were applicable to him prior to his termination and outplacement services for the eighteen-month period.

In addition, in the event we terminate his employment without cause or he terminates his employment for good reason, Mr. Bazemore is entitled to the automatic vesting and exercisability of any options and other equity awards granted to him that vest solely based on his continued employment that would have vested if his employment had continued for twelve months following such termination, and any performance-based grants with the performance period ending within one year after the termination shall be treated as having satisfied any service requirement with respect thereto and shall vest subject to, and only to the extent of, the satisfaction of the applicable performance goals at the end of the applicable performance period.

In the event we terminate his employment without cause or he terminates his employment for good reason in contemplation of a change of control, as defined in the letter agreement, or within the twenty-four-month period following a change of control, Mr. Bazemore is entitled to the automatic vesting and exercisability of 100% of any options and other equity awards granted to him that vest solely based on his continued employment, and any performance based grants with a performance period ending within one year after the termination will be treated as having satisfied any service requirement with respect such grant, and will vest subject to, and only to the extent of, the satisfaction of the applicable performance goals at the end of the applicable performance period.

Letter Agreement with Dr. Brazzell

Dr. Brazzell was appointed to serve on a full-time basis as our Chief Medical Officer pursuant to a letter agreement with us dated May 10, 2016, which amended and restated a prior letter agreement. Dr. Brazzell is an at-will employee, and his employment with us can be terminated by him or us at any time and for any reason.

Brazzell's base salary is subject to annual review and adjustment by our compensation committee. In December 2022, Dr. Brazzell's annual base salary was increased to $520,000, effective January 1, 2023. In addition, Dr. Brazzell is eligible to receive a discretionary bonus in a target amount of 45% of his annual base salary, as determined by our compensation committee in its sole discretion.

On March 11, 2019, Dr. Brazzell's employment letter agreement was amended to revise the severance benefits he is entitled to receive upon termination in connection with the following events. Subject to his execution and nonrevocation of a release of claims in our favor, in the event of the termination of Dr. Brazzell's employment by us without cause or by him for good reason, each as defined in his employment letter agreement, and such termination is not within the twenty-four month period following a change of control, as defined in his employment letter agreement, Dr. Brazzell will be entitled to a lump sum payment in an amount equal to (i) twelve months of his then-current annual base salary, (ii) any bonus earned for the year prior to the year of termination that has not yet been paid, (iii) a pro-rated portion of any bonus attributable to the year of termination based upon performance against company but not individual objectives and (iv) an amount equal to 100% of his target bonus for the year of termination. In addition, Dr. Brazzell is entitled to twelve months of COBRA premiums for continued health benefit coverage on the same terms as were applicable to him prior to his termination and outplacement services for the twelve-month period.

Further, in the event of the termination of Dr. Brazzell's employment by us without cause or by him for good reason within the twenty-four month period following a change of control, Dr. Brazzell will be entitled to a lump sum payment in an amount equal to (i) eighteen months of his then-current annual base salary, (ii) any bonus earned for the year prior to the year of termination that has not yet been paid, (iii) a pro-rated portion of any bonus attributable to the year of termination based upon performance against company but not individual objectives and (iv) 150% of the greater of (A) the average bonus Dr. Brazzell received during the two years prior to termination or resignation, or (B) the target bonus for the year of termination or resignation. In addition, Dr. Brazzell is entitled to eighteen months of COBRA premiums for continued health benefit coverage on the same terms as were applicable to him prior to his termination and outplacement services for the eighteen-month period.

In addition, in the event we terminate his employment without cause or he terminates his employment for good reason, Dr. Brazzell is entitled to the automatic vesting and exercisability of any options and shares granted to him that vest solely based on his continued employment that would have vested if his employment had continued for twelve months following such termination. In the event of a change of control, as defined in his employment letter agreement, during his employment, Dr. Brazzell is entitled to the automatic vesting and exercisability of 100% of any options and restricted shares granted to him that vest solely based on his continued employment, and certain options are exercisable for a period of up to six months following his termination date.

In addition, in the event we terminate his employment without cause or he terminates his employment for good reason within the twenty-four-month period following a change of control, Dr. Brazzell is entitled to the automatic vesting and exercisability of any options and shares granted to him following a change of control that vest solely based on his continued employment and have not vested.

Employee Non-Competition, Non-Solicitation, Confidentiality, and Assignment of Inventions Agreements

Each of our named executive officers has entered into a standard form agreement with respect to non-competition, non-solicitation, confidential information and assignment of inventions. Under this agreement, each executive officer has agreed not to compete with us during his or her employment and for a period of one year after the termination of his or her employment and to protect our confidential and proprietary information indefinitely. Under this agreement, each of Mr. Iwicki and Dr. Brazzell has agreed not to solicit our employees or consultants during his employment and for a period of twelve months after the termination of his employment, and Mr. Bazemore has agreed not to solicit our employees or consultants during his employment and for a period of eighteen months after the termination of his employment, and each executive officer has agreed to protect our confidential and proprietary information indefinitely. In addition, under this agreement, each executive officer has agreed that we own all inventions, as defined in the agreement, that are developed during such executive officer's employment and for a period of one year after the termination of his or her employment, to the extent such invention is our field of interest, as defined in the agreement. Each executive officer also agreed to assign to us any inventions which were not prepared or originated in the performance of employment but that were provided to us or incorporated into any of our products or systems.

Stock Option and Other Compensation Plans

In this section we describe our 2009 Plan, our 2017 Plan, and our Amended and Restated 2017 Employee Stock Purchase Plan, or 2017 ESPP. Prior to our initial public offering of common stock, or IPO, which closed on July 25, 2017, we granted awards to eligible participants under the 2009 Plan. Following the closing of our IPO, we ceased granting awards under the 2009 Plan and started granting awards to eligible participants under the 2017 Plan.

2009 Plan

Our 2009 Plan was adopted by our board of directors and approved by our stockholders on December 11, 2009 and subsequently amended by our board in 2012, 2013, 2014 and 2015. The 2009 Plan provided for the grant of incentive stock options, non-qualified options, shares, restricted or otherwise, of our common stock, and other stock-based awards. We refer to awards granted under our 2009 Plan as stock rights. Our employees, directors and consultants were eligible to receive stock rights under our 2009 Plan; however incentive stock options could only be granted to our employees who are deemed to be residents of the United States.

The type of stock right granted under our 2009 Plan and the terms of such stock right are set forth in the applicable stock right award agreement.

Our board of directors (or a committee to which our board delegates its authority) administers the 2009 Plan. Subject to the provisions of the 2009 Plan, our board of directors is authorized to:

- interpret the provisions of the 2009 Plan and all stock rights and make all rules and determinations that it deems necessary or advisable for the administration of the 2009 Plan;
- amend any term or condition of an outstanding stock right, including, without limitation, to reduce or increase the exercise price or purchase price, accelerate the vesting or extend the expiration date, provided that no such change will impair a participant's rights under any prior grant unless we obtain the participant's consent;
- purchase and/or cancel a stock right previously granted and grant other stock rights in substitution, which may cover the same or a different number of shares and which may have a lower or higher exercise or purchase price per share, based on such terms and conditions as the board of directors establishes and the participant accepts; and
- adopt any sub-plans applicable to residents of any specified jurisdiction as it deems necessary or appropriate to facilitate the 2009 Plan or to comply with or take advantage of any tax or other laws applicable to us, any of our affiliates, or to participants, which sub-plans may include additional restrictions or conditions applicable to stock rights or shares issuable pursuant to a stock right.

Effect of certain changes in capitalization

If our shares of common stock are subdivided or combined into a greater or smaller number of shares, if we issue shares of common stock as a stock dividend, or if we make any distribution of additional, new or different shares or securities of ours or any distribution of non-cash assets with respect to our shares of common stock, then, subject to the terms of the 2009 Plan, our board of directors shall proportionately and appropriately adjust:

- the number of shares of our common stock deliverable upon the exercise of an option or acceptance of a stock grant;
- the exercise or purchase price per share; and
- any other term or condition of a stock right.

Effect of certain corporate transactions

In the event that we are consolidated with or acquired by another entity in a merger, consolidation, or sale of all or substantially all of our assets (other than a transaction to merely change the state of incorporation), which we refer to as corporate transactions, our board of directors, or the board of directors of any entity assuming our obligations under the 2009 Plan, must take one of the following actions pursuant to the 2009 Plan as to outstanding options, subject to the terms of the 2009 Plan:

- provide for the continuation of the outstanding options by equitably substituting for the shares of our common stock then underlying such options either with securities of any successor or acquiring entity or the consideration payable with respect to the outstanding shares of our common stock in connection with the corporate transaction;

- provide by written notice to the participants that the outstanding options will terminate unless exercised (to the extent then exercisable or made partially or fully exercisable by our board of directors for purposes of the corporate transaction) within a specified period following the date of the notice; or

- terminate each outstanding option in exchange for a payment equal to the consideration payable upon consummation of the corporate transaction to a holder of the number of shares of our common stock into which such option would have been exercisable (to the extent then exercisable or made partially or fully exercisable by our board of directors for purposes of the corporate transaction), minus the aggregate exercise price of such option.

If there is a corporate transaction, our board of directors, or the board of directors of any entity assuming our obligations under the 2009 Plan, must take one of the following actions pursuant to the 2009 Plan as to outstanding stock grants, restricted or otherwise, subject to the terms of the 2009 plan:

- provide for the continuation of the outstanding stock grants on the same terms and conditions by equitably substituting for the shares of our common stock then subject to such stock grants either with securities of any successor or acquiring entity or the consideration payable with respect to the outstanding shares of our common stock in connection with the corporate transaction; or

- provide that each outstanding stock grant will terminate in exchange for a payment equal to the consideration payable upon consummation of the corporate transaction to a holder of the number of shares of our common stock comprising such stock grant (to the extent such stock grant is no longer subject to any forfeiture or repurchase rights or our board of directors waives all forfeiture and repurchase rights upon the corporate transaction).

In taking any of the above actions with respect to stock rights, our board of directors will not be obligated to treat all stock rights, all stock rights held by a participant, or all stock rights of the same type, identically.

As of February 21, 2023, options to purchase 31,681 shares of common stock were outstanding under the 2009 Plan at a weighted average exercise price of $188.32 per share.

We no longer grant awards under our 2009 Plan; however, awards outstanding under our 2009 Plan continue to be governed by their existing terms.

2017 Equity Incentive Plan

Our 2017 Plan, which became effective on July 19, 2017, was adopted by our board of directors and approved by our stockholders in July 2017. An amendment to our 2017 Plan was adopted by our board of directors on April 2020 and approved by our stockholders at the 2020 annual meeting of stockholders. The 2017 Plan provides for the grant of incentive stock options, non-qualified options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The number of shares of our common stock reserved for issuance under the 2017 Plan is the sum of: (1) 75,737; plus (2) 4,830 shares available for issuance under the 2009 Plan at the time of our IPO and the number of shares of our common stock subject to outstanding awards under the 2009 Plan that expire, terminate or are

otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right; plus (3) an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2018 and continuing until, and including, the fiscal year ending December 31, 2027, equal to the lowest of 71,475 shares of our common stock, 4% of the number of shares of our common stock outstanding on the first day of such fiscal year and an amount determined by our board of directors. The number of shares authorized for issuance under the 2017 Plan has further increased each year, pursuant to the terms of the 2017 Plan, on the first of January beginning in 2018 by an amount equal to 4% of our then-outstanding common stock.

Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2017 Plan. Incentive stock options, however, may only be granted to our employees.

Pursuant to the terms of the 2017 Plan, our board of directors (or a committee delegated by our board of directors or, subject to certain limitations, officers delegated by our board of directors) administers the plan and, subject to any limitations in the plan, selects the recipients of awards and determines:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;
- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- the exercise price of options, which must be at least equal to the fair market value of our common stock on the date of grant; and
- the number of shares of our common stock subject to and the terms of any stock appreciation rights, restricted stock awards, restricted stock units or other stock-based awards and the terms and conditions of such awards, including conditions for repurchase, issue price and repurchase price (though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years).

If our board of directors delegates authority to an executive officer to grant awards under the 2017 Plan, the executive officer will have the power to make awards to all of our employees, except executive officers. Our board of directors will fix the terms of the awards to be granted by such executive officer, including the exercise price of such awards (which may include a formula by which the exercise price will be determined), and the maximum number of shares subject to awards that such executive officer may make.

Effect of certain changes in capitalization

Upon the occurrence of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, our board of directors shall equitably adjust:

- the number and class of securities available under the 2017 Plan;
- the share counting rules under the 2017 Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and the measurement price of each outstanding stock appreciation right;
- the number of shares subject to, and the repurchase price per share subject to, each outstanding restricted stock award; and

- the share and per-share related provisions and the purchase price, if any, of each other stock-based award.

Effect of certain corporate transactions

Upon a merger or other reorganization event (as defined in our 2017 Plan), our board of directors may, on such terms as our board determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and us), take any one or more of, or a combination of, the following actions pursuant to the 2017 Plan as to some or all outstanding awards, other than restricted stock awards:

- provide that all outstanding awards shall be assumed, or substantially equivalent awards shall be substituted, by the acquiring or successor corporation (or an affiliate thereof);

- upon written notice to a participant, provide that all of the participant's unvested awards will be forfeited, and/or vested but unexercised awards will terminate, immediately prior to the consummation of such reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of the notice;

- provide that outstanding awards shall become exercisable, realizable or deliverable, or restrictions applicable to an award shall lapse, in whole or in part, prior to or upon such reorganization event;

- in the event of a reorganization event pursuant to which holders of shares of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to participants with respect to each award held by a participant equal to (1) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award; and/or

- provide that, in connection with a liquidation or dissolution, awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings).

Our board of directors does not need to take the same action with respect to all awards, all awards held by a participant or all awards of the same type.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than a liquidation or dissolution, the repurchase and other rights with respect to outstanding restricted stock awards will continue for the benefit of the successor company and will, unless our board of directors may otherwise determine, apply to the cash, securities or other property into which shares of our common stock are converted or exchanged pursuant to the reorganization event. Upon the occurrence of a reorganization event involving a liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award or any other agreement between the participant and us.

At any time, our board of directors may, in its sole discretion, provide that any award under the 2017 Plan will become immediately exercisable in full or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part as the case may be.

No award may be granted under the 2017 Plan on or after July 19, 2027. Our board of directors may amend, suspend or terminate the 2017 Plan at any time, except that stockholder approval may be required to comply with applicable law or stock market requirements.

As of February 21, 2023, options to purchase 157,512 shares of common stock were outstanding under the 2017 Plan at a weighted average exercise price of $259.54 per share, and 1,521 options to purchase shares of our common

stock had been exercised. As of February 21, 2023, restricted stock units with respect to 148,870 shares of common stock were outstanding under the 2017 Plan. As of February 21, 2023, 8,876 shares of common stock were available for future issuance under our 2017 Plan.

Amended and Restated 2017 Employee Stock Purchase Plan

Our 2017 ESPP, which became effective on July 19, 2017, was adopted by our board of directors and approved by our stockholders in July 2017 and amended and restated by our board of directors in December 2018. The 2017 ESPP is administered by our board of directors or by a committee appointed by our board of directors. The 2017 ESPP initially provides participating employees with the opportunity to purchase an aggregate of 4,466 shares of our common stock. The number of shares of our common stock reserved for issuance under the 2017 ESPP will automatically 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) 17,868 shares of our common stock; (2) 1% of the total number of shares of our common stock outstanding on the first day of the applicable fiscal year; and (3) an amount determined by our board of directors. The number of shares authorized for issuance under the 2017 ESPP has increased each year, pursuant to the terms of the 2017 ESPP, on the first of January beginning in 2019 by an amount equal to 1% of our then-outstanding common stock.

All of our employees and employees of any of our designated subsidiaries, as defined in the 2017 ESPP, are eligible to participate in the 2017 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year; and

- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2017 ESPP.

We retain the discretion to determine which eligible employees may participate in an offering under applicable Treasury regulations.

We may make one or more offerings to our eligible employees to purchase stock under the 2017 ESPP beginning at such time and on such dates as our board of directors may determine, or the first business day thereafter. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors or a committee appointed by our board, may, at its discretion, choose a different period of not more than 12 months for offerings. Offering periods under our 2017 ESPP commenced on each January 1 and July beginning with January 1, 2019.

On each offering commencement date, each participant will be granted the right to purchase, on the last business day of the offering period, up to 500 shares of our common stock. No employee may be granted an option under the 2017 ESPP that permits the employee's rights to purchase shares under the 2017 ESPP and any other employee stock purchase plan of ours or of any of our subsidiaries to accrue at a rate that exceeds $25,000 of the fair market value of our common stock (determined as of the first day of each offering period) for each calendar year in which the option is outstanding. In addition, no employee may purchase shares of our common stock under the 2017 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock or the stock of any of our subsidiaries.

On the commencement date of each offering period, each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2017 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of our common stock that his or her accumulated payroll deductions on such date will buy, not in excess of the maximum numbers set forth above. Under the terms of the 2017 ESPP, the purchase price shall be determined by our board of directors for each offering period and will be at least 85% of the applicable closing price of our common stock. If our board of directors does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee may at any time prior to the close of business on the fifteenth business day prior to the end of an offering period, and for any reason, permanently withdraw from participation in an offering prior to the end of an offering period and permanently withdraw the balance accumulated in the employee's account. Any balance remaining in an employee's payroll deduction account at the end of an offering period will be automatically refunded to the employee. If a participating employee's employment ends before the last business day of an offering period, no additional payroll deductions will be taken and the balance in the employee's account will be paid to the employee.

We are required to make equitable adjustments to the extent determined by our board of directors or a committee of our board of directors to the number and class of securities available under the 2017 ESPP, the share limitations under the 2017 ESPP and the purchase price for an offering period under the 2017 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event (as defined in the 2017 ESPP), our board of directors or a committee of our board of directors may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2017 ESPP on such terms as our board of directors or committee determines:

- provide that options shall be assumed, or substantially equivalent options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);

- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by our board of directors or committee in such notice, which date shall not be less than ten days preceding the effective date of the reorganization event;

- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;

- in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (1) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the cash payment for each share surrendered in the reorganization event is treated as the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2017 ESPP minus (2) the result of multiplying such number of shares by the purchase price; and/or

- provide that, in connection with our liquidation or dissolution, options shall convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Our board of directors may at any time, and from time to time, amend or suspend the 2017 ESPP, or any portion of the 2017 ESPP. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Internal Revenue Code of 1986, as amended, or the Code. Further, our board of directors may not make any amendment that would cause the 2017 ESPP to fail to comply with Section 423 of the Code. The 2017 ESPP may be terminated at any time by our board of directors. Upon termination, we will refund all amounts in the accounts of participating employees.

401(k) Plan

We maintain a defined contribution employee retirement plan for our employees. Our 401(k) plan is intended to qualify as a tax-qualified plan under Section 401 of the Code so that contributions to our 401(k) plan, and income earned

on such contributions, are not taxable to participants until withdrawn or distributed from the 401(k) plan. Our 401(k) plan provides that each participant may contribute up to 90% of his or her pre-tax compensation, up to a statutory limit, which was $20,500 for 2022. Participants who are at least 50 years old can also make "catch-up" contributions, which in 2022 was up to an additional $6,500 above the statutory limit. We also make discretionary matching contributions to our 401(k) plan equal to 50% of the employee contributions up to 4% of the employee's salary, subject to the statutorily prescribed limit, which was equal to $20,500 in 2022. The discretionary matching contributions were capped at $6,100 in 2022. Under our 401(k) plan, each employee is fully vested in his or her deferred salary contributions and our discretionary match. Employee contributions are held and invested by the plan's trustee, subject to participants' ability to give investment directions by following certain procedures.

Rule 10b5-1 Sales Plans

Our directors and executive officers have adopted and may in the future adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. It also is possible that the director or officer could amend or terminate the plan when not in possession of material, nonpublic information. In addition, our directors and executive officers may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Anti-Hedging Policies

Our insider trading policy expressly prohibits all of our employees, including our executive officers, and our directors from engaging in any purchases of financial instruments (including prepaid variable forward contracts, equity swaps, collars and exchange funds) that are designed to hedge or offset any decrease in the market value of our securities.

Director Compensation

The table below shows all compensation to our non-employee directors during 2022.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)[1][2][3]	Stock Awards ($)[1]	Total ($)
Mark S. Blumenkranz	56,083	10,152	—	66,235[4]
Marjan Farid[5]	9,266	7,527	—	16,793
Gregory Grunberg[6]	27,692	—	—	27,692
Andrew I. Koven	88,750	12,690	—	101,440
C. Daniel Myers	62,500	10,152	—	72,652
Robert Paull	70,000	10,152	—	80,152
Gregory D. Perry	70,000	10,152	—	80,152
Howard B. Rosen	67,500	10,152	—	77,652

(1) The aggregate amount of outstanding options and RSUs held by each non-employee director as of December 31, 2022 were as follows:

Name	Aggregate Options Outstanding (#)	Aggregate Restricted Stock Units Outstanding (#)
Mark S. Blumenkranz	1,640	—
Marjan Farid	1,600	—
Gregory Grunberg	—	—
Andrew I. Koven	2,197	1,060
C. Daniel Myers	1,640	—
Robert Paull	1,738	800
Gregory D. Perry	1,738	800
Howard B. Rosen	2,502	800

(2) The amounts reported in the "Option Awards" column reflects the aggregate grant date fair value of options awarded during the year computed in accordance with the provisions of FASB ASC Topic 718. For the assumptions underlying the valuation of the stock option grants, see Note 14 to our financial statements appearing in this Annual Report on Form 10-K.

(3) The number of shares of common stock underlying stock options granted to the following non-employee directors in 2022 were as follows:

Name	Grant Date	Number of Shares Underlying Stock Options Granted in 2022 (#)
Mark S. Blumenkranz	6/16/2022	800
Marjan Farid	10/31/2022	1,600
Gregory Grunberg	—	—
Andrew I. Koven	6/16/2022	1,000
C. Daniel Myers	6/16/2022	800
Robert Paull	6/16/2022	800
Gregory D. Perry	6/16/2022	800
Howard B. Rosen	6/16/2022	800

(4) Does not include consideration received by Dr. Blumenkranz from us in his capacity as an equityholder of Combangio in connection with the acquisition of Combangio. For a further description of such consideration, see Item 13, "Certain Relationships and Related Transactions, and Director Independence".

(5) Dr. Farid was appointed to our board of directors in October 2022.

(6) Dr. Grunberg's term as a member of the board expired, and he ceased being a director on June 16, 2022.

Mr. Iwicki, one of our directors who also serves as our Chief Executive Officer, does not receive any additional compensation for his service as a director. The compensation that we pay to our Chief Executive Officer is discussed under "-Summary Compensation Table" and "-Narrative Disclosure to Summary Compensation Table."

During the year ended December 31, 2022, our non-employee directors were entitled to compensation for their services on our board of directors as follows:

Each member of our board of directors also is entitled to be reimbursed for reasonable travel and other expenses incurred in connection with attending meetings of our board of directors and any committee of our board of directors on which he or she serves.

This director compensation policy is currently in effect for directors serving during the year ending December 31, 2023.

- each non-employee director was entitled to receive an option to purchase 1,600 shares of our common stock, upon his or her initial election or appointment to our board of directors, which option vests with respect to one third of the shares on the first anniversary of the grant and with respect to an additional 1/36th of the shares on each monthly anniversary thereafter and vest automatically as to 100% of the unvested portion of such option upon specified change in control events;

- each non-employee director who has then served on our board of directors for at least six months was entitled to receive, on the date of the first board meeting held after each annual meeting of stockholders, an option to purchase 800 shares of our common stock, and if then serving as the lead independent director, an option to purchase 1,000 shares of our common stock, which options will vest (A) on the earlier of (i) the first anniversary date of the previous year's annual meeting or (ii) the date of the first annual meeting following the grant date, and (B) automatically as to 100% of the unvested portion of such options upon specified change in control events;

- each non-employee director was entitled to receive an annual fee of $50,000;

- the lead independent director was entitled to receive an additional annual fee of $18,750; and

- each non-employee director who served as member of a committee of our board of directors was entitled to receive additional compensation as follows:

- audit committee-an annual non-chair retainer of $10,000; chair annual retainer of $20,000;
- compensation committee-an annual non-chair retainer of $7,500; chair annual retainer of $15,000; and
- nominating and corporate governance committee-an annual non-chair retainer of $5,000; chair annual retainer of $10,000.

Each member of our board of directors also is entitled to be reimbursed for reasonable travel and other expenses incurred in connection with attending meetings of our board of directors and any committee of our board of directors on which he or she serves.

This director compensation policy is currently in effect for directors serving during the year ending December 31, 2023.

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

Security Ownership of Certain Beneficial Owners and Management

Unless otherwise provided below, the following table sets forth information regarding beneficial ownership of our common stock as of February 21, 2023 by:

- each person, or group of affiliated persons, known to us to be the beneficial owner of 5% or more of the outstanding shares of our common stock;
- each of our current directors;
- our principal executive officer and two other most highly compensated executive officers who served during the year ended December 31, 2022, whom, collectively, we refer to as our named executive officers; and
- all of our executive officers and directors as a group.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Percentage of beneficial ownership is based on 2,025,495 shares of our common stock outstanding as of February 21, 2023, plus an aggregate of 19,350 shares of common stock that were initially held back as partial security for the satisfaction of indemnification obligations and other payment obligations of the Combangio equityholders and that will be issued in March 2023, or the Holdback Shares, for a total of 2,044,845 shares of our common stock utilized in the percentage of beneficial ownership calculations below. In addition, shares of common stock subject to options or other rights currently exercisable, or exercisable within 60 days of February 21, 2023, are deemed outstanding and beneficially owned for the purpose of computing the percentage beneficially owned by (i) the individual holding such options, warrants or other rights (but not any other individual) and (ii) the directors and executive officers as a group. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o Kala Pharmaceuticals, Inc., 1167 Massachusetts Avenue, Arlington, Massachusetts 02476.

Name and Address of Beneficial Owner	Shares of Common Stock Beneficially Owned	Percentage of Common Stock
5% Stockholders:		
Entities affiliated with Baker Bros. Advisors LP[1]	218,427	9.99 %
Entities affiliated with Longitude Venture Partners[2]	108,239	5.29 %
Integrated Core Strategies (US) LLC[3]	107,200	5.24 %
Entities affiliated with Lagunita[4]	103,599	5.07 %
Directors and Named Executive Officers:		
Mark Iwicki[5]	58,519	2.79 %
Todd Bazemore[6]	17,019	*
Kim Brazzell, Ph.D.[7]	17,911	*
Mark S. Blumenkranz, M.D.[8]	107,149	5.24 %
Marjan Farid, M.D.	—	*
Andrew I. Koven[9]	1,197	*
C. Daniel Myers[10]	419	*
Robert Paull[11]	727	*
Gregory D. Perry([12]	938	*
Howard B. Rosen[13]	1,964	*
All current executive officers and directors as a group (13 persons)[14]	238,590	11.07 %

* **Less than one percent**

(1) Based, in part, on a Schedule 13G filed with the SEC on February 14, 2023. Includes 141,614 shares of common stock issuable upon conversion of Series E Preferred Stock directly held by the Funds (as defined below). The Funds hold 53,144 shares of Series E Preferred Stock, each of which is convertible into 100 shares of common stock (subject to adjustment as provided in the Company's Certificate of Designations) at any time at the option of the holder, provided that the holder will be prohibited, subject to certain exceptions, from converting its Series E Preferred Stock for shares of common stock to the extent that immediately prior to or following such conversion, the holder, together with its affiliates and other attribution parties, would own in excess of 9.99% of the total number of shares of common stock then issued and outstanding after giving effect to such conversion, which percentage may be changed at the holder's election to a lower percentage at any time or to a higher percentage not to exceed 19.99% upon 61 days' notice to us (collectively, the "Beneficial Ownership Limitation"). Percentage of common stock held based on 2,044,845 shares of common stock outstanding as of February 21, 2023 inclusive of the Holdback Shares to be issued in March 2023, plus 141,614 shares of common stock issuable upon the conversion of the Series E Preferred Stock that are subject to the Beneficial Ownership Limitation. The Schedule 13G was filed jointly by Baker Bros. Advisors LP, Baker Bros. Advisors (GP) LLC, Felix J. Baker and Julian C. Baker. Consists of shares of common stock held by Baker Brother Life Sciences, L.P. ("Life Sciences") and 667, L.P. ("667", and together with Life Sciences, the "Funds") which may be deemed to be indirectly beneficially owned by the reporting persons, as well as shares

of common stock that may be acquired upon conversion of Series E Preferred Stock. The address for each of the reporting persons is 860 Washington Street, 3rd Floor, New York, NY 10014.

(2) Based solely on a Schedule 13D/A filed with the SEC on February 14, 2023. Consists of (a) 57,541 shares of common stock held by Longitude Venture Partners II, L.P. ("LVPII") and (b) 50,698 shares of common stock held by Longitude Venture Partners IV, L.P. ("LVPIV"). Longitude Capital Partners II, LLC ("LCPII") is the sole general partner of LVPII and may be deemed to share voting and investment power over the shares held by LVPII. Longitude Capital Partners IV, LLC ("LCPIV") is the general partner of LVPIV and may be deemed to share voting and investment power with respect to the shares held by LVPIV. Patrick G. Enright and Juliet Tammenoms Bakker are managing members of LCPII and LCPIV and may be deemed to share voting and investment power over the shares held by LVPII and LVPIV. Each of LCPII, LCPIV, Mr. Enright and Ms. Tammenoms Bakker disclaims beneficial ownership of such shares, except to the extent of its, his or her pecuniary interest therein. The address for LVPII and LVPIV is 2740 Sand Hill Road, 2nd Floor, Menlo Park, CA 94025.

(3) Based solely on a Schedule 13G filed with the SEC on January 17, 2023. The Schedule 13G was jointly filed by Integrated Core Strategies (US) LLC ("Integrated Core Strategies"), which reported shared voting and dispositive power with regard to 107,200 shares of common stock, and Millennium Management LLC ("Millennium Management"), Millennium Group Management LLC ("Millennium Group Management") and Israel A. Englander ("Mr. Englander"), which each reported shared voting and dispositive power with regard to 133,703 shares of common stock, including the 107,200 shares of common stock held by Integrated Core Strategies. The shares of common stock disclosed as potentially beneficially owned by Millennium Management, Millennium Group Management and Mr. Englander are held by entities subject to voting control and investment discretion by Millennium Management and/or other investment managers that may be controlled by Millennium Group Management (the managing member of Millennium Management) and Mr. Englander (the sole voting trustee of the managing member of Millennium Group Management). The address for each of the reporting persons is 399 Park Avenue, New York, NY 10022.

(4) Based, in part, on a Schedule 13D filed with the SEC on November 26, 2021. Consists of (a) 90,721 shares of common stock held by Lagunita Biosciences, LLC ("Lagunita Biosciences") and 12,099 Holdback Shares issuable to Lagunita Biosciences in March 2023 and (b) 688 shares of common stock held by Garland Investments, L.P. ("Garland") and 91 Holdback Shares issuable to Garland in March 2023. Lagunita, LLC ("Lagunita") is the manager of Lagunita Biosciences and Lagunita may be deemed to share voting and dispositive power over the shares held by Lagunita Biosciences. Dr. Blumenkranz, a member of our board, is managing partner of Lagunita and Garland and may be deemed to share voting and dispositive power over the shares held by Lagunita Biosciences and Garland. Dr. Blumenkranz disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest therein. The address for Lagunita, Lagunita Biosciences, Garland and Dr. Blumenkranz is 1440 O'Brien Drive, Suite D, Menlo Park, CA 94028.

(5) Consists of (i) 3,759 shares of common stock beneficially owned by Mr. Iwicki and (ii) 54,760 shares of common stock underlying options held by Mr. Iwicki that are exercisable as of February 21, 2023 or will become exercisable within 60 days after such date.

(6) Consists of (i) 1,852 shares of common stock beneficially owned by Mr. Bazemore and (ii) 15,167 shares of common stock underlying options held by Mr. Bazemore that are exercisable as of February 21, 2023 or will become exercisable within 60 days after such date.

(7) Consists of (i) 5,552 shares of common stock beneficially owned by Dr. Brazzell and (ii) 12,359 shares of common stock underlying options held by Dr. Brazzell that are exercisable as of February 21, 2023 or will become exercisable within 60 days after such date.

(8) Consists of (i) the shares described in note 4 above, (ii) 2,783 shares of common stock held by Dr. Blumenkranz, (iii) 371 Holdback Shares issuable to Dr. Blumenkranz in March 2023 and (iv) 396 shares of common stock underlying options held by Dr. Blumenkranz that are exercisable as of February 21, 2023 or will become exercisable within 60 days after such date.

(9) Consists of shares of common stock underlying options held by Mr. Koven that are exercisable as of February 21, 2023 or will become exercisable within 60 days after such date.

(10) Consists of shares of common stock underlying options held by Mr. Myers that are exercisable as of February 21, 2023 or will become exercisable within 60 days after such date.

(11) Consists of (i) 48 shares of common stock owned by Mr. Paull and (ii) 679 shares of common stock underlying options held by Mr. Paull that are exercisable as of February 21, 2023 or will become exercisable within 60 days after such date.

(12) Consists of shares of common stock underlying options held by Mr. Perry that are exercisable as of February 21, 2023 or will become exercisable within 60 days after such date.

(13) Consists of (i) 97 shares of common stock owned by Mr. Rosen, (ii) 165 shares of common stock owned by the Rosen/Doherty Revocable Trust Dated June 11, 2001, of which Mr. Rosen is a co-trustee, and (iii) 1,702 shares of common stock underlying options held by Mr. Rosen that are exercisable as of February 21, 2023 or will become exercisable within 60 days after such date.

(14) Includes (i) 110,433 shares of common stock underlying options that are exercisable as of February 21, 2023 or will become exercisable within 60 days after such date and (ii) 1,656 Holdback Shares issuable in March 2023.

Securities Authorized for Issuance under Equity Compensation Plans

The following table contains information about our equity compensation plans as of December 31, 2022. As of December 31, 2022, we had three equity compensation plans, our 2009 Plan, our 2017 Plan and our 2017 ESPP, each of which was approved by our stockholders. We have also made inducement awards to certain new hires, which awards were not approved by our stockholders.

Equity Compensation Plan Information

	Number of securities to be issued upon exercise of outstanding options warrants and rights (a)	Weighted-Average exercise price of outstanding options warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders	207,791[(1)]	$ 252.07[(2)]	92,923[(3)(4)(5)]
Equity compensation plans not approved by security holders	11,080[(6)]	$ 336.62	—
Total	218,871	$ 256.35	92,923

(1) Includes shares of our common stock issuable upon exercise of options to purchase common stock awarded under our 2009 Plan and 2017 Plan and shares of our common subject to outstanding restricted stock units awarded under our 2017 Plan. The number in the table assumes maximum performance for all outstanding unvested performance-based stock options.

(2) The calculation does not take into account the 8,347 shares of common stock subject to outstanding restricted stock units. Such shares will be issued at the time such awards vest (or upon the earlier of the director's

cessation of service or certain "change in control events", if a non-employee director elects to defer the receipt of such restricted stock units), without any cash consideration payable for those shares. The number of shares available for issuance under the 2017 Plan, as reflected in this table, assumes maximum performance of outstanding performance-based stock options.

(3) Includes 77,375 shares of our common stock available for issuance under our 2017 Plan and 15,548 shares of common stock available for issuance under our 2017 ESPP.

(4) The number of shares of common stock reserved for issuance under the 2017 Plan will be increased on the first day of each fiscal year through January 1, 2027, in amount equal to the lowest of: (i) 71,475 shares of common stock, (ii) 4% of the total number of shares of our common stock outstanding on the first day of the applicable fiscal year or (iii) an amount determined by our board of directors. On January 1, 2023, the shares under the 2017 Plan were increased by 68,278 shares pursuant to the annual increase described above.

(5) The number of shares of our common stock reserved for issuance under the 2017 ESPP will be increased on the first day of each fiscal year through January 1, 2029, in an amount equal to the lowest of: (1) 17,868 shares of common stock, (2) 1% of the total number of shares of our common stock outstanding on the first day of the applicable fiscal year or (3) an amount determined by our board of directors. On January 1, 2023, the shares under the 2017 ESPP were increased by 17,069 shares pursuant to the annual increase described above.

(6) Represents inducement option awards granted to employees in accordance with Nasdaq Listing Rule 5635(c)(4) each with an exercise price equal to closing price of our common stock on the date of grant and vesting over four years with 25% of the shares underlying each option vesting on the first anniversary of the applicable employee's new hire date and 2.0833% vesting monthly thereafter. Includes inducement option awards to purchase 2,000 shares of our common stock granted on November 15, 2021 to Darius Kharabi.

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

Certain Relationships and Related Transactions

Policies and Procedures for Related Person Transactions

Our board of directors has adopted written policies and procedures for the review of any transaction, arrangement or relationship in which our company is a participant, the amount involved exceeds $120,000, and one of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, each of whom we refer to as a "related person," has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a "related person transaction," the related person must report the proposed related person transaction to our general counsel or, if none, to our chief financial officer, or individual performing a similar function. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person's interest in the transaction. As appropriate for the circumstances, the audit committee will review and consider:

- the related person's interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;

- the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;

- whether the transaction was undertaken in the ordinary course of our business;

- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;

- the purpose of, and the potential benefits to us of, the transaction; and

- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

Our audit committee may approve or ratify the transaction only if it determines that, under all of the circumstances, the transaction is in our best interests. Our audit committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC's related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person's position as an executive officer of another entity, whether or not the person is also a director of the entity, that is a participant in the transaction where the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction and the amount involved in the transaction is less than the greater of $200,000 or 5% of the annual gross revenues of the company receiving payment under the transaction; and

- a transaction that is specifically contemplated by provisions of our certificate of incorporation or by-laws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by our compensation committee in the manner specified in the compensation committee's charter.

With respect to related person transactions, it is the practice of our board of directors to consider the nature of and business reasons for such transactions, how the terms of such transactions compared to those which might be obtained from unaffiliated third parties and whether such transactions were otherwise fair to and in the best interests of, or not contrary to, our best interests.

Related Person Transactions

In addition to the compensation arrangements with directors and executive officers described elsewhere in this Annual Report on Form 10-K, since January 1, 2021, we have engaged in the following transactions with our directors, executive officers and holders of more than 5% of our voting securities, and affiliates of our directors, executive officers and holders of more than 5% of our voting securities. These transactions were approved in accordance with our Related Person Transaction Policy to the extent required, and we believe that all of these transactions were on terms as favorable as could have been obtained from unrelated third parties.

Private Placement

On November 28, 2022, we entered into a Securities Purchase Agreement, or the Securities Purchase Agreement, with 667, L.P. and Bakers Brothers Life Sciences, L.P., or the Purchasers, pursuant to which we agreed to issue and sell, in a private placement priced at-the-market under Nasdaq rules, shares of our common stock and shares of our Series E Convertible Non-Redeemable Preferred Stock, or Series E Preferred Stock, in two tranches for aggregate

gross proceeds of up to $31.0 million, which we refer to collectively as the Private Placement. At the first closing of the Private Placement on December 1, 2022, we issued and sold to the Purchasers (i) 76,813 shares of common stock, at a price per share equal to $5.75 and (ii) 9,666 shares of Series E Preferred Stock, at a price per share equal to $575.00, for aggregate gross proceeds of approximately $6.0 million. On December 27, 2022, following the certification by our Chief Executive Officer that the U.S. Food and Drug Administration accepted our investigational new drug application for KPI-012, we issued and sold to the Purchasers at a second closing of the Private Placement a total of 43,478 shares of Series E Preferred Stock, at a price per share equal to $575.00, for aggregate gross proceeds of approximately $25.0 million.

The Purchasers have certain participation rights. If at any time during the four-year period following the date of the first tranche closing, or the Participation Period, we propose to offer and sell new equity securities in an offering that is conducted pursuant to an exemption from registration under the Securities Act of 1933, as amended, or the Securities Act, or in an offering that is registered under the Securities Act that is not conducted as a firm-commitment underwritten offering, then, subject to compliance with securities laws and regulations, we have agreed to offer each Purchaser the right to purchase its pro rata share of the total amount of the new equity securities, subject to certain conditions and limitations. In addition, if during the Participation Period, we propose to offer and sell new equity securities in a firm-commitment underwritten offering registered under the Securities Act, then subject to compliance with securities laws and regulations, we have agreed to use our commercially reasonable efforts to cause the managing underwriters of such offering to contact the Purchasers about potentially participating in such offering and to provide to each Purchaser the opportunity to purchase its pro rata share of such new equity securities, subject to certain conditions and limitations. The participation rights will terminate if the Purchasers are offered the opportunity to participate in an offering pursuant to the participation rights and do not purchase at least 50% of their aggregate pro rata share of the new equity securities offered for sale in such offering.

The Purchasers also have the right to have up to two non-voting observers attend and participate in all Board and committee meetings and, subject to the Purchasers owning directly specified minimum amounts of our common stock, the right to have the Board nominate and recommend for election by the stockholders up to three Purchaser designees to the Board (one designee at 9.9%, two designees at 15.0% and three designees at 25.0%) designated by the Purchasers, provided that at such time as the Purchasers have designated three Board designees, at least one such designee must qualify as an "independent" director under Nasdaq rules and be acceptable to the members of the Board who are not Purchaser designees.

The Purchasers' participation rights, observer rights and Board designation rights also will terminate at such time as the Purchasers and their affiliates cease to own, in the aggregate, specified minimum amounts of the shares purchased in the Private Placement.

We also agreed that we will not without the prior approval of the requisite Purchasers (i) issue or authorize the issuance of any equity security that is senior or *pari passu* to the Series E Preferred Stock with respect to liquidation preference, (ii) incur any additional indebtedness for borrowed money in excess of $1,000,000, in the aggregate, outside the ordinary course of business, subject to specified exceptions, including the refinancing of our existing indebtedness or (iii) pay or declare any dividend or make any distribution on, any shares of our capital stock, subject to specified exceptions.

Combangio Acquisition

On November 15, 2021, we and our newly formed, direct wholly owned subsidiary, Ceres Merger Sub, Inc., or the Merger Subsidiary, entered into an Agreement and Plan of Merger, or the Merger Agreement, with 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 ours, or the Combangio Acquisition. In connection with the Closing of the Combangio Acquisition, we made an upfront payment of an aggregate of $5.0 million in cash to former Combangio equityholders, subject to customary adjustments, and agreed to issue an aggregate of 155,664 shares of our common stock to the Combangio equityholders with an aggregate value of approximately $16.1 million, consisting of (i) an aggregate of 136,314 shares of common stock which were issued on January 3, 2022, or the Initial Shares, and (ii) an aggregate of 19,350 shares of common stock that were held back as partial security for the satisfaction of indemnification obligations and other payment obligations of the former Combangio equityholders and that will be issued in March 2023, or the Holdback Shares. The Combangio equityholders

included Dr. Blumenkranz, Mr. Kharabi, Lagunita Biosciences, LLC, of which Dr. Blumenkranz is a managing member, and Garland Investments, L.P., of which Dr. Blumenkranz is a managing member.

In connection with the closing of the Combangio Acquisition, we appointed Dr. Blumenkranz, a then-member of the board of directors of Combangio, to our board of directors, and we appointed Mr. Kharabi, the then-President and Chief Executive Officer of Combangio, as our Chief Business Officer.

The following table sets forth the consideration paid and payable by us to Dr. Blumenkranz, Mr. Kharabi, Lagunita Biosciences, LLC and Garland Investments, L.P. pursuant to the Merger Agreement.

Name	Cash Consideration at Closing	Initial Shares Issued on January 3, 2022	Holdback Shares Issuable in March 2023
Mark S. Blumenkranz	$ 29,675	2,783(1)	371(1)
Darius Kharabi	$ 437,703	4,620(2)	1,285(2)
Lagunita Biosciences, LLC (3)	$ 967,638	90,721(4)	12,099(4)
Garland Investments, L.P.	$ 7,329	688(5)	91(5)

(1) In exchange for 2,618,875 shares of Combangio's common stock.

(2) In exchange for 323,415 shares of Combangio's common stock and for an option to purchase 8,754,216 shares of Combangio's common stock.

(3) Upon the issuance of the Initial Shares, Lagunita Biosciences, LLC became a holder of more than 5% of our outstanding voting securities.

(4) In exchange for 85,395,439 shares of Combangio's common stock.

(5) In exchange for 646,830 shares of Combangio's common stock.

In addition to the foregoing consideration, former equityholders of Combangio are entitled to receive from us contingent consideration in the form of cash and additional shares of our common stock upon the achievement of various milestones. As a result of the dosing of the first patient in our CHASE Phase 2b clinical trial of KPI-012 for PCED in the United States in February 2023, or the Dosing Milestone, we will pay to the former Combangio equityholders in March 2023 an aggregate of $2.5 million in cash and $2.4 million in shares of our common stock (representing an aggregate of 105,039 shares of our common stock). The remaining amount of $0.1 million in cash will be paid to the former Combangio equityholders in January 2024.

The following table sets forth the consideration as result of the achievement of the Dosing Milestone payable by us to Dr. Blumenkranz, Mr. Kharabi, Lagunita Biosciences, LLC and Garland Investments, L.P. pursuant to the Merger Agreement.

Name	Cash Consideration in March 2023	Shares in March 2023	Cash in January 2024
Mark S. Blumenkranz	$ 44,528.76	2,013	$ 2,606.70
Darius Kharabi	$ 154,347.06	6,977	$ 9,035.42
Lagunita Biosciences, LLC	$ 1,451,979.58	65,634	$ 84,998.37
Garland Investments, L.P.	$ 10,998.06	497	$ 643.82

Following payment of the Dosing Milestone, any contingent consideration payable under the Merger Agreement in the future will be paid only in cash.

Registration Rights

We are a party to a registration rights agreement, as amended, with Mr. Iwicki. This registration rights agreement, as amended, provides Mr. Iwicki the right, subject to certain conditions, beginning after January 16, 2018, to request that his shares be covered by a registration statement that we are otherwise filing.

We are a party to a registration rights agreement with the Purchasers in our Private Placement, who are beneficial owners of more than 5% of our common stock. This registration rights agreement provides the Purchasers with certain resale registration rights with respect to the 76,813 shares of common stock issued in the Private Placement, the 5,314,400 shares of common stock issuable upon conversion of the Series E Preferred Stock issued in the Private Placement and any other shares of our common stock held by the Purchasers.

Indemnification Agreements

Our certificate of incorporation provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with all of our directors and officers.

Board Determination of Independence

Applicable Nasdaq rules require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934 and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Securities Exchange Act of 1934. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In April 2022, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each then-sitting director, including Gregory Grunberg, who served as a director during 2022 until his term expired at our 2022 annual meeting of stockholders. In October 2022, our board of directors undertook a similar review of the independence of Marjan Farid, who joined our board of directors in October 2022. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors determined that each of our directors, with the exception of Mark Iwicki, is an "independent director" as defined under applicable Nasdaq rules. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. Mr. Iwicki is not an independent director under these rules because he is our Chief Executive Officer.

Item 14. Principal Accountant Fees and Services

Audit Fees and Services

Deloitte was our independent registered public accounting firm for the years ended December 31, 2022 and December 31, 2021. The following table summarizes the fees Deloitte billed to us for the last two fiscal years. All such services and fees were pre-approved by our audit committee in accordance with the "Pre-Approval Policies and Procedures" described below.

	Years Ended December 31,	
Fee Category	**2022**	**2021**
Audit Fees(1)	$ 782,094	$ 866,480
Audit-Related Fees	—	—
Tax Fees(2)	158,475	147,808
All Other Fees(3)	1,895	1,895
Total Fees	$ 942,464	$ 1,016,192

(1) Audit fees consist of fees billed for professional services rendered by Deloitte & Touche LLP for the audits of our annual consolidated financial statements, the reviews of our interim consolidated financial statements, and related services that are normally provided in connection with statutory and regulatory filings or engagements, including, our registration statements.

(2) Tax fees consist of fees for professional services with respect to tax compliance, tax advice and tax planning.

(3) All other fees include fees and expenses for services which do not fall within the categories described above. All other fees consisted of a subscription to Deloitte & Touche LLP's Accounting and Research Tool.

Pre-approval Policies and Procedures

The audit committee of our board of directors has adopted policies and procedures for the pre-approval of audit and non-audit services for the purpose of maintaining the independence of our independent auditor. We may not engage our independent auditor to render any audit or non-audit service unless either the service is approved in advance by the audit committee, or the engagement to render the service is entered into pursuant to the audit committee's pre-approval policies and procedures. In 2020, the audit committee delegated to its chair the authority to pre-approve any audit or non-audit services to be provided to us by our independent registered public accounting firm. By the terms of this delegated authority, the chair must be report on any such approval of services pursuant to such authority at the first regularly scheduled meeting of the audit committee following such approval. The audit committee does not delegate its responsibility to approve services performed by the independent auditor to any member of management.

The standard applied by the audit committee, or the chair of the audit committee, in determining whether to grant approval of any type of non-audit service, or of any specific engagement to perform a non-audit service, is whether the services to be performed, the compensation to be paid therefore and other related factors are consistent with the independent registered public accounting firm's independence under guidelines of the SEC and applicable professional standards. Relevant considerations include whether the work product is likely to be subject to, or implicated in, audit procedures during the audit of our financial statements, whether the independent registered public accounting firm would be functioning in the role of management or in an advocacy role, whether the independent registered public accounting firm's performance of the service would enhance our ability to manage or control risk or improve audit quality, whether such performance would increase efficiency because of the independent registered public accounting firm's familiarity with our business, personnel, culture, systems, risk profile and other factors, and whether the amount of fees involved, or the non-audit services portion of the total fees payable to the independent registered public accounting firm in the period would tend to reduce the independent registered public accounting firm's ability to exercise independent judgment in performing the audit.

Part IV

Item 15. Exhibits and 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 the Registrant, 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)
2.2#	Asset Purchase Agreement, by and between the Registrant, Alcon Pharmaceuticals Ltd. and Alcon Vision, LLC (incorporated by reference to Exhibit 2.1 to the Registrant's current report on Form 8-K (File No. 001-38150) filed on May 23, 2022)
3.1*	Restated Certificate of Incorporation of the Registrant, as amended as of November 28, 2022, including Certificate of Designation of the Series D Preferred Stock of Registrant, Certificate of Elimination of Number of Shares of Preferred Stock Designated as Series D Preferred Stock of Registrant, Certificate of Designations, Preferences and Rights of Series E Convertible Non-Redeemable Preferred Stock of Registrant
3.2	Amended and Restated By laws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on November 8, 2022
4.1*	Specimen Stock Certificate evidencing the shares of common stock
4.2	Third Amended and Restated Registration Rights Agreement of the Registrant dated April 6, 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
4.4	Form of Series E Preferred Stock Certificate (incorporated by reference to Exhibit 4.1 to the Registrant's current report on Form 8-K (File No. 001-38150) filed on November 28, 2022)

Exhibit Number	Description of Exhibit
4.5*	Registration Rights Agreement, dated March 2, 2023, by and among the Registrant and the persons party thereto
10.1+	2009 Employee, Director and Consultant Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.2+	Form of Stock Option Agreement under the 2009 Employee, Director and Consultant Equity Incentive Plan (incorporated by reference to Exhibit 10.2 to the Registrant's registration statement on Form S-1 (File No. 333-218936) filed on June 23, 2017)
10.3+	Amended and Restated 2017 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.1 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on May 9, 2019)
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 October 11, 2019, by and between Combangio, Inc. and The Board of Trustees of the Leland Stanford Junior University (incorporated by reference to Exhibit 10.18 to the Registrant's annual report on Form 10-K (File No. 001-38150) filed on March 29, 2022)
10.12+	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)
10.13+	Letter Agreement, dated March 25, 2018, by and between the Registrant and Eric L. Trachtenberg (incorporated by reference to Exhibit 10.3 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on August 9, 2018)
10.14+	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)
10.15+	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)
10.16+	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)
10.17+	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)
10.18+	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)
10.19	Common Stock Purchase Warrant (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)

Exhibit Number	Description of Exhibit
10.20#	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)
10.21#	First Amendment to Loan and Security Agreement, dated November 15, 2021, by and among the Registrant, Combangio, Inc. and Oxford Finance LLC, as collateral agent and lender (incorporated by reference to Exhibit 10.1 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on August 11, 2022)
10.22	Second Amendment to Loan and Security Agreement, dated May 21, 2022, by and among the Registrant, Combangio, Inc. and Oxford Finance LLC, as collateral agent and lender (incorporated by reference to Exhibit 10.2 to the Registrant's quarterly report on Form 10-Q (File No. 001-38150) filed on August 11, 2022)
10.23	Third Amendment to Loan and Security Agreement, dated December 27, 2022, by and among the Registrant, Combangio, Inc. 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 December 27, 2022)
10.24	Securities Purchase Agreement, dated November 28, 2022, by and among the Registrant and the purchasers party thereto (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38150) filed on November 28, 2022)
10.25	Open Market Sale Agreement℠, dated as of January 19, 2023, by and between Registrant and Jefferies LLC (incorporated by reference to Exhibit 1.1 to the Registrant's current report on Form 8-K (File No. 001-38150) filed on January 19, 2023)
21.1*	Subsidiaries of the Registrant
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
99.1*	Unaudited Pro Forma Financial Statements and accompanying notes for the year ended December 31, 2022
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.

** Furnished herewith.

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 3, 2023

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 3, 2023
/s/ MARY REUMUTH Mary Reumuth	Chief Financial Officer (Principal Financial and Accounting Officer)	March 3, 2023
/s/ MARK S. BLUMENKRANZ Mark S. Blumenkranz, M.D.	Director	March 3, 2023
/s/ MARJAN FARID Marjan Farid, M.D.	Director	March 3, 2023
/s/ ANDREW I. KOVEN Andrew I. Koven	Director	March 3, 2023
/S/ C. DANIEL MYERS C. Daniel Myers	Director	March 3, 2023
/s/ ROBERT PAULL Robert Paull	Director	March 3, 2023
/s/ GREGORY PERRY Gregory Perry	Director	March 3, 2023
/s/ HOWARD B. ROSEN Howard B. Rosen	Director	March 3, 2023

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

Basis for Opinion

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

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

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which they relate.

Sale of Commercial Business to Alcon - Refer to Note 1 and Note 3 to the financial statements

Critical Audit Matter Description

On July 8, 2022, the Company sold the rights to manufacture, sell, distribute, market and commercialize EYSUVIS and INVELTYS and to develop, manufacture, market and otherwise exploit the Company’s AMPPLIFY Drug Delivery Technology (collectively, the “Commercial Business”) to Alcon Pharmaceuticals Ltd. and Alcon Vision, LLC (together referred to as “Alcon”), (the “Alcon Transaction”). The Company received an upfront cash payment of $60 million and is eligible to receive from Alcon up to four commercial-based sales milestone payments totaling up to $325 million. The

Company has determined that the disposition of the Commercial Business does not qualify for reporting as a discontinued operation as it was not considered a component of an entity that comprises operations and cash flows that can be clearly distinguished, operationally and for financial reporting purposes, from the rest of the Company.

In connection with the Alcon Transaction, Alcon may purchase any remaining inventory owned by the Company ("Remaining Inventory") at an agreed upon discounted price. The Company deferred a portion of the upfront consideration related to the discounted pricing on the Remaining Inventory. Determining the recoverability of the Remaining Inventory requires management to make significant assumptions and estimates on future purchases of inventory by Alcon.

We identified the Company's accounting for the Alcon Transaction that included: (1) the overall accounting presentation as continuing operations (2) the recognition of a gain and (3) the recoverability of the Remaining Inventory as our critical audit matter given the extent of effort and high degree of auditor judgement, including the involvement of specialists.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the accounting for the Alcon Transaction and the recoverability of the Remaining Inventory included the following, among others:

- We obtained and reviewed the Alcon Transaction agreements to evaluate the reasonableness of the methodology management used to record the transaction, including the recognition of a gain.

- With the assistance of professionals with specialized skill and knowledge, we evaluated management's assessment of the discontinued operations criteria, including the quantitative and qualitative factors surrounding the qualification for discontinued operations treatment.

- We evaluated the reasonableness of management's methodology, significant assumptions and estimates used to determine the estimate of future purchases of the Remaining Inventory by Alcon and tested the accuracy of the data utilized in the estimates for INVELTYS and EYSUVIS, including expiration dates, industry data and activity subsequent to December 31, 2022.

- We made inquiries of management and tested the mathematical accuracy of management's significant assumptions and estimates.

- We evaluated the accuracy and completeness of management's disclosure for the Alcon Transaction.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 3, 2023

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, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 70,495	$ 92,136
Short-term restricted cash	—	2,042
Accounts receivable, net	195	15,345
Inventory	—	8,639
Prepaid expenses and other current assets (Note 7)	7,657	6,204
Current assets held for sale (Note 4)	7,595	—
Total current assets	85,942	124,366
Non-current assets:		
Property and equipment, net	400	2,722
Long-term inventory	—	9,578
Right-of-use assets	16	1,299
Restricted cash and other long-term assets	462	1,462
Total assets	$ 86,820	$ 139,427
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,832	$ 4,899
Accrued expenses and other current liabilities	8,910	20,986
Deferred gain on sale of commercial business	4,189	—
Current portion of lease liabilities	13	711
Current portion of long-term debt	5,000	—
Current portion of contingent consideration	4,146	3,817
Current portion of deferred purchase consideration	595	7,009
Total current liabilities	25,685	37,422
Long-term liabilities:		
Long-term lease liabilities	—	548
Long-term debt	37,937	78,929
Long-term contingent consideration	4,224	4,841
Long-term deferred purchase consideration	—	883
Total long-term liabilities	42,161	85,201
Total liabilities	67,846	122,623
Commitments and Contingencies (Note 17)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized as of December 31, 2022 and December 31, 2021; 53,144 and 0 shares of Series E Convertible Non-Redeemable Preferred Stock issued and outstanding as of December 31, 2022 and December 31, 2021, respectively	—	—
Common stock, $0.001 par value; 120,000,000 shares authorized as of December 31, 2022 and December 31, 2021; 1,706,971 and 1,322,464 shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively	2	1
Additional paid-in capital	606,182	559,191
Accumulated deficit	(587,210)	(542,388)
Total stockholders' equity	18,974	16,804
Total liabilities and stockholders' equity	$ 86,820	$ 139,427

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,	
	2022	**2021**
Product revenues, net	$ 3,892	$ 11,240
Costs and expenses:		
Cost of product revenues	2,560	4,097
Selling, general and administrative	65,035	105,061
Research and development	17,653	11,515
Acquired in-process research and development	—	26,617
Loss (gain) on fair value remeasurement of deferred purchase consideration	638	(5,805)
Gain on fair value remeasurement of contingent consideration	(288)	—
Total costs and expenses	85,598	141,485
Loss from operations	(81,706)	(130,245)
Other income (expense):		
Interest income	664	104
Interest expense	(7,266)	(8,380)
Loss on extinguishment of debt	(2,583)	(5,395)
Gain on sale of commercial business	46,995	—
Gain on lease modification	—	1,311
Other income (expense), net	(926)	—
Total interest and other income (expense)	36,884	(12,360)
Net loss	$ (44,822)	$ (142,605)
Net loss per share attributable to common stockholders—basic and diluted	$ (29.48)	$ (108.32)
Weighted average shares outstanding—basic and diluted	1,520,611	1,316,495
Net loss	$ (44,822)	$ (142,605)
Other comprehensive loss:		
Change in unrealized gains on investments	—	(4)
Total other comprehensive loss	—	(4)
Total comprehensive loss	$ (44,822)	$ (142,609)

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

KALA PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CHANGES IN MEZZANINE EQUITY AND STOCKHOLDERS' EQUITY

(In thousands, except share amounts)

	Mezzanine Equity		Stockholders' Equity							
	Series D Preferred Stock $0.001 Par Value		Series E Preferred Stock $0.001 Par Value		Common Stock $0.001 Par Value		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance as of December 31, 2020	—	$ —	—	$ —	1,190,763	$ 1	$ 499,773	$ 4	$ (399,783)	$ 99,995
At the market offering, net of offering costs of $1,176	—	—	—	—	115,204	—	41,232	—	—	41,232
Exercise of stock options	—	—	—	—	1,778	—	248	—	—	248
Issuance of common stock for vested restricted stock units	—	—	—	—	9,204	—	1	—	—	1
Issuance of common stock under employee stock purchase plan	—	—	—	—	5,515	—	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	—	$ —	—	$ —	1,322,464	$ 1	$ 559,191	$ —	$ (542,388)	$ 16,804
At the market offering, net of offering costs $29	—	—	—	—	148,461	1	1,036	—	—	1,037
Exercise of stock options	—	—	—	—	102	—	3	—	—	3
Issuance of common stock for vested restricted stock units	—	—	—	—	9,026	—	—	—	—	—
Issuance of common stock under employee stock purchase plan	—	—	—	—	13,791	—	298	—	—	298
Issuance of common stock to satisfy deferred purchase consideration	—	—	—	—	136,314	—	7,936	—	—	7,936
Issuance of redeemable Series D preferred stock	73,208	—	—	—	—	—	—	—	—	—
Redemption of redeemable Series D preferred stock	(73,208)	—	—	—	—	—	—	—	—	—
Issuance of common stock, net of issuance cost of $3	—	—	—	—	76,813	—	438	—	—	438
Issuance of convertible Series E preferred stock and Second Closing Right, net of issuance costs of $43	—	—	9,666	—	—	—	5,515	—	—	5,515
Issuance of convertible Series E preferred stock upon settlement of Second Closing Right, net of issuance costs of $194	—	—	43,478	—	—	—	24,807	—	—	24,807
Stock-based compensation expense	—	—	—	—	—	—	6,958	—	—	6,958
Net loss	—	—	—	—	—	—	—	—	(44,822)	(44,822)
Balance as of December 31, 2022	—	$ —	53,144	$ —	1,706,971	$ 2	$ 606,182	$ —	$ (587,210)	$ 18,974

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,	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (44,822)	$ (142,605)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation and amortization	537	975
Non-cash operating lease cost	439	1,335
Gain on sale of commercial business	(46,995)	—
Loss on extinguishment of debt	2,583	5,395
Gain on lease modification	—	(1,311)
Acquired in-process research and development	—	26,617
Loss (gain) on fair value remeasurement of deferred purchase consideration	638	(5,805)
Gain on fair value remeasurement of contingent consideration	(288)	—
Amortization of debt discount and other non-cash interest	1,425	1,519
Stock-based compensation	7,008	16,088
Other non-cash losses, net	76	173
Change in operating assets and liabilities:		
Accounts receivable	15,138	(5,756)
Prepaid expenses and other current assets	(2,009)	(2,859)
Inventory	1,708	(6,257)
Accounts payable	(2,076)	3,231
Accrued expenses and other current liabilities	(11,926)	1,714
Lease liabilities and other long-term liabilities	(344)	(689)
Net cash used in operating activities	(78,908)	(108,235)
Cash flows from investing activities:		
Cash paid for acquisition of in-process research and development, net of cash acquired	—	(4,653)
Proceeds from sale of commercial business, net of transaction costs	62,908	—
Purchases of property and equipment and other assets	(313)	(886)
Proceeds from sale of property and equipment	114	92
Purchases of short-term investments	(4,992)	—
Proceeds from sales or maturities of short-term investments	5,000	76,250
Net cash provided by investing activities	62,717	70,803
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 final payment fee on debt	(40,000)	(78,010)
Proceeds from issuance of common stock and Series E preferred stock, net of transaction costs of $240	30,760	—
Proceeds from common stock offerings, net of offering costs	1,036	41,232
Payment of principal on finance lease	(39)	(35)
Proceeds from exercise of stock options and issuance of common stock under employee stock purchase plan	301	1,585
Net cash (used in) provided by financing activities	(7,942)	42,554
Net (decrease) increase in cash, cash equivalents and restricted cash:	(24,133)	5,122
Cash, cash equivalents and restricted cash at beginning of period	94,878	89,756
Cash, cash equivalents and restricted cash at end of period	$ 70,745	$ 94,878
Reconciliation of cash, cash equivalents and restricted cash:		
Cash, cash equivalents, and restricted cash at end of period	$ 70,745	$ 94,878
Less restricted cash (Notes 10 and 11)	(250)	(2,742)
Cash and cash equivalents at end of period	$ 70,495	$ 92,136
Non-cash investing and financing activities:		
Purchases of property and equipment in accounts payable and accrued expenses	$ 9	$ 139
Supplemental disclosure:		
Cash paid for interest	$ 5,958	$ 6,837
Right-of-use assets obtained in exchange of operating lease obligations	424	1,210

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

Note 1: Nature of Business

Nature of Business— Kala Pharmaceuticals, Inc. (the "Company") was incorporated on July 7, 2009, and is a clinical-stage biopharmaceutical company dedicated to the research, development and commercialization of innovative therapies for rare and severe diseases of the eye.

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 "Combangio Acquisition"). In connection with the Combangio Acquisition, the Company acquired Combangio's mesenchymal stem cell secretomes ("MSC-S") platform, including its lead product candidate for the treatment of persistent corneal epithelial defects ("PCED"), which the Company now refers to as KPI-012. PCED is a rare disease of impaired corneal healing. The Company submitted an investigational new drug application, ("IND") to the U.S. Food and Drug Administration, ("FDA"), which was accepted in December 2022. In February 2023, the Company dosed its first patient in the CHASE ("**C**orneal **H**ealing **A**fter **SE**cretome therapy") Phase 2b clinical trial of KPI-012 for PCED in the United States. The Company expects to commercialize in the United States any of its product candidates that receive marketing approval.

In connection with the determination to focus its research and development efforts on KPI-012, in 2022, the Company ceased the development of its preclinical pipeline programs that are unrelated to its MSC-S platform, including the development of KPI-287, its receptor tyrosine kinase inhibitor, and its selective glucocorticoid receptor modulators.

The Company previously developed and commercialized two marketed products, 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 applied a proprietary mucus-penetrating particle drug delivery technology, which the Company referred to as the AMPPLIFY® Drug Delivery Technology. On July 8, 2022, the Company closed the transaction (the "Alcon Transaction"), contemplated by the asset purchase agreement, dated as of May 21, 2022 (the "Asset Purchase Agreement"), by and between the Company, Alcon Pharmaceuticals Ltd. and Alcon Vision, LLC (together referred to as "Alcon"), pursuant to which Alcon purchased the rights to manufacture, sell, distribute, market and commercialize EYSUVIS and INVELTYS and to develop, manufacture, market and otherwise exploit the Company's AMPPLIFY Drug Delivery Technology (collectively, the "Commercial Business"). Alcon also assumed certain liabilities with respect to the Commercial Business at the closing of the Alcon Transaction. See Note 3, "Acquisitions and Divestitures", for additional information about the Alcon Transaction.

The Company's success is dependent upon its ability to develop, obtain regulatory approval for and commercialize KPI-012 and any other product candidate it may develop in the future, the success of its research and development efforts, whether it receives any commercial-based sales milestone payments from Alcon, its ability to raise additional capital when needed and, ultimately, attain profitable operations.

Refer to Note 3, "Acquisitions and Divestitures", for further discussion of the Combangio Acquisition.

Reverse Stock Split— On October 20, 2022, the Company effected a 1-for-50 reverse stock split of the Company's shares of common stock either issued and outstanding or held by the Company as treasury stock (the "Reverse Stock Split"). As a result of the Reverse Stock Split, every 50 shares of issued and outstanding common stock were automatically combined into one issued and outstanding share of common stock, without any change in the par

value per share. No fractional shares were issued as a result of the Reverse Stock Split. Any fractional shares that would otherwise have resulted from the Reverse Stock Split were rounded up to the next whole number. The number of authorized shares of common stock under the Company's Restated Certificate of Incorporation, as amended, remained unchanged at 120,000,000 shares. All historical share and per share amounts reflected throughout these financial statements have been adjusted to reflect the Reverse Stock Split. Proportionate adjustments were made to the per share exercise price and the number of shares of common stock that may be purchased upon exercise of outstanding stock options and warrants, and the number of shares of common stock reserved for future issuance under the Company's 2017 Equity Incentive Plan and Employee Stock Purchase Plan.

Recent Financings—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 (the "Amended and Restated Sales Agreement") with Jefferies LLC ("Jefferies") pursuant to which the Company could issue and sell, from time to time, up to an aggregate of $75,000 of its common stock in an at-the-market equity offering (the "ATM Offering") through Jefferies, as a sales agent. During the year ended December 31, 2021, the Company issued and sold 115,205 shares of its common stock under its ATM Offering pursuant to the terms of the Amended and Restated Sales Agreement, resulting in net proceeds of $41,232. During the year ended December 31, 2022, the Company issued and sold an additional 148,461 shares of its common stock under its ATM Offering pursuant to the terms of the Amended and Restated Sales Agreement, resulting in net proceeds of $1,036. As of December 31, 2022, there were $10,278 of shares of common stock remaining under the ATM Offering, and excluding these shares of common stock, there was approximately $275,000 of securities available to be issued under the 2020 Shelf Registration.

From January 1, 2023 through January 10, 2023, the Company issued and sold an additional 245,887 shares of its common stock under its ATM Offering resulting in net proceeds of $9,995. On January 10, 2023, the Amended and Restated Sales Agreement terminated in accordance with its terms when the Company completed the sale of $75,000 of its shares of common stock thereunder. As of the date of termination of the Amended and Restated Sales Agreement, the Company had sold an aggregate of 565,974 shares of its common stock under such agreement for aggregate gross proceeds of $75,000. On January 19, 2023, the Company entered into an Open Market Sale Agreement with Jefferies (the "Open Market Sale Agreement"), pursuant to which the Company may issue and sell, from time to time, shares its common stock under an ATM Offering. The Company filed a prospectus supplement relating to the Open Market Sale Agreement under its 2020 Shelf Registration, pursuant to which the Company may offer and sell shares of common stock having an aggregate offering price of up to $40,000 under the Open Market Sale Agreement. Through the date of filing of this Annual Report on Form 10-K, the Company sold 69,974 shares of its common stock under its ATM Offering pursuant to the Open Market Sale Agreement, resulting in net proceeds of $1,386. In the aggregate, subsequent to December 31, 2022 through the date of filing of this Annual Report on Form 10-K, the Company sold 315,861 shares of its common stock in ATM Offerings pursuant to the Amended and Restated Sales Agreement and the Open Market Sale Agreement for total net proceeds of $11,381.

On November 28, 2022, the Company entered into a Securities Purchase Agreement (the "Securities Purchase Agreement") with certain institutional investors named therein (the "Purchasers"), pursuant to which the Company agreed to issue and sell, in a private placement priced at-the-market under Nasdaq rules, shares of common stock of the Company and shares of Series E Convertible Non-Redeemable Preferred Stock, par value $0.001 per share, of the Company (the "Series E Preferred Stock"), in two tranches for aggregate gross proceeds of up to $31,000 (collectively, the "Private Placement"). Pursuant to the Securities Purchase Agreement, on December 1, 2022 the Company issued and sold to the Purchasers at the first closing of the Private Placement, (i) 76,813 shares of common stock, at a price per common share equal to $5.75 and (ii) 9,666 shares of Preferred Stock, at a price per share equal to $575.00, for aggregate gross proceeds of approximately $6,000. On December 27, 2022, following the certification by the Chief

Executive Officer of the Company that the FDA accepted the Company's IND for KPI-012, the Company issued and sold to the Purchasers at a second closing of the Private Placement a total of 43,478 Preferred Shares, at a price per share equal to $575.00, for aggregate gross proceeds of approximately $25,000. Costs incurred in connection with the Private Placement were $240, which have been recorded as a reduction to additional paid-in capital.

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

COVID-19 – In order to safeguard the health of its employees from 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 does not know the extent to which the COVID-19 pandemic will impact its development of KPI-012 or any other product candidate it develops. In addition, government restrictions have at times led to moratoria on elective ocular surgeries in many jurisdictions, which had significantly reduced the demand for INVELTYS, which is indicated for the treatment of post-operative inflammation and pain following ocular surgery. The COVID-19 pandemic had negatively impacted the Company's revenues from INVELTYS. In addition, the COVID-19 pandemic has generally had an adverse impact on the launch of pharmaceutical products, and the Company believes the pandemic impacted the launch of EYSUVIS. The Company cannot predict whether the COVID-19 pandemic will impact Alcon's ability to commercialize EYSUVIS and INVELTYS, and as a result, it cannot be certain whether the COVID-19 pandemic might adversely affect when the Company may receive milestone payments from Alcon, which milestone payments the Company may receive and if the Company will receive any milestone payments at all. Any impact of COVID-19 on Alcon's commercialization efforts of EYSUVIS and INVELTYS, the Company's development of KPI-012 and any other product candidate it may develop in the future and the Company's operational and financial performance will depend on certain developments, including the length and severity of the 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 treatments, and the impact of the foregoing on 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 generated only limited revenues from product sales prior to the sale of the Commercial Business to Alcon in July 2022 and has incurred recurring losses and negative cash flows from operations, including a net loss of $44,822 and $142,605, for the years ended December 31, 2022 and 2021, respectively, and used cash in operations of $78,908 and $108,235, in the years ended December 31, 2022 and 2021, 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 common stock and 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, prior to the sale of its Commercial Business to Alcon in July 2022, 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, 2022 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. To the extent these conditions or events change, 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, deferred purchase consideration, contingent consideration, assets held for sale 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— Following the sale of its Commercial Business to Alcon in July 2022, the Company no longer has any commercial products in its portfolio. The Company sold 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 resold the Company's products to specialty and other retail pharmacies. In addition to agreements with Customers, the Company entered into arrangements with third-party payors that provided for government-mandated and/or privately-negotiated rebates, chargebacks and discounts for the purchase of its products.

The Company accounted 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 performed 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 recognized revenue when it was probable that it would collect the consideration to which it was entitled in exchange for the goods or services that would be transferred to the customer.

Performance Obligations

The Company determined that performance obligations were satisfied and revenue was recognized when a customer took control of the Company's products, which occurred at a point in time. This generally occurred upon delivery of the products to customers, at which point the Company recognized revenue and recorded accounts receivable. Payment was typically received 70 to 90 days after satisfaction of the Company's performance obligations.

(In thousands, except share and per share amounts)

Transaction Price and Variable Consideration

Revenue was measured as the amount of consideration the Company expected to receive in exchange for transferring products to a customer ("transaction price"). The transaction price for product sales included variable consideration related to chargebacks, rebates, sales incentives and allowances, distribution service fees, and returns. The Company estimated the amount of variable consideration that should have been included in the transaction price. These estimates took into consideration a range of possible outcomes that were 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 reflected the Company's best estimates of the amount of consideration to which it was entitled based on the terms of the contract. The amount of variable consideration that was included in the transaction price may be constrained and was included in net sales only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized would not occur in a future period. In general, performance obligations did not include any estimated amounts of variable consideration that were 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, 2022 and 2021:

	Trade Discounts, Allowances and Chargebacks (1)	Product Returns (2)	Rebates and Incentives (3)
Balance as of January 1, 2021	$ 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
Provision related to current period sales	5,005	291	28,915
Changes in estimate related to prior period sales	(47)	(24)	(200)
Credit/payments made	(7,619)	(889)	(39,223)
Balance as of December 31, 2022	$ 11	$ 518	$ 772

(1) Trade discounts, allowances and chargebacks included fees for distribution service fees, prompt pay and other discounts, and chargebacks. Estimated trade discounts, allowances and chargebacks were deducted from gross revenue at the time revenues were recognized and were recorded as a reduction to accounts receivable on the Company's consolidated balance sheets.

(2) Estimated provisions for product returns were deducted from gross revenues at the time revenues were recognized and were included in accrued expenses and other current liabilities on the Company's consolidated balance sheets.

(3) Rebates and incentives included managed care rebates, government rebates, co-pay program incentives, and sales incentives and allowances. Estimated provisions for rebates and discounts were deducted from gross revenues at the time revenues were recognized and were included in accrued expenses and other current liabilities on the Company's consolidated balance sheets.

As of December 31, 2022 and 2021, 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.

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, 2022 or December 31, 2021. The Company recorded an allowance of $11 and $2,672 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, 2022 and December 31, 2021, 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 Combangio 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 Combangio Acquisition of $26,617 as there was 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. 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 the Company's 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, if any, 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, if any, 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.

The Company's accounts receivable balance as of December 31, 2022 was *de minimis*. Three Customers comprised 10% or more of the Company's accounts receivable balance as of December 31, 2021. These Customers comprised 44%, 31% and 24% of the accounts receivable balance, respectively, as of December 31, 2021. 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, 2022. The same three Customers comprised 10% or more of the Company's revenue during the years ended December 31, 2022 and 2021. These Customers comprised 47%, 28% and 21% of revenue, respectively, during the year ended December 31, 2022 and 48%, 29% and 22% of revenue, respectively, during the year ended December 31, 2021. 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, 2022, the Company had long-term restricted cash of $250. 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 former 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).

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, *Investments—Debt and Equity Securities*. 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, 2022 or 2021.

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. The determination of whether inventory costs will be realizable requires estimates by management. Prior to the sale of the Commercial Business in July 2022, such impairment charges were recorded within cost of product revenues, unless associated with samples inventory, in which case the charges were recorded to selling, general and administrative expense. Following the sale of the Commercial Business, any adjustments to the Remaining Inventory are recorded within other expense in the consolidated statements of operations and comprehensive loss. Following the sale of the Commercial Business, the only customer for the Company's current inventory is Alcon. If Alcon does not purchase any additional inventory, the remaining inventory balance, net of the deferred gain on sale of the Commercial Business, will be recorded to other expense 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.

Assets Held for Sale—The Company classifies its long-lived assets to be sold as held for sale, as specified by ASC 360, *Property, Plant, and Equipment*, in the period (i) it has approved and committed to a plan to sell the asset, (ii) the asset is available for immediate sale in its present condition, (iii) an active program to locate a buyer and other actions required to sell the asset have been initiated, (iv) the sale of the asset is probable, (v) the asset is being actively marketed for sale at a price that is reasonable in relation to its current fair value and (vi) it is unlikely that significant changes to the plan will be made or that the plan will be withdrawn. The Company initially measures a long-lived asset that is classified as held for sale at the lower of its carrying value or fair value less any costs to sell. Any loss resulting from this measurement is recognized in the period in which the held for sale criteria are met. Conversely, gains are not recognized on the sale of a long-lived asset until the date of sale. Upon designation as an asset held for sale, the Company stops recording depreciation and amortization expense on long-lived assets. The Company assesses the fair value of a long-lived asset less any costs to sell at each reporting period and until the asset is no longer classified as held for sale.

As of December 31, 2022, certain assets, including EYSUVIS and INVELTYIS inventory, met the criteria to be classified as held for sale. Fair value was determined based on the estimated proceeds from the sale of the assets. The Company reclassified the inventory and property and equipment, which had a combined net realizable value of $7,595, to current assets held for sale on the consolidated balance sheet as of December 31, 2022. See Note 4, "Assets Held for Sale", for additional information. There were $211 of property and equipment, net that met the criteria for classification as held for sale as of December 31, 2021, which were classified in prepaid expenses and other current assets.

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, 2022 and 2021, advertising expenses were $11,249 and $11,692, 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 years ended December 31, 2022 and 2021, impairment charges recorded were *de minimis*.

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 Attributable to Common Stockholders—The Company follows the two-class method when computing net income (loss) per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed. The two-class method is not applicable during periods with a net loss, as the holders of the convertible preferred stock have no contractual obligation to share in losses. For all periods presented, the two-class method was not applicable.

Basic net loss per share attributable to common stockholders is computed using the weighted-average number of common shares outstanding during the period. Diluted net loss per share attributable to common stockholders 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, the issuance of unvested RSUs and PSUs and convertible preferred stock using the if-converted method.

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, unvested RSUs and PSUs and convertible preferred stock using the if-converted method. Common stock equivalent shares are excluded from the computation of diluted net loss per share attributable to common stockholders 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, 2022 and 2021. (See Note 15).

Recent Accounting Pronouncements

Management has considered all recent accounting pronouncements issued since the last audit of our consolidated financial statements. The Company's management believes that these recent pronouncements will not have a material effect on our company's consolidated financial statements.

Note 3: Acquisitions and Divestitures

Sale of Commercial Business to Alcon

On July 8, 2022, the Company closed the Alcon Transaction contemplated by the Asset Purchase Agreement, pursuant to which Alcon purchased the Commercial Business and assumed certain liabilities with respect to the Commercial Business. Alcon paid to the Company an upfront cash payment of $60,000 upon the closing of the Alcon Transaction. In addition, pursuant to the Asset Purchase Agreement, the Company is eligible to receive from Alcon up to four commercial-based sales milestone payments as follows: (1) $25,000 upon the achievement of $50,000 or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2028, (2) $65,000 upon the achievement of $100,000 or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2028, (3) $75,000 upon the achievement of $175,000 or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2029 and (4) $160,000 upon the achievement of $250,000 or more in aggregate worldwide net sales of EYSUVIS and INVELTYS in a calendar year from 2023 to 2029. Each milestone payment will only become payable once, if at all, upon the first time such milestone is achieved, and only one milestone payment will be paid with respect to a calendar year. In the event that more than one milestone is achieved in a calendar year, the higher milestone payment will become payable and the lower milestone payment will become payable only if the corresponding milestone is achieved again in a subsequent calendar year.

Pursuant to the Asset Purchase Agreement, on July 8, 2022, the Company entered into supply and commercial agreements under which the Company agreed to supply EYSUVIS and INVELTYS to Alcon and distribute EYSUVIS and INVELTYS to third-party customers of the Commercial Business on behalf of Alcon for a period of six months following the closing of the Alcon Transaction, subject to early termination. In addition, the Company entered into a transition services agreement under which the Company agreed to provide certain transition services to Alcon on a cost-plus pricing arrangement for up to six months following the closing of the Alcon Transaction. Pursuant to the supply agreement, Alcon purchased from the Company, at the closing of the Alcon Transaction, $5,027 of EYSUVIS and INVELTYS inventory on-hand at the Company. Together, the supply, commercial and transition services agreements are referred to herein as the "Transition Agreement."

(In thousands, except share and per share amounts)

The Company has determined that the disposition of these assets does not qualify for reporting as a discontinued operation as it was not considered a component of an entity that comprises operations and cash flows that can be clearly distinguished, operationally and for financial reporting purposes, from the rest of the Company. During the year ended December 31, 2022, the Company recognized a net gain on the sale of the Commercial Business as follows:

Gross consideration from the sale of the Commercial Business	$	65,027
Closing and transaction costs		2,119
Net proceeds from the sale of the Commercial Business		62,908
Book value of assets transferred		
Inventories		8,915
Prepaid expenses and other current assets		556
Property and equipment, net		1,819
Other long-term assets		434
Total book value of assets transferred		11,724
Gain on sale of Commercial Business		51,184
Deferred gain on sale of Commercial Business		4,189
Net gain on sale of Commercial Business	$	46,995

Alcon may purchase any remaining inventory owned by the Company ("Remaining Inventory") at an agreed upon discounted price. As the overall components of the Alcon Transaction should be reflected at fair value, the Company has deferred a portion of the gross consideration related to the discounted pricing on the Remaining Inventory. The deferred gain on the sale of the Commercial Business of $4,189 was recorded on the consolidated balance sheet as of the transaction date as deferred gain on sale of Commercial Business and will be reduced at the time of recoverability of the Remaining Inventory.

The Company collected on behalf of Alcon for revenue generated by sales of EYSUVIS and INVELTYS from July 8, 2022 through the transition period and the Company transferred all cash generated by such sales to Alcon as of December 31, 2022.

As of December 31, 2022, the receivables due from Alcon for reimbursement for services performed under the Transition Agreement and invoices processed on Alcon's behalf were $1,418 and $3,618, respectively. The Company also has receivables due from Alcon for Remaining Inventory sold and other amounts due as of December 31, 2022 of $358 for a total receivable due from Alcon of $5,394 included in prepaid and other current assets on the consolidated balance sheet as of December 31, 2022. The Company also has $26 of receivables due from third parties in connection with the Transition Agreement. The Company recorded income from the Transition Agreement of $3,611 which is presented in other income on the consolidated statement of operations for the year ended December 31, 2022 and which offsets $3,533 of operating expenses related to the Transition Agreement captured within loss from operations. The Company's consolidated balance sheet as of December 31, 2022 reflected an additional $3,981 in payables to third parties of which $1,737 was included within accounts payable and $2,244 was included within accrued expenses and other current liabilities related to invoices the Company is obligated to pay on Alcon's behalf. As of December 31, 2022, the Company has a net receivable due from Alcon and third parties in connection with the Transition Agreement of $1,439.

Acquisition of Combangio, Inc.

In connection with the closing of the Combangio 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 155,664 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 136,314 shares of common stock which were issued on January 3, 2022 (the "Upfront Shares") and (ii) an aggregate of 19,350 shares of common stock that were initially held back as partial security for the satisfaction of indemnification obligations and other payment obligations of the Combangio Equityholders (the "Holdback Shares") and that will be issued in March 2023 upon escrow release (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 are entitled to receive from the Company up to $105,000 in payments that are contingent upon the achievement of specified development, regulatory and commercialization milestones (the "Contingent Consideration") and are payable in cash and shares of the Company's common stock, subject to the Share Cap (as defined below). If the issuance of the Deferred Purchase Consideration or any contingent consideration payable in shares of the Company's common stock (the "Contingent Stock Consideration") would result in the aggregate number of shares of 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 such consideration in excess of the Share Cap in cash. The portion of any payment of Contingent Consideration payable in cash is referred to as "Contingent Cash Consideration".

Upon dosing of the first patient in the CHASE Phase 2b clinical trial of KPI-012 for PCED in the United States in February 2023 (the "Dosing Milestone"), the Company became obligated to pay to the former Combangio Equityholders an aggregate of $2,500 in cash and $2,354 in shares of our common stock (representing an aggregate of 105,039 shares of the Company's common stock) which will be made in March 2023 and will pay the remaining amount due for the Dosing Milestone of $146 in January 2024. Upon payment of the Dosing Milestone, the Company reached the Share Cap and any Contingent Consideration payable under the Merger Agreement in the future will be paid only in cash.

Subject to the terms and conditions of the Merger Agreement, the former Combangio Equityholders, are entitled to receive from the Company the following remaining Contingent Consideration in cash:

- (i) $5,000 would become payable 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 pivotal clinical trial, (ii) $12,500 payable upon regulatory approval by the FDA of marketing and sale of a Product Candidate in the United States, subject to certain specified reductions; (iii) $17,500 payable upon the first commercial sale of a Product Candidate in the United States, subject to certain specified reductions, and (iv) an aggregate of up to $65,000 payable 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.

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.

(In thousands, except share and per share amounts)

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 Combangio Acquisition, the Company owns 100% of the outstanding common stock of Combangio. The cost of the Combangio Acquisition, which represents the total consideration transferred to Combangio stockholders in the Combangio 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 136,314 Upfront Shares issued on January 3, 2022 and 19,350 Holdback Shares which will be issued on the Escrow Release Date in March 2023.

(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 are contingent upon the achievement of specified development, regulatory and commercial milestones. Upon achievement of the Dosing Milestone in February 2023, the Company became obligated to pay to the former Combangio Equityholders an aggregate of $2,500 in cash and $2,354 in shares of the Company's common stock (representing an aggregate of 105,039 shares of the Company's common stock) which will be made in March 2023 and will pay the remaining amount of $146 in cash in January 2024. 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, 2022 or 2021, such contingencies have not been recorded in the Company's consolidated financial statements.

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 Combangio 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: Assets Held for Sale

As of December 31, 2022, the Company presented assets to be disposed of that met the criteria as held for sale as a single asset in its consolidated financial statements. The EYSUVIS and INVELTYS product inventory classified as held for sale represents the net realizable value of the Remaining Inventory which Alcon, and solely Alcon, has the right to purchase. As noted in Note 3, "Acquisitions and Divestitures" above, the Company deferred a portion of the gain on the sale of the Commercial Business related to the discounted pricing on the Remaining Inventory of $4,189.

(In thousands, except share and per share amounts)

The following is a summary of the major categories of assets that have been reclassified to held for sale on the consolidated balance sheet as of December 31, 2022:

	December 31, 2022
Inventories	$ 7,544
Property and equipment, net	51
Total assets held for sale	$ 7,595

Since the closing of the Alcon Transaction, the Company has made adjustments to the held for sale inventory balance of $4,560 for expiring Remaining Inventory, which are recorded in other income (expense), net on the consolidated statement of operations and comprehensive loss. The balance in the table above reflects these adjustments.

See Note 2, “Summary of Significant Accounting Policies”, and Note 3, “Acquisitions and Divestitures”, for further information on the sale of the Commercial Business.

Note 5: Fair Value of Financial Instruments

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, 2022 and 2021 consisted primarily of cash equivalents and contingent consideration. Cash equivalents and contingent consideration are reported at their respective fair values on the Company’s consolidated balance sheets.

As discussed in Note 3, “Acquisitions and Divestitures”, the Company acquired Combangio in November 2021 and in connection with the closing of the Combangio 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 Combangio 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 years ended December 31, 2022 and 2021, the change in the fair value of the Deferred Purchase Consideration was a loss of $638 and a gain of $5,805, respectively, primarily due to the change in the fair value of the underlying stock price and was recognized as the loss (gain) on fair value remeasurement of deferred purchase consideration in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2022 and 2021.

(In thousands, except share and per share amounts)

Additionally, the purchase price in connection with the Combangio Acquisition included potential future payments of up to $105,000 that are contingent upon the achievement of specified development, regulatory and commercialization milestones and are required to be recorded at fair value. To date, of the $105,000 in contingent milestone payments, the Company has paid to the Combangio Equityholders an aggregate of $2,500 in cash and $2,354 in shares of the Company's common stock (representing an aggregate of 105,039 shares of the Company's common stock) upon dosing of the first patient in the Company's CHASE Phase 2b clinical trial of KPI-012 for PCED in the United States in February 2023 and will pay the remaining amount due in connection with the Dosing Milestone of $146 in January 2024. 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, 2022, the change in the fair value of the contingent consideration liabilities was a gain of $288, primarily due to changes in discount rates, partially offset by the passage of time, and was recognized as a gain on fair value remeasurement of contingent consideration in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2022. During the year ended December 31, 2021, the change in the fair value of the contingent consideration liabilities was *de minimis*.

The following tables set forth the fair value of the Company's financial instruments by level within the fair value hierarchy as of December 31, 2022 and 2021:

	December 31, 2022			
	Fair Value	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$ 31,587	$ 31,587	$ —	$ —
Total Assets	$ 31,587	$ 31,587	$ —	$ —
Liabilities:				
Deferred purchase consideration	$ 595	$ —	$ —	$ 595
Contingent consideration	8,370	—	—	8,370
Total Liabilities	$ 8,965	$ —	$ —	$ 8,965

	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

(In thousands, except share and per share amounts)

The following tables summarize quantitative information and assumptions pertaining to the fair value measurement of the Level 3 inputs as of December 31, 2022 and 2021:

Financial Instrument	Fair Value at December 31, 2022	Valuation Technique	Unobservable Input	Range (Average)
Deferred purchase consideration	$ 595	Option pricing model	Discount for lack of marketability	20%
Contingent consideration	$ 8,370	Probability-adjusted discounted cash flow model	Period of expected milestone achievement	2023 - 2027 (2025)
			Probabilities of achievement	19.9% - 95.0% (44.9%)
			Discount rate	19.0%
			Discount for lack of marketability	20.0%

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%

The following table summarizes the changes in the Deferred Purchase Consideration and contingent consideration liabilities measured at fair value using Level 3 inputs for the year ended December 31, 2022:

Deferred purchase consideration	
Balance at January 1, 2021	$ —
Additions	13,697
Fair value adjustments	(5,805)
Balance at January 1, 2022	$ 7,892
Fair value adjustments	638
Settlements	(7,935)
Balance at December 31, 2022	$ 595
Contingent consideration	
Balance at January 1, 2021	$ —
Additions	8,658
Balance at January 1, 2022	$ 8,658
Fair value adjustments	(288)
Balance at December 31, 2022	$ 8,370

During the years ended December 31, 2022 and 2021, 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.

(In thousands, except share and per share amounts)

Note 6: Inventory

Inventory consists of the following:

	December 31, 2022	December 31, 2021
Raw materials	$ —	$ 1,328
Work in progress	—	9,799
Finished goods	—	7,090
Total inventory	$ —	$ 18,217

As of December 31, 2022, the Company had $7,544 of inventory classified as held for sale (see Note 4, "Assets Held for Sale"). As of December 31, 2021, the Company had $8,639 of current inventory and $9,578 of long-term inventory.

Note 7: Prepaid Expenses and Other Current Assets

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

	December 31, 2022	December 31, 2021
Due from Alcon	$ 5,394	$ —
Other non-trade receivables	908	2,110
Insurance	698	1,307
Deposits	77	911
Other	580	1,876
Prepaid expenses and other current assets	$ 7,657	$ 6,204

(In thousands, except share and per share amounts)

Note 8: Property and Equipment, Net

Property and equipment, net, consists of the following:

	December 31, 2022	December 31, 2021
Computer hardware and software	$ 1,204	$ 1,184
Equipment	391	2,647
Furniture and office equipment	29	37
Construction in progress	—	1,715
Property and equipment—at cost	1,624	5,583
Less: Accumulated depreciation	(1,224)	(2,861)
Property and equipment—net	$ 400	$ 2,722

Depreciation expense for the years ended December 31, 2022 and 2021 was $421 and $933, 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) and in connection with the Alcon Transaction, the Company disposed of and sold certain property and equipment.

Note 9: Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2022	December 31, 2021
Compensation and benefits	$ 3,334	$ 6,324
Due to third parties in connection with Transition Agreement (1)	2,244	—
Professional services	948	881
Accrued revenue reserves (2)	807	10,300
Contract manufacturing	453	396
Development costs	446	127
Commercial costs	271	2,134
Other	407	824
Accrued expenses	$ 8,910	$ 20,986

(1) There were additional amounts due to third parties in connection with the Transition Agreement included in accounts payable of $1,737 as of December 31, 2022.
(2) As of December 31, 2022 and 2021, $483 and $2,120 of additional revenue reserves were included 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

(In thousands, except share and per share amounts)

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 a lease termination agreement (the "Lease Termination Agreement") with the landlord of the Watertown Lease, which Lease Termination Agreement was amended on December 22, 2021, which modified 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 during the year ended December 31, 2022. 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 was 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 during the year ended December 31, 2022 that was pledged as collateral under a letter of credit with cash on deposit. The restricted cash was included within short-term restricted cash on the consolidated balance sheet as of December 31, 2021.

Terminated 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 leased vehicles. The Vehicle Fleet Lease commenced upon the delivery of the initial vehicles in March 2019 and has been subject to modifications as the number of leased vehicles has increased or decreased. In connection with the closing of the Alcon Transaction, the Company initiated the termination of the Vehicle Fleet Lease and as of December 31, 2022 there is no remaining right-of-use asset or corresponding lease liability. In connection with the Vehicle Fleet Lease, the Company issued a letter of credit for $450, which was reported as restricted cash on the consolidated balance sheet as of December 31, 2021. The letter of credit was released during the year ended December 31, 2022. As of December 31, 2022, the Company had a receivable of $775 due from the vendor for the sale of used vehicles following the lease termination, which is included within prepaid expenses and other current assets on the consolidated balance sheet.

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

	Year Ended December 31,	
	2022	2021
Lease cost		
Operating lease cost	$ 414	$ 3,822
Short-term lease cost	173	20
Variable lease cost	758	2,270
Total lease cost	$ 1,345	$ 6,112
Operating cash outflows from operating leases	$ 1,318	$ 7,350

(In thousands, except share and per share amounts)

As of December 31, 2022, the Company's lease liabilities were *de minimis*.

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

	December 31, 2022	December 31, 2021
Weighted average remaining lease term	0.5 years	2.4 years
Weighted average discount rate	10.4%	2.6%

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.

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 for the year ended December 31, 2021, consisting of the prepayment premium, the unamortized debt discount and issuance costs and the unaccreted exit fee. Additionally, in May 2021, the Company released $10,000 of restricted cash previously recorded to comply with a financial covenant required by the Athyrium Credit Facility.

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, 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 was 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, prior to the Second Loan Amendment and Third Loan Amendment (as defined below), provided 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 were 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 make partial repayments of the term loan to the Lender, subject to specified conditions, including the payment of applicable fees and accrued and unpaid interest on the principal amount of the term loan being repaid.

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 and the Commercial Business. 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, 2022. The derivative liability will be remeasured at fair value at each reporting date, with changes in fair value being recorded as other income (expense) in the consolidated statements of operations and comprehensive loss.

On May 21, 2022, in connection with its entry into the Asset Purchase Agreement with Alcon, the Company entered into an amendment to the Loan Agreement (the "Second Loan Amendment"). Pursuant to the Second Loan Amendment, the Lender and Agent consented to the entry by the Company into the Asset Purchase Agreement and the sale of the Commercial Business to Alcon and agreed to release its liens on the Commercial Business in consideration for the payment by the Company at the closing of the Alcon Transaction of an aggregate amount of $40,000 (the "Second Amendment Prepayment") to the Lender and Agent, representing a partial prepayment of principal in the amount of $36,697 of the $80,000 principal amount outstanding under the term loan advanced by the Lender under the Loan Agreement, plus a prepayment fee of $734 and a final payment fee of $2,569. In addition, the Company was required to pay all accrued and unpaid interest on the principal amount of the term loan being repaid.

In addition, under the Second Loan Amendment, the Lender and Agent agreed that, following the closing of the Alcon Transaction and the Second Amendment Prepayment, the Amortization Date would be extended from December 1, 2024 to January 1, 2026, at which time the aggregate principal balance of the term loan then outstanding under the Loan Agreement is required to be repaid in five monthly installments. Pursuant to the Second Loan Amendment, the Company may also make partial prepayments of the term loan to the Lender, subject to specified conditions, including the payment of applicable fees and accrued and unpaid interest on the principal amount of the term loan being repaid.

On July 8, 2022, the Second Amendment Prepayment was paid in connection with the closing of Alcon Transaction, and as such, the Amortization Date was extended to January 1, 2026. The transaction resulted in a loss on extinguishment of debt of $2,583 for the year ended December 31, 2022, consisting of the prepayment premium, a pro-rata portion of the unamortized debt discount and issuance costs and the unaccreted exit fee due upon the Second Amendment Prepayment.

On December 27, 2022, the Company entered into an amendment to the Loan Agreement (the "Third Loan Amendment"). Pursuant to the Third Loan Amendment, the Lender and Agent agreed to amend certain provisions of the Loan Agreement to permit the transfer of the listing of the Company's common stock from The Nasdaq Global Select Market to The Nasdaq Capital Market. Pursuant to the Third Loan Amendment, the Company agreed (A) to make partial prepayments of the principal amount of the term loan outstanding under the Loan Agreement as follows (the "Third Amendment Prepayments"): (1) a payment of $5,000 on or before June 30, 2023, representing a partial prepayment of principal in the amount of $4,673, plus a final payment fee of $327 and (2) a payment of $5,000 on or before January 31, 2024, representing a partial prepayment of principal in the amount of $4,673, plus a final payment fee of $327 and (B) that the Amortization Date under the Loan Agreement shall be changed from January 1, 2026 to January 1, 2025.

Pursuant to the Third Loan Amendment, in addition to the Third Amendment Prepayments, if the Company makes an additional prepayment under the Loan Agreement equal to $5,000 (inclusive of the final payment fee) on or prior to December 31, 2024 (the "First Extension Prepayment"), the Amortization Date will be automatically changed to July 1, 2025, and the maturity date of the Loan Agreement will be automatically changed from May 1, 2026 to November 1, 2026. If, in addition to the Third Amendment Prepayments and the First Extension Prepayment, the Company makes an additional prepayment under the Loan Agreement equal to $2,500 (inclusive of the final payment fee) on or prior to June 30, 2025 (the "Second Extension Prepayment"), the Amortization Date will be automatically changed to January 1, 2026, and the maturity date of the Loan Agreement will be automatically changed to May 1, 2027.

Under the Third Loan Amendment, the Lender and Agent also agreed to waive the prepayment fees for the Third Amendment Prepayments, the First Extension Prepayment, the Second Extension Prepayment and any other prepayments under the Loan Agreement. Pursuant to the Loan Agreement, the Company also will be required to pay all accrued and unpaid interest on the principal amounts of the term loan being repaid at the time of repayment. The Company paid the Third Amendment Prepayments on January 25, 2023. The principal loan balance under the Loan Agreement following the Third Amendment Prepayments was $33,957.

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 are being 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 consolidated statements of operations and comprehensive loss. As of December 31, 2022, the effective interest rate was 15.63%, which takes into consideration the non-cash accretion of the exit fee and the amortization of the debt discount and issuance costs.

During the year ended December 31, 2022, the Company recognized interest expense of $7,280 for the Loan Agreement. This consisted of amortization of debt discount of $342, accretion of the final payment fee of $1,083 and the contractual coupon interest expense of $5,855. During the year ended December 31, 2021, the Company recognized interest expense of $8,351 for the Loan Agreement and the Athyrium Credit Facility. This consisted of amortization of debt discount of $613, accretion of the final payment fee of $905 and the contractual coupon interest expense of $6,833.

(In thousands, except share and per share amounts)

The components of the carrying value of the debt as of December 31, 2022 and December 31, 2021 are detailed below:

	December 31, 2022	December 31, 2021
Principal loan balance	$ 43,303	$ 80,000
Unamortized debt discount and issuance cost	(806)	(1,927)
Cumulative accretion of exit fee	440	856
Total debt	$ 42,937	$ 78,929
Less: current portion of long-term debt	(5,000)	—
Long-term debt, net	$ 37,937	$ 78,929

The annual principal payments due under the Loan Agreement as of December 31, 2022 were as follows:

Years Ending December 31,	
2023	$ 4,673
2024	4,673
2025	23,970
2026	9,987
2027	—
Total	$ 43,303

Note 12: Warrants

The Company has issued warrants in connection with debt transactions that were completed prior to 2017.

The following table summarizes the common stock warrants outstanding as of December 31, 2022 and 2021, each exercisable into the number of shares of common stock set forth below as of the specified dates:

Issued	Exercise Price Per Share	Expiration Date	Exercisable From	Shares Exercisable at December 31, 2022	Shares Exercisable at December 31, 2021
2014	$ 375.00	November 2024	July 2017	320	320
2016	$ 413.50	October 2026	September 2017	290	290
2018	$ 609.23	October 2025	October 2018	3,693	3,693
				4,303	4,303

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, 2022 and 2021. As of December 31, 2022, the Company designated 54,000 shares of preferred stock as Series E Preferred Stock of which 53,144 shares were outstanding as of December 31, 2022. There was no preferred stock outstanding as of December 31, 2021.

Series D Convertible Redeemable Preferred Stock

On August 18, 2022, the Board of Directors (the "Board") declared a dividend of one one-thousandth of a share of the Company's Series D Preferred Stock ("Series D Preferred Stock"), for each outstanding share of the Company's common stock held of record as of 5:00 p.m. Eastern Time on August 29, 2022. The Certificate of Designation of Series D Preferred Stock was filed with the Delaware Secretary of State and became effective on August 19, 2022. The dividend was based on the number of outstanding shares of common stock prior to the Reverse Stock Split. The outstanding shares of Series D Preferred Stock were entitled to vote together with the outstanding shares of common stock, as a single class, exclusively with respect to a proposal giving the Board the authority, as it determined appropriate, to implement a reverse stock split within twelve months following the approval of such proposal by the Company's stockholders (the "Reverse Stock Split Proposal"), as well as any proposal to adjourn any meeting of stockholders called for the purpose of voting on the Reverse Stock Split Proposal (the "Adjournment Proposal").

The Company held a special meeting of stockholders on October 19, 2022 (the "Special Meeting") for the purpose of voting on the Reverse Stock Split Proposal and an Adjournment Proposal. All shares of Series D Preferred Stock that were not present in person or by proxy at the Special Meeting were automatically redeemed by the Company immediately prior to the opening of the polls at Special Meeting (the "Initial Redemption"). All shares that were not redeemed pursuant to the Initial Redemption were redeemed automatically upon the approval by the Company's stockholders of the Reverse Stock Split Proposal at the Special Meeting (the "Subsequent Redemption" and, together with the Initial Redemption, the "Redemption"). Each share of Series D Preferred Stock was entitled to receive $0.10 in cash for each 100 whole shares of Series D Preferred Stock immediately prior to the Redemption. As of September 30, 2022, there were 73,208 shares of Series D Preferred Stock issued and outstanding. As of December 31, 2022, both the Initial Redemption and the Subsequent Redemption have occurred. As a result, no shares of Series D Preferred Stock remain outstanding.

On November 28, 2022, the Company filed a Certificate of Elimination of Number of Shares of Preferred Stock Designated as Series D Preferred Stock with the Secretary of State of the State of Delaware which, effective upon filing, eliminated all matters set forth in the Certificate of Designation of Series D Preferred Stock previously filed by the Company and all shares of Preferred Stock previously designated as Series D Preferred Stock resumed their status as undesignated shares of preferred stock of the Company.

Series E Convertible Non-Redeemable Preferred Stock

Pursuant to the Company's Certificate of Designations, Preferences and Rights of Series E Convertible Non-Redeemable Preferred Stock (the "Certificate of Designations"), filed with the Secretary of State of the State of Delaware with respect to the Series E Preferred Stock, the Company designated 54,000 shares of its authorized and unissued preferred stock as Series E Preferred Stock, and established the rights, preferences and privileges of the Series E Preferred Stock. As discussed more fully in Note 1, "Nature of Business," the Company entered into a Securities Purchase Agreement pursuant to which it issued 9,666 shares of Series E Preferred Stock at a per share price of $575.00 on December 1, 2022 and 43,478 shares of Series E Preferred Stock at a per share price of $575.00 on December 27, 2022. Each share of Series E Preferred Stock has a par value of $0.001.

Conversion

Each share of Series E Preferred Stock is initially convertible into 100 shares of common stock (subject to adjustment as provided in the Certificate of Designations) at any time at the option of the holder, provided that the holder will be prohibited, subject to certain exceptions, from converting its Series E Preferred Stock for shares of common stock to the extent that immediately prior to or following such conversion, the holder, together with its affiliates and other attribution parties, would own in excess of 9.99% of the total number of shares of common stock of the Company then issued and outstanding after giving effect to such conversion, which percentage may be changed at the holder's election to a lower percentage at any time or to a higher percentage not to exceed 19.99% upon 61 days' notice to the Company (collectively, the "Beneficial Ownership Limitation").

Voting

Shares of Series E Preferred Stock will generally have no voting rights, except to the extent provided by applicable law, and except that the consent of the holders of a majority of the outstanding Series E Preferred Stock will be required to waive any provisions of the Certificate of Designations.

Dividends

Shares of Series E Preferred Stock will be entitled to receive dividends equal to (on an as-if-converted-to-common stock basis), and in the same form and manner as, dividends actually paid on shares of common stock.

Liquidation Rights

Upon any dissolution, liquidation or winding up of the Company, whether voluntary or involuntary ("Dissolution"), subject to any prior or superior rights of holders of senior securities, if any, holders of Series E Preferred Stock will be entitled to receive an amount per share of Series E Preferred Stock equal to (i) $575.00 (as adjusted for stock splits, combinations, reorganizations and the like) plus any dividends declared but unpaid thereon or (ii) such amount per share as would have been payable had all shares of Series E Preferred Stock been converted into common stock (without regard to any restrictions on conversion, including the Beneficial Ownership Limitation) immediately prior to such Dissolution, in either case, before any distributions shall be made to holders of common stock or any series of preferred stock ranked junior to the Series E Preferred Stock.

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, 2022 and 2021. The Company had 1,706,971 and 1,322,464 shares of common stock issued and outstanding as of December 31, 2022 and 2021, respectively.

(In thousands, except share and per share amounts)

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, subject to any preferential dividend rights of any preferred stock that the Company may issue in the future.

In the event of the Company's Dissolution, whether voluntary or involuntary, 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 the Series E Preferred Stock and any preferred stock that the Company may issue in the future. 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 Series E Preferred Stock and shares of any series of its preferred stock that the Company may designate and issue in the future.

Reserved Shares

As of December 31, 2022 and 2021, 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 (the "ESPP"), upon the exercise of stock options, upon the vesting of RSUs and PSUs, upon the issuance of the Deferred Purchase Consideration in connection with the Combangio Acquisition (see Note 5) and upon conversion of the Series E Preferred Stock:

	December 31, 2022	December 31, 2021
Warrant rights to acquire common stock	4,303	4,303
ESPP	15,548	16,178
Outstanding inducement stock option awards	11,080	25,838
2009 Plan	32,642	42,817
2017 Plan	248,221	194,730
Deferred Purchase Consideration	19,350	155,664
Series E Preferred Stock (as converted to common shares)	5,314,400	—
Total	5,645,544	439,530

Second Closing Right

The Company determined that the common stock and the Series E Preferred Stock issued on December 1, 2022 and the Series E Preferred Stock issued on December 27, 2022 (the "Second Closing Right") each represented separate freestanding financial instruments and were not within the scope of ASC 480, *Distinguishing Liabilities from Equity*. The instruments did not contain any embedded derivatives required to be bifurcated from the Series E Preferred Stock and the instruments were each equity classified within permanent equity. The Company determined that the relative fair value of the Second Closing Right was *de minimis*.

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, 2022, there were 77,375 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 32,642 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) 71,475 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.

Stock Option Awards

During the year ended December 31, 2022, the Company granted options for the purchase of 83,221 shares of common stock, including options with performance criteria as described below, options to directors and inducement grant options to purchase 2,800 shares of common stock to new employees made outside of the 2017 Plan in accordance with Nasdaq Listing Rule 5635(c)(4) and 6,910 restricted stock units. During the year ended December 31, 2021, the Company granted options for the purchase of 44,727 shares of common stock, including inducement grant options to purchase 12,988 shares of common stock to new employees made outside of the 2017 Plan and 11,090 restricted stock units. Vesting of each option award is subject to such employee's continued service with the Company through the applicable vesting dates.

A summary of option activity for awards under the 2009 Plan, the 2017 Plan and inducement grants for the year ended December 31, 2022 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, 2022	199,805	$ 338.33	6.4	$ 14
Granted	83,221	62.46		
Exercised	(102)	29.15		
Forfeited	(76,703)	250.01		
Outstanding as of December 31, 2022	206,221	$ 260.00	6.2	$ 203
Vested or expected to vest as of December 31, 2022	206,221	$ 260.00	6.2	$ 203
Options exercisable as of December 31, 2022	131,254	$ 345.33	5.1	$ 1

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, 2022 and 2021 are as follows:

	Year Ended December 31,					
	2022			2021		
Expected volatility	72.9%	–	87.0%	72.7%	–	74.2%
Risk-free interest rate	1.43%	–	4.19%	0.50%	–	1.39%
Expected dividend yield	0%			0%		
Expected term (in years)	5.50	–	6.10	5.13	–	6.10

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.

(In thousands, except share and per share amounts)

The weighted average grant-date fair value of options granted during the years ended December 31, 2022 and 2021, was $40.40 and $181.43, 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, 2022, there was $4,410 of unrecognized compensation cost related to the stock options granted, which is expected to be expensed over a weighted-average period of 1.95 years. Stock-based compensation expense was classified in the consolidated statements of operations and comprehensive loss as follows:

	Year Ended December 31,	
	2022	2021
Cost of product revenues	$ 166	$ 169
Research and development	1,292	3,145
Selling, general and administrative	5,550	12,774
Total	$ 7,008	$ 16,088

Stock-based compensation costs capitalized into inventory totaled $190 and $1,157 for the years ended December 31, 2022 and 2021, respectively. Capitalized stock-based compensation was recognized as an expense in cost of product revenues when the related product was sold or in selling, general and administrative expense when the related product was designated as a sample.

The Company received cash proceeds from the exercise of stock options of $3 and $248 during the years ended December 31, 2022 and 2021, respectively. The total intrinsic value of options exercised for the years ended December 31, 2022 and 2021, was $3 and $406, respectively.

In January 2022, the Company granted stock options to purchase up to 14,850 shares of common stock to certain executives tied to certain performance criteria. The options will vest, if at all, upon satisfying the performance criteria. The Company has assessed the probability of achievement of the performance criteria and has recorded related stock compensation expense to the extent they are determined to be probable as of December 31, 2022.

Restricted Stock Units and Performance-Based Restricted Stock Units—In June 2020, the Company issued 13,854 PSUs to certain executives and other employees tied to certain performance criteria, which vested as to 50% of the PSUs in October 2021 on the first anniversary of satisfying the performance criteria and the remaining 50% vested in October 2022 upon the second anniversary of satisfying the performance criteria.

In 2021, the Company issued 8,590 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 2,500 RSUs to members of the Board which vested upon the 2022 Annual Meeting of Stockholders. In 2022, the Company issued 6,910 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 of December 31, 2022, a total of 8,347 RSUs were outstanding, consisting of 4,887 unvested shares and 3,460 vested and deferred shares by directors. This results in unrecognized stock-based compensation of $585 to be recognized as stock-based compensation expense over the remaining weighted-average vesting period of 1.29 years.

(In thousands, except share and per share amounts)

A summary of activity for RSUs and PSUs for the year ended December 31, 2022 is as follows:

	Shares	Weighted Average Grant Date Fair Value
Unvested and outstanding balance as of January 1, 2022	16,287	$ 443.05
Changes during the period:		
Granted	6,910	63.50
Vested	(10,726)	$ 475.83
Forfeited	(7,584)	$ 187.96
Unvested and outstanding balance as of December 31, 2022	4,887	$ 230.29
Vested and deferred balance as of December 31, 2022	3,460	

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 4,466 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) 17,868 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 and 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, 2022, employees of the Company purchased an aggregate of 13,791 shares under the ESPP. During the year ended December 31, 2021, employees of the Company purchased an aggregate of 5,515 shares under the ESPP.

(In thousands, except share and per share amounts)

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, 2022 and 2021:

	Year Ended December 31,	
	2022	2021
Numerator:		
Net loss attributable to common stockholders	$ (44,822)	$ (142,605)
Denominator:		
Weighted-average common shares outstanding, basic and diluted(1)	1,520,611	1,316,495
Net loss per share attributable to common stockholders, basic and diluted	$ (29.48)	$ (108.32)

(1) Included in the weighted-average common shares outstanding, basic and diluted for the years ended December 31, 2022 and 2021 is an aggregate of 19,350 shares of common stock that were held back by the Company and will be issued in March 2023 upon the Escrow Release Date. Also included in the weighted-average common shares outstanding, basic and diluted for the year ended December 31, 2021 is an aggregate of 136,314 shares of common stock issued to Combangio Equityholders on January 3, 2022.

The following potential common stock equivalents were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect. The share amounts presented below represent the average of the quarters' incremental shares:

	Year Ended December 31,	
	2022	2021
Options to purchase shares of common stock	233,231	201,477
Unvested RSUs and PSUs	9,718	23,530
Unexercised warrants	4,303	4,470
Convertible preferred stock (as converted to common shares)	1,328,600	—
	1,575,852	229,477

Note 16: Income Taxes

The Company has had no income tax expense due to operating losses incurred for the years ended December 31, 2022 and 2021. 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.

(In thousands, except share and per share amounts)

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,	
	2022	2021
Federal statutory income tax rate	21.0 %	21.0 %
Effect of:		
Change in valuation allowance	7.5	(23.0)
State income taxes, net of federal benefit	5.4	4.8
Stock-based compensation	(4.6)	(1.3)
Losses and Credits Limited by Section 382 & Section 383	(28.8)	1.3
Research and development tax credits	—	0.5
Acquired in-process research and development	—	(3.9)
Other	(0.5)	0.6
Effective income tax rate	— %	— %

Net deferred tax assets as of December 31, 2022 and 2021 consisted of the following:

	December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 102,565	$ 102,935
Capitalized research and development and start-up expenditures	8,230	4,615
Stock-based compensation	7,243	8,408
Deferred gain on sale of Commercial Business	1,145	—
Rebates, incentives, trade discounts and allowances	223	3,334
Lease liabilities	4	321
Research and development tax credit carryforwards	—	3,591
Other	2,000	1,260
Total deferred tax assets	$ 121,410	$ 124,464
Deferred tax liabilities:		
Right-of-use assets	(4)	(331)
Total deferred tax liabilities	$ (4)	$ (331)
Valuation allowance	$ (121,406)	$ (124,133)
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, 2022 and 2021. The valuation allowance decreased by $2,727 and increased by $36,568 during the years ended December 31, 2022 and 2021, respectively. The current year decrease is primarily the result of a material reduction to the net operating loss carryforward and the research and development tax credits deferred tax assets caused by limitations under Section 382 and Section 383 of the Internal Revenue Code of 1986, thus lowering the valuation allowance required. The prior year increase is due to additional net operating loss carryforwards and research and development tax credits, partially offset by a small increase to the Section 382 limit. Management reevaluates the positive and negative evidence at each reporting period.

In 2017, the Tax Cuts and Jobs Act of 2017 ("2017 Tax Act") was signed into law. Amongst other provisions, the 2017 Tax Act requires taxpayers to capitalize and amortize research and experimental ("R&D") expenditures under Section 174 for tax years beginning after December 31, 2021. As such, the rule noted became effective for the Company during the year ended December 31, 2022 and resulted in the capitalization of certain R&D costs within its tax provision.

The Company will amortize such costs for tax purposes over 5 years if the R&D was performed in the United States and over 15 years if the R&D was performed outside the United States.

As of December 31, 2022 and 2021, the Company had federal net operating loss carryforwards of $349,378 and $364,425, respectively, which may be available to offset future federal tax liabilities and expire at various dates beginning in 2030. As of December 31, 2022 and 2021, the Company had state net operating loss carryforwards of $390,607 and $352,863, respectively, which may be available to offset future state income tax liabilities and expire at various dates beginning in 2023. As of December 31, 2022, the Company had $0 federal and state research and development credit carryforwards. As of December 31, 2021, the Company had combined federal and state research and development credit carryforwards of approximately $3,591, which were set to begin to expire in 2039 (federal) and 2034 (state).

Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. Under the provisions of Section 382 of the Internal Revenue Code of 1986, certain substantial changes in the Company's ownership, including a sale of the Company, or significant changes in ownership due to sales of equity, may have limited, or may limit in the future, the amount of net operating loss carryforwards, which could be used annually to offset future taxable income. The Company previously completed an analysis and determined that an ownership change materially limited the net operating loss carryforwards. During December 2022, an additional ownership change occurred as a result of the Company's entry into the Securities Purchase Agreement. As a result of the most recent ownership change, the utilization of the Company's net operating loss carryforwards is subject to an annual limitation of $222.

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, 2022 and 2021 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, 2022 and 2021.

Note 17: Commitments and Contingencies

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 Combangio Acquisition. Pursuant to the license agreement with Stanford (the "Stanford Agreement"), the Company has a worldwide, exclusive, sublicensable license under certain patent rights ("licensed patents") directed to methods to promote eye wound healing, to make, have made, use, import, offer to sell and sell products ("licensed products") that are covered by the licensed patents 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. Amounts paid to Stanford in the year ended December 31, 2022 were *de minimis*. There were no amounts paid to Stanford in the year ended December 31, 2021.

Johns Hopkins University License Agreement - In connection with the closing of the Alcon Transaction on July 8, 2022, the Company's exclusive license agreement with John Hopkins University was assigned to Alcon, and the Company has no further obligations under the agreement.

(In thousands, except share and per share amounts)

The Company's minimum obligations due under the Stanford License Agreement as of December 31, 2022, are as follows:

Years Ending December 31,		
2023	$	30
2024		30
2025		65
2026		65
2027		65
Thereafter		390
Total minimum license payments	$	645

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 commitments due under the commercial supply agreement for 2023 and beyond were transferred to Alcon upon the closing of the Alcon Transaction.

Contingencies related to the Merger Agreement—In connection with the Combangio Acquisition, 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. Upon achievement of the Dosing Milestone in February 2023, the Company became obligated to pay to the former Combangio Equityholders an aggregate of $2,500 in cash and $2,354 in shares of the Company's common stock (representing an aggregate of 105,039 shares of the Company's common stock) which will be made in March 2023 and will pay the remaining amount due in connection with the Dosing Milestone of $146 in January 2024. 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, 2022 or 2021, such contingencies have not been recorded in the Company's consolidated 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.

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, 2022 and 2021, 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 $396 and $612 to the 401(k) Plan during for the years ended December 31, 2022 and 2021, respectively.