# KODIAK

THE OPHTHALMOLOGY MEDICINES COMPANY

2019
ANNUAL
REPORT

TRAILBLAZING

# SCIENCE

Our creative & thoughtful foundation

GENERATION 2.0

# MEDICINES

Our challenge to the status quo

SINGULAR FOCUS IN

# OPHTHALMOLOGY

Our 24/7/365

## TO OUR KODIAK
# STOCKHOLDERS

***We made tremendous progress in 2019 toward our goal of developing a next-generation platform for retinal medicines.*** We remain very pleased with the emerging clinical profile of KSI-301, our first product candidate built on our ABC platform. We continue to see impressive safety, efficacy and durability across our active clinical studies. We initiated our first pivotal clinical study (DAZZLE) assessing KSI-301 in wet age-related macular degeneration (wet AMD) patients. We held a productive End-of-Phase-2 meeting with the FDA in which we reached agreement on an innovative clinical plan for registration. We secured substantive resources to fund accelerated clinical, manufacturing, and commercial plans for KSI-301. We continued to attract top talent and to deepen our drug development pipeline while remaining focused on achieving our 2022 Vision of filing a BLA in wet AMD, Diabetic Macular Edema (DME), and Retinal Vein Occlusion (RVO) in 2022.

Kodiak aims to resolve fierce challenges in treating retinal diseases. Clinical studies establish that anti-VEGF therapy can improve and maintain patients' vision for years when dosed at a high frequency. However, patients often cannot be treated often enough to maintain therapeutic benefits in the real world. The insufficient durability of today's anti-VEGF therapies severely limits real-world efficacy. These shortcomings often lead to permanent retina damage and blindness starting just a few months after treatment. Clinicians, patients, and health systems are forced to bear the burden placed by the limitations of today's medicines. We believe that these trends can be prevented. The solution is to develop a new generation of medicines that fits seamlessly into the lives of our patients.

*Over twenty-five million intravitreal injections of anti-VEGF biologics are performed globally every year. Our lead medicine, KSI-301, fits into this established treatment paradigm as an anti-VEGF antibody-based biologic dosed via intravitreal injection.* ***Data generated to date make us optimistic that KSI-301 can offer meaningful differentiation and improve real-world outcomes.***

All cohorts of our Phase 1b open-label multiple-dose study of KSI-301 are fully enrolled. In the wake of favorable data presented at Angiogenesis 2020 this February, we expect to continue providing updates on safety, efficacy, and durability from this study at major medical meetings or company-organized virtual events this year.

Our clinical development plans are designed to meet FDA guidance, respond effectively to a changing macro environment and position KSI-301 as the leading first-line anti-VEGF therapy in wet AMD, DME, and RVO. At our End-of-Phase-2 meeting with the FDA, we confirmed that approval of KSI-301 in these key retinal indications could be achieved with only four successful pivotal clinical studies. We successfully launched a global Phase 2/3 head-to-head study of KSI-301 versus aflibercept in wet AMD (DAZZLE). Clinician enthusiasm for KSI-301 remains high, as demonstrated by the strong patient recruitment into DAZZLE. Additionally, we are prepared to initiate pivotal clinical studies of KSI-301 in DME, RVO, and, potentially, earlier diabetic retinopathy this year with the goal to submit a single BLA in 2022.

Looking to 2020, we are well-positioned to continue development of KSI-301. In 2019, we closed the sale of a capped royalty right on global net sales of KSI-301 and also closed a public offering of common stock. These substantive financing events provide us with the capital necessary to execute against our 2022 Vision.

***The COVID-19 pandemic reminds us of the importance of our patients and clinical study sites.*** The safety of our patients, investigators, and study site staff continues to be a primary focus. We are also acutely aware of the seriousness of the retinal diseases we treat and the necessity for continuous anti-VEGF treatment to prevent permanent vision loss. Given this dire need, patients continue to participate in DAZZLE, and we have implemented numerous measures to maximize their safety and the safety of our clinical study sites. We are vigilantly and proactively monitoring study participation and engaging with our community to safeguard the integrity of our study data. Importantly, the sequencing of our pivotal trials enables us to adapt to fluid public health and economic landscapes.

Being well-capitalized and addressing very serious diseases, we are well-positioned to navigate the unknowns and complexities caused by the ongoing COVID-19 pandemic.

We are also designing and developing additional pipeline molecules with a focus on multi-inhibitor medicines. KSI-501, our dual-inhibitor bioconjugate, targets vascular leakage, abnormal angiogenesis, and concurrent inflammation. Inflammation is intimately linked to the pathology of high prevalence retinal diseases, to VEGF-non-responder populations in these diseases and particularly to the very high levels of disease activity seen in diabetic eye disease. Additionally, we continue to make solid progress on our triplet inhibitors, such as KSI-601, to address multifactorial diseases of the retina like dry AMD.

***On behalf of Kodiak's board of directors and leadership team, I want to thank you for your investment and support. I also want to thank our dedicated employees and corporate partners around the world for their commitment to our mission of using trailblazing science to create disruptive products and platforms to tackle the biggest challenges in ophthalmology.***

***Victor Perlroth*** MD Chairman & CEO

# FORWARD-LOOKING STATEMENTS

This communication contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. These forward-looking statements are not based on historical fact and include statements regarding the potential licensure of KSI-301 and a BLA submission in wet AMD, DME, RVO and diabetic retinopathy; the sufficiency of our cash, cash equivalents and marketable securities; our platform technology and potential therapies; future development plans; clinical and regulatory objectives and the timing thereof, anticipated design of planned clinical trials, expectations regarding the potential efficacy and commercial potential of our product candidates; the anticipated presentation of data; the results of our research and development efforts and our ability to advance our product candidates into later stages of development. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "expect," "plan," "believe," "intend," "pursue," and other similar expressions among others. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the preliminary safety, efficacy and durability data for our KSI-301 product candidate will not continue or persist; cessation or delay of any of the ongoing clinical studies and/or our development of KSI-301 may occur, including as a result of the COVID-19 pandemic; future potential regulatory milestones of KSI-301, including those related to current and planned clinical studies may be insufficient to support regulatory submissions or approval; anticipated presentation of data at upcoming conferences may not occur; our research and development efforts and our ability to advance our product candidates into later stages of development may fail; any one or more of our product candidates may not be successfully developed, approved or commercialized; adverse conditions in the general domestic and global economic markets, including the COVID-19 pandemic, which may significantly impact our business and operations, including out of our headquarters in the San Francisco Bay Area and our clinical trial sites, as well as the business or operations of our manufacturers, contract research organizations or other third parties with whom we conduct business; as well as the other risks identified in our filings with the Securities and Exchange Commission. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and Kodiak undertakes no obligation to update forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements.

Kodiak®, Kodiak Sciences®, ABC™, ABC Platform™ and the Kodiak logo are registered trademarks or trademarks of Kodiak Sciences Inc. in various global jurisdictions.

# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, DC 20549**

# FORM 10-K

**(Mark One)**

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

**For the fiscal year ended December 31, 2019**

**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: 001-38682**

# KODIAK SCIENCES INC.

**(Exact Name of Registrant as Specified in its Charter)**

| **Delaware** | **27-0476525** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(I.R.S. Employer Identification No.)** |
| **2631 Hanover Street Palo Alto, CA** | **94304** |
| **(Address of principal executive offices)** | **(Zip Code)** |

**Registrant's telephone number, including area code: (650) 281-0850**

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

| **Title of each class** | **Trading Symbol(s)** | **Name of each exchange on which registered** |
|---|---|---|
| Common stock, par value $0.0001 | KOD | The Nasdaq Stock Market LLC |

**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 Exchange Act 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 is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the common stock held by non-affiliates of the registrant, based on the closing price of a share of the registrant's common stock on June 28, 2019 as reported by the Nasdaq Global Market on such date, was approximately $273.7 million. Shares of common stock held by each executive officer and director and by each other person who may be deemed to be an affiliate of the registrant, have been excluded from this computation. The determination of affiliate status for this purpose is not necessarily a conclusive determination for other purposes.

As of March 2, 2020, the registrant had 44,420,028 shares of common stock, $0.0001 par value per share, outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive Proxy Statement relating to the 2020 Annual Meeting of Stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K to the extent stated herein. The proxy statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2019.

[THIS PAGE INTENTIONALLY LEFT BLANK]

**Table of Contents**

**Kodiak Sciences Inc.**
**Annual Report on Form 10-K for the Fiscal Year Ended December 31, 2019**

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or Exchange Act. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends affecting the financial condition of our business. Forward-looking statements should not be read as a guarantee of future performance or results and will not necessarily be accurate indications of the times at, or by, which such performance or results will be achieved. Forward-looking statements are based on information available at the time those statements are made and/or management's good faith beliefs as of that time with respect to future events, and are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in or suggested by the forward-looking statements.

Forward-looking statements include all statements that are not historical facts. In some cases, you can identify forward-looking statements by terms such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "anticipate," "project," "target," "design," "estimate," "predict," "potential," "plan" or the negative of these terms, or similar expressions and comparable terminology intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties, including those set forth under the section titled "Risk Factors" and elsewhere in this report. Forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our development activities, preclinical studies, clinical trials and regulatory filings;
- the translation of our preclinical results and data and early clinical trial results in particular relating to safety, efficacy and durability into future clinical trials in humans;
- the continued durability, efficacy and safety of our product candidates;
- our ability to achieve our "2022 Vision" of a Biologics License Application of KSI-301 in 2022;
- the number, size and design of clinical trials that regulatory authorities may require to obtain marketing approval, including the order and number of clinical studies required to support a Biologics License Application, or BLA, in wet age-related macular degeneration, or wet AMD, diabetic macular edema, or DME, retinal vein occlusion, or RVO, and diabetic retinopathy, or DR;
- the timing or likelihood of regulatory filings and approvals, including the potential to achieve FDA approval of KSI-301 in wet AMD, DME, RVO and DR;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- our ability to obtain funding for our operations, including funding necessary to develop, manufacture and commercialize our product candidates;
- the rate and degree of market acceptance of our product candidates;
- the success of competing products or platform technologies that are or may become available;
- our plans and ability to establish sales, marketing and distribution infrastructure to commercialize any product candidates for which we obtain approval;
- our expectation as to the concentration of retinal specialists in the United States and its impact on our sales and marketing plans;
- our expectations regarding our ability to enter into manufacturing-related commitments, and the timing thereof;
- future agreements with third parties in connection with the commercialization of our product candidates;
- the size and growth potential of the markets for our product candidates, if approved for commercial use, and our ability to serve those markets;
- existing regulations and regulatory developments in the United States and foreign countries;
- the expected potential benefits of strategic collaboration agreements and our ability to attract collaborators with development, regulatory and commercialization expertise;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- potential claims relating to our intellectual property and third-party intellectual property;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the pricing and reimbursement of our product candidates, if approved;

- our ability to attract and retain key managerial, scientific and medical personnel;
- the accuracy of our estimates regarding the sufficiency of our cash resources, expenses, future revenue, capital requirements and needs for additional financing;
- our financial performance; and
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act.

All forward-looking statements are based on information available to us on the date of this Annual Report on Form 10-K and we will not update any of the forward-looking statements after the date of this Annual Report on Form 10-K, except as required by law. Our actual results could differ materially from those discussed in this Annual Report on Form 10-K. The forward-looking statements contained in this Annual Report on Form 10-K, and other written and oral forward-looking statements made by us from time to time, are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements, and you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. Factors that might cause such a difference include, but are not limited to, those discussed in the following discussion and within Part I, Item 1A "Risk Factors" of this Annual Report on Form 10-K.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

*All brand names or trademarks appearing in this report are the property of their respective holders. Unless the context requires otherwise, references in this report to "Kodiak" the "Company," "we," "us," and "our" refer to Kodiak Sciences Inc.*

[THIS PAGE INTENTIONALLY LEFT BLANK]

# PART I

## ITEM 1. BUSINESS

### Overview

Our goal is to prevent and treat the major causes of blindness by developing next-generation therapeutics for chronic, high-prevalence retinal diseases.

Throughout 2019 and into 2020, we have generated clinical data with our most advanced product candidate, KSI-301, a biologic therapy built with our antibody biopolymer conjugate platform, or ABC Platform, which is designed to maintain potent and effective drug levels in ocular tissues for longer periods than the currently-marketed biologic medicines used to treat retinal diseases. To date, KSI-301 has been administered more than 500 times to over 200 patients. We believe that KSI-301, if approved, has the potential to be an important therapy to treat patients with wet age-related macular degeneration, or wet AMD, diabetic retinopathy, or DR, including diabetic macular edema, or DME, and macular edema due to retinal vein occlusion, or RVO.

In our ongoing Phase 1b clinical study, we have completed enrollment and administered multiple doses of KSI-301 to treatment-naïve patients with wet AMD, DME or RVO, and we are observing promising safety, efficacy, and clinical durability in the emerging data in each of the retinal diseases under study. We believe the data support an acceleration of efforts to bring KSI-301 to the market in these retinal diseases and that the data lend confidence to the design of our current and planned pivotal studies of KSI-301, which studies we believe, if successful, may demonstrate a meaningfully differentiated clinical profile of KSI-301 as compared to current therapies. Based on this encouraging data, we are entering into the manufacturing-related commitments necessary for pre-commercial scale-up and BLA submission.

We have completed an end of phase 2 meeting with the U.S. Food and Drug Administration, or FDA, where we agreed on the order and number of clinical studies required to support the licensure of KSI-301 in wet AMD, DME, RVO and DR (without DME). Two pivotal studies will be required in RVO and one study each in wet AMD, DME, and DR in order to support the potential U.S. approval of KSI-301 across these four indications. The pivotal study for wet AMD began recruiting patients in the third quarter of 2019, and we plan to initiate the pivotal studies in DME, RVO and DR in 2020.

The ABC Platform and KSI-301 were developed at Kodiak, and we own worldwide rights to these assets. We have applied our ABC Platform to develop additional product candidates beyond KSI-301, including KSI-501, our bispecific anti-IL-6/VEGF bioconjugate, and we are expanding our early research pipeline to include ABC Platform-based triplet inhibitors for multifactorial retinal diseases such as dry AMD and the neurodegenerative aspects of glaucoma. We intend to progress these and other product candidates to address high-prevalence ophthalmic diseases.

Our overall objective is to develop our product candidates, seek FDA and worldwide health authority marketing authorization approvals, and ultimately commercialize our product candidates.

### Recent developments

On December 1, 2019, we and our subsidiary, Kodiak Sciences GmbH, entered into a funding agreement with Baker Bros. Advisors, or BBA, pursuant to which BBA purchased the right to receive a capped 4.5% royalty on future net sales of KSI-301 in exchange for $225,000,000 in committed development funding payable to us. Unless earlier terminated or re-purchased by us, the royalty terminates upon the date that BBA has received an aggregate amount equal to 4.5 times the funding amount paid to us. On February 4, 2020, BBA paid us the first $100,000,000 of the funding amount, and the remaining $125,000,000 of the funding amount will be paid following the achievement of 50% enrollment in each of (i) the planned Phase 3 clinical trial of KSI-301 for branch RVO and (ii) the planned Phase 3 clinical trial of KSI-301 for central RVO. We have the option, exercisable at any point during the term of the funding agreement, to repurchase from BBA 100% of the royalties due to BBA under the funding agreement for a purchase price equal to the funding amount paid to us as of such time times 4.5, less amounts paid by us to BBA. The funding agreement was the result of a competitive process overseen by independent and disinterested directors with the assistance of outside counsel. For further details, see the section titled "— Funding Agreement" below.

On December 6, 2019, we completed a follow-on equity offering and issued and sold 6,900,000 shares of the Company's common stock at a price to the public of $46.00 per share. The gross proceeds from this offering were $317.4 million, resulting in aggregate net proceeds of $297.6 million after deducting underwriting discounts and commissions and other offering costs payable by us.

Proceeds from the royalty funding agreement together with our current cash, cash equivalents and marketable securities, which includes proceeds from the equity offering, are expected to advance the clinical programs for KSI-301 towards achieving our "2022 Vision" of a Biologics License Application, or BLA, of KSI-301 in 2022 for wet AMD, DME, RVO and potentially DR without DME, including the manufacturing activities necessary for BLA submission, as well as to advance our pipeline of drug candidates including KSI-501 and our triplet inhibitor drug candidates and for working capital and general corporate purposes.

In 2019 and into the first quarter of 2020, highlights of our activities included:

- Initiation of enrollment and on-going recruitment in our pivotal DAZZLE clinical trial of KSI-301 in patients with treatment naïve wet AMD. As of March 6, 2020, more than 175 patients have been enrolled in the study randomized 1:1 between KSI-301 and Eylea as active comparator;
- Completion of recruitment into our ongoing Phase 1b study of KSI-301 in 121 treatment-naïve patients with wet AMD, DME and RVO;
- Presentation of promising on-going clinical safety, efficacy and durability data at the American Society of Retina Specialists 2019 Annual Meeting, the Macula Society 2019 Annual Meeting, the American Academy of Ophthalmology 2019 Annual Meeting Retina Subspecialty Day, and the Angiogenesis, Exudation, and Degeneration 2020 Annual Meeting;
- Completion of a Type B (End of Phase 2 or EOP) meeting with the FDA where we discussed and agreed on:
    - Certain recommended clinical, non-clinical, and manufacturing activities to support the licensure of KSI-301, and
    - The order and number of clinical studies required to support a BLA in wet AMD, DME, RVO and DR;
- Announcement of an accelerated registration strategy for KSI-301 which includes: (i) running our pivotal clinical studies in the major retinal vascular disease indications in parallel (rather than in series), and (ii) engaging in BLA and pre-commercial manufacturing validation and scale-up activities;
- Expansion of our Board of Directors with the appointment of Taiyin Yang, Ph.D., Executive Vice President, Pharmaceutical Development and Manufacturing of Gilead Sciences, who brings expertise and experience in the relevant pre-commercial areas of clinical and commercial manufacturing, quality and supply chain operations;
- Entry into a royalty funding agreement with BBA in which we sold a capped, pre-payable 4.5% royalty on future net sales of KSI-301 in exchange for $225,000,000 in committed development funding payable to us.; and
- Closing of a $317.4 million follow-on offering of our common stock.

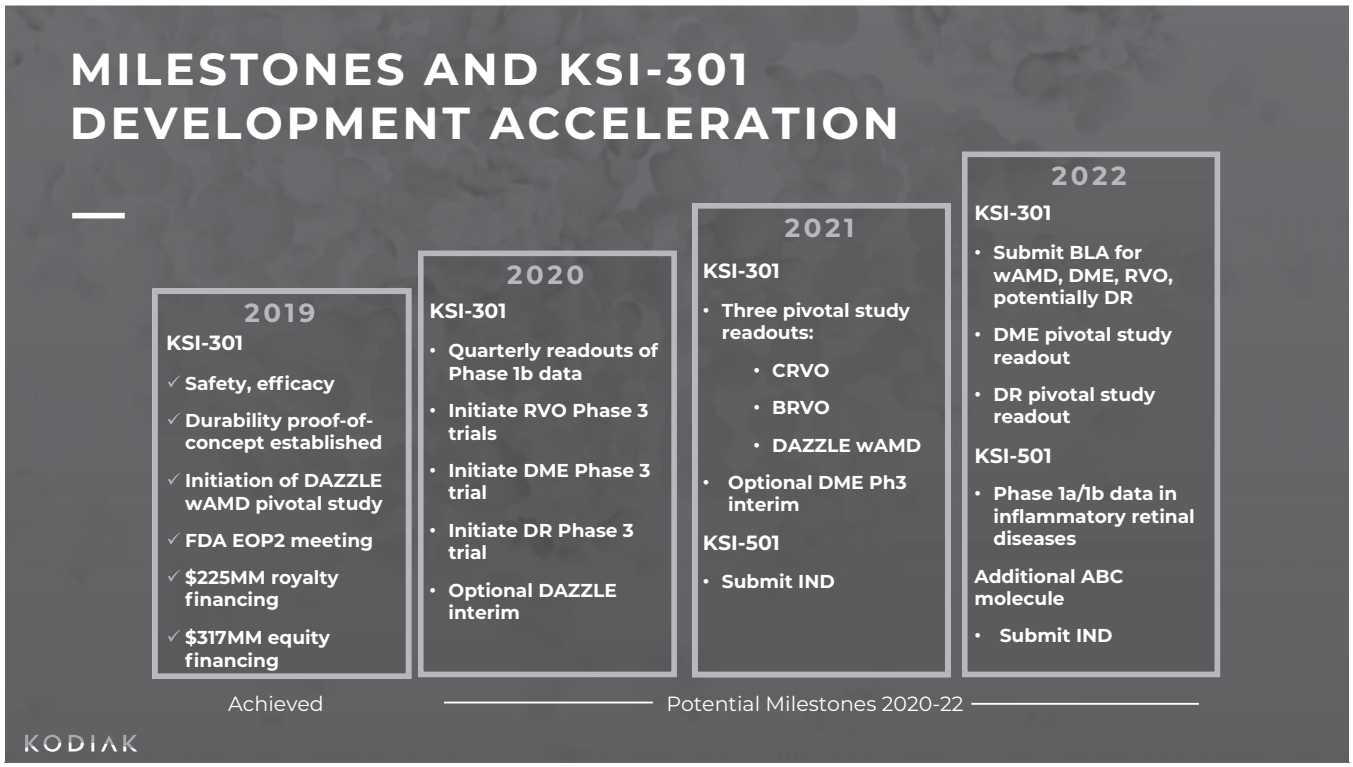
Based on the emerging clinical data, our productive EOP meeting with the FDA, and our substantive financing events, we are accelerating our BLA- and pre-commercial manufacturing activities to match the clinical timelines for KSI-301, with the goal of demonstrating a meaningfully-differentiated (*i.e.,* first line) clinical profile in each of wet AMD, DME, RVO, and DR as compared to currently-marketed medicines.

Our current cash, cash equivalents and marketable securities which includes the net proceeds from the December 2019 public offering, and together with the royalty funding agreement, provide the resources for us to advance the KSI-301 program towards achieving our "2022 Vision," and also to advance our pipeline of drug candidates including KSI-501 and our triplet inhibitor drug candidates, and for working capital and general corporate purposes.

**Kodiak's 2022 Vision and KSI-301 accelerated development strategy**

We believe that we can achieve our "2022 Vision" of a BLA submission and initial FDA approval for KSI-301 in wet AMD, DME, RVO and DR with a total of five pivotal trials— two in RVO, one in wet AMD, one in DME and one in DR without DME. Consequently, we now intend to initiate at least four US/EU-based pivotal trials in 2020 – one in DME, one in central RVO (CRVO), one in branch RVO (BRVO), and one in DR without DME. These studies, together with our ongoing pivotal study in wet AMD, will be the basis of our intended BLA and sBLA submissions. We currently expect to submit the wet AMD, DME, and RVO indications in a single initial BLA for KSI-301 and the DR indication in a supplemental BLA in the United States. We continue to invest in our science and our pipeline, including our bispecific ABC product candidate KSI-501 for retinal vascular diseases with a strong inflammatory component and our new triplet inhibitors for the high prevalence multifactorial retinal diseases dry AMD and the neurodegenerative aspects of glaucoma.

Our 2022 Vision includes the following potential catalysts and milestones in 2020, 2021 and 2022, along with the important milestones achieved in 2019 that support the accelerated development program:




Further details of our ongoing KSI-301 Phase 1b trial and our accelerating development strategy are discussed below.

**Opportunity for clinically meaningful differentiation**

Current intravitreal anti-VEGF agents require frequent eye injections in order to achieve the best clinical results. When patients do not follow product labeling or miss treatments, improvements in their vision following treatment may be transient or decline over time. Real-world data demonstrate that most patients are not currently receiving their anti-VEGF therapy at the recommended intervals. We believe that our ABC Platform medicines could address this problem by requiring less frequent dosing, and the emerging Phase 1b clinical data with KSI-301 support meaningfully differentiated clinical profiles of KSI-301 relative to standard of care in each of the major retinal diseases treated today with anti-VEGF therapy. The current and emerging standard of care treatment regimens and the dosing regimens Kodiak intends to test in its pivotal trials with KSI-301 are shown in the below table.

| **Retinal disease:** | **Wet AMD** | **Diabetic macular edema** | **Retinal vein occlusion** | **Non-proliferative diabetic retinopathy** |
|---|---|---|---|---|
| *Current and emerging standard of care* | (Current:) Aflibercept once every 2 months, after 3 monthly loading doses | Aflibercept once every 2 months, after 5 monthly loading doses | Aflibercept once monthly (for both Branch and Central RVO) | (Current:) None<br><br>(Emerging:) Aflibercept once every 2 months, after 5 monthly loading doses |
| *Kodiak's Potential Dosing Regimen for KSI-301 (as studied in ongoing or anticipated pivotal trials)* | KSI-301 once every 3, 4 or 5 months, after 3 monthly loading doses | KSI-301 once every 2 to 6 months, after 3 monthly loading doses | Branch RVO: KSI-301 once every 2 months, after 2 monthly loading doses<br>Central RVO: KSI-301 once monthly for six months, followed by less-frequent dosing | KSI-301 once every 4 or 6 months, after 3 initial doses every other month |

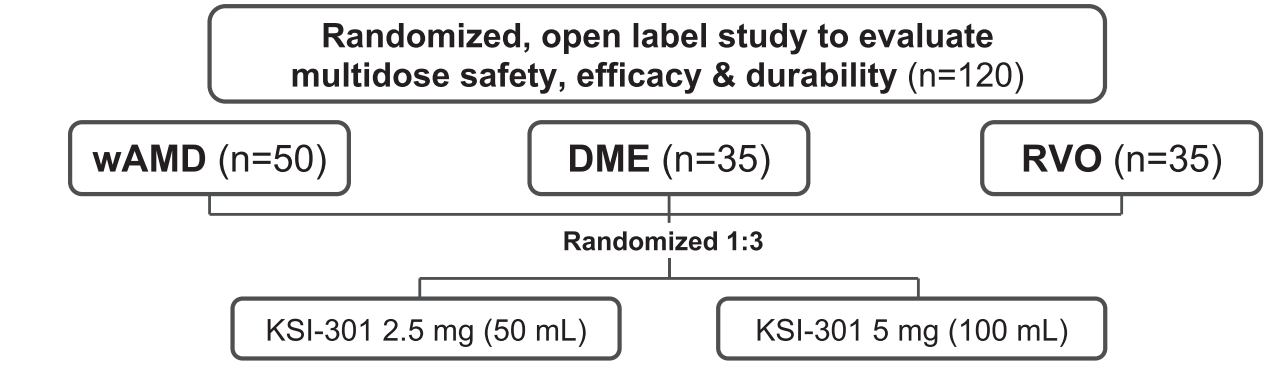
**Emerging phase 1b data support a differentiated profile of KSI-301 in each disease**

We have been studying the safety, efficacy and durability data of KSI-301 in patients with treatment-naïve wet AMD, DME and RVO treated in an ongoing, open-label, multiple-dose Phase 1b study of KSI-301. This Phase 1b study was initiated in the United States in the fourth quarter of 2018 and followed a successful first-in-human, single ascending dose Phase 1a clinical study of KSI-301 that was also undertaken in 2018. The Phase 1b study is designed to provide a scientific and clinical proof of concept for the safety, efficacy and durability of KSI-301 and the ABC Platform in patients with retinal vascular disease. All cohorts are fully enrolled in the Phase 1b study. In the study, patients are being treated with three monthly doses of either 2.5 mg or 5 mg KSI-301 and followed thereafter, with additional treatments according to disease-specific, protocol-specified retreatment criteria.

On February 8, 2020, we presented additional interim data from the ongoing Phase 1b study of KSI-301 at the Angiogenesis, Exudation, and Degeneration 2020 Annual Meeting. We are observing promising clinical durability in the emerging data in each of the retinal diseases under study. We believe the Phase 1b data we are generating in treatment naïve patients with wet AMD, DME and RVO lend confidence to the design of our current and proposed pivotal studies of KSI-301, and that these pivotal studies, if successful, may demonstrate meaningfully differentiated profiles in each of the four retinal vascular diseases as compared to current agents.

The Phase 1b study design, retreatment criteria, and patient baseline characteristics are described below. In the Phase 1b study, treatment-naïve patients with wet AMD, DME or RVO receive three monthly loading doses of KSI-301 at either the 2.5 mg or 5 mg dose levels and are followed thereafter; retreatment with KSI-301 is administered as per the protocol-specified retreatment criteria.

# KSI-301 Phase 1b
## *insight into durability among treatment naïve subjects*




| | Loading Phase | | | Durability Assessment Phase |
|---|---|---|---|---|
| Weeks | 0 | 4 | 8 | 12 to 72 (months 3 to 18) |
| Treatment Schedule | ■ | ■ | ■ | Monthly monitoring with protocol guided retreatment |

■ Fixed Treatment

wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion; Clinicaltrials.gov ID: NCT03790852

# KSI-301 Phase 1b Retreatment Criteria
## *prespecified by disease state*

- **wAMD**
  - Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12, *OR*
  - Decrease in BCVA of > 5 letters compared to Day 1, due to worsening wAMD activity, *OR*
  - Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening wAMD activity, *OR*
  - 6 months have elapsed since the last retreatment
- **DME and RVO**
  - Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12 or the prior visit, *OR*
  - Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening DME/RVO disease activity

**For all subjects, investigators can retreat at their discretion if significant disease activity is present that does not meet the above criteria**

wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion; CST = central subfield retinal thickness; BCVA = best corrected visual acuity.
Clinicaltrials.gov ID: NCT03790852

# KSI-301 Phase 1b Baseline Characteristics

| Variable | wet AMD cohort (n=51) | DME cohort (n=35) | RVO cohort (n=35) |
|---|---|---|---|
| Age, mean (SD), years | 77.9 (10.5) | 59.7 (11.7) | 63.6 (12.6) |
| Gender, n (%), female | 32 (62.7) | 14 (40.0) | 13 (37.1) |
| Race, n (%), White | 48 (94.1) | 28 (80.0) | 31 (88.6) |
| BCVA, mean (SD), ETDRS letters | 63.3 (13.3) | 66.8 (10.2) | 54.9 (15.4) |
| Snellen equivalent | ~20/50 | ~20/50 | ~20/80 |
| BCVA, Snellen 20/40 or better, n (%) | 20 (39.2) | 16 (45.7) | 6 (17.1) |
| OCT CST, mean (SD), microns | 430 (162) | 453 (110) | 675 (237) |

Includes all patients randomized as of 21 January 2020, SD = standard deviation; BCVA = best corrected visual acuity; OCT = optical coherence tomography; CST = central subfield thickness

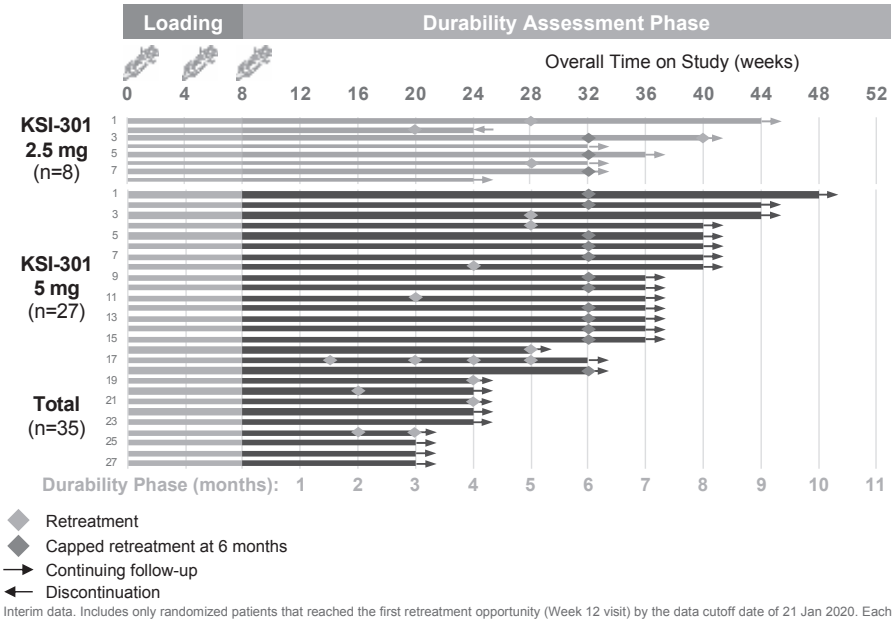
The figures below present additional new data on durability and efficacy outcomes from the ongoing Phase 1b study that were presented at the Angiogenesis 2020 Annual Meeting. Across all three diseases under the study, improvements in vision and retinal anatomy were observed through 24 weeks of patient follow-up, with stability in OCT and BCVA over time in the monthly follow-up intervals following the three mandatory loading doses. Vision is measured as change in best corrected visual acuity, or BCVA, on a standardized eye chart, and retinal anatomy is measured as change in retinal central subfield thickness, or CST, using optical coherence tomography, or OCT, imaging.

***Wet AMD***

In wet AMD, with current agents, only approximately 40% of patients can be maintained on an every 12-week (3 month) dosing interval over a two-year period. The remaining 60% of patients require either every other month therapy, monthly therapy, or even on occasion treatment as often as every two weeks. Our objective with KSI-301 in wet AMD is to develop a therapy where the vast majority of patients are on every 12-week dosing or better, with at least 50% of patients maintained on an every four or five month dosing regimen.

In our Phase 1b study, we have observed thus far that 91.4% of wet AMD treated eyes have been extended to three months or longer after the last loading dose of KSI-301 without receiving retreatment, and 84% have been extended to four months or longer after the last loading dose. Many patients have not received their first retreatment until five or even six months after the last loading dose. In the Phase 1b study, the maximum retreatment interval for wet AMD patients is capped at six months. The following results have been observed as of January 21, 2020.

## KSI-301 in wAMD: Durability Assessment
### *Emerging data support 3 to 6 month durability*



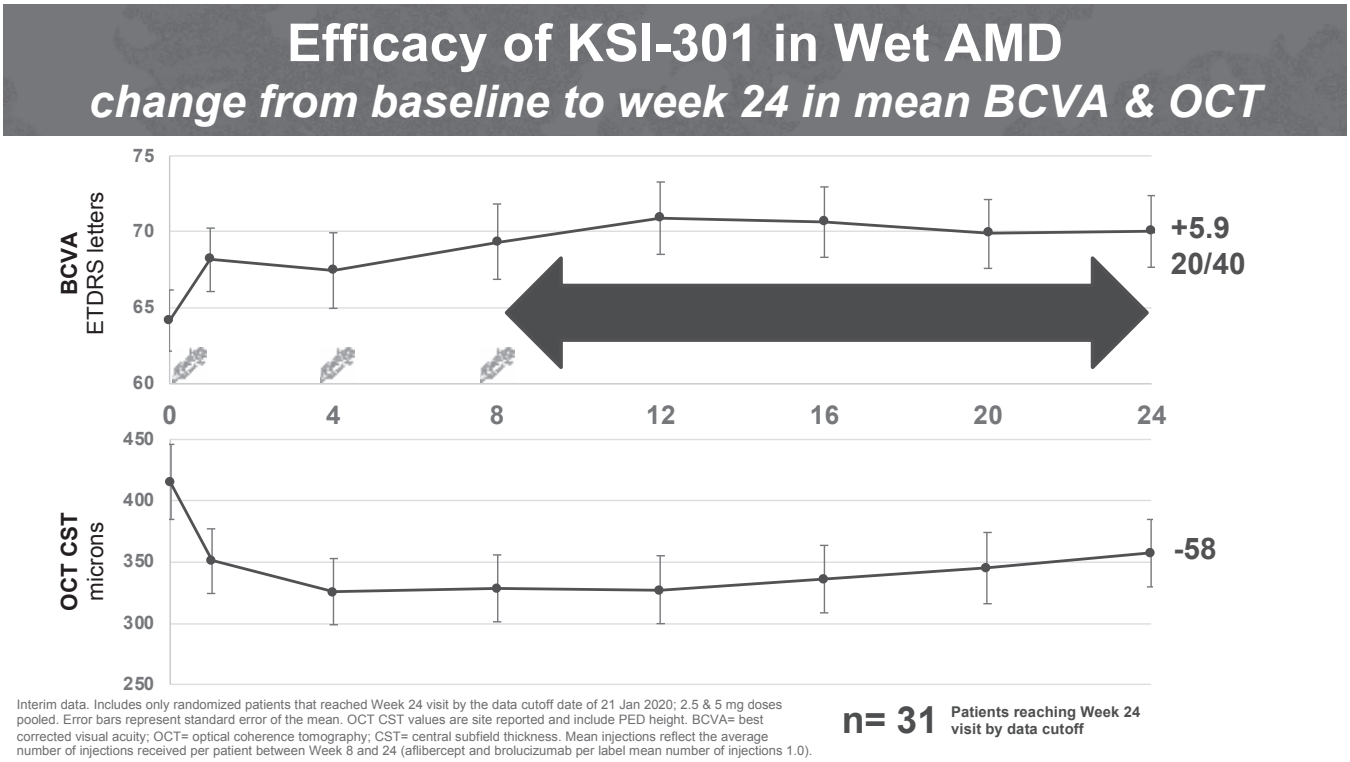

| First Retreatment | Percentage |
|---|---|
| At or before 3 months | 14% (5/35) |
| 4 months or longer | 84% (27/32) |
| 5 months or longer | 72% (21/29) |
| 6 months | 55% (16/29) |

**55% (16/29) have achieved a 6-month interval before a mandated first retreatment**

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 21 Jan 2020. Each bar represents an individual patient.

Intriguingly, we are observing that a high proportion of Phase 1b patients, approximately 55% as of January 21, 2020, have reached six months without retreatment after the initial loading doses, and 72% have reached a five months or longer interval. These emerging data underscore the potential of KSI-301 and the ABC Platform to achieve truly long-interval dosing with an intravitreally-administered therapy.

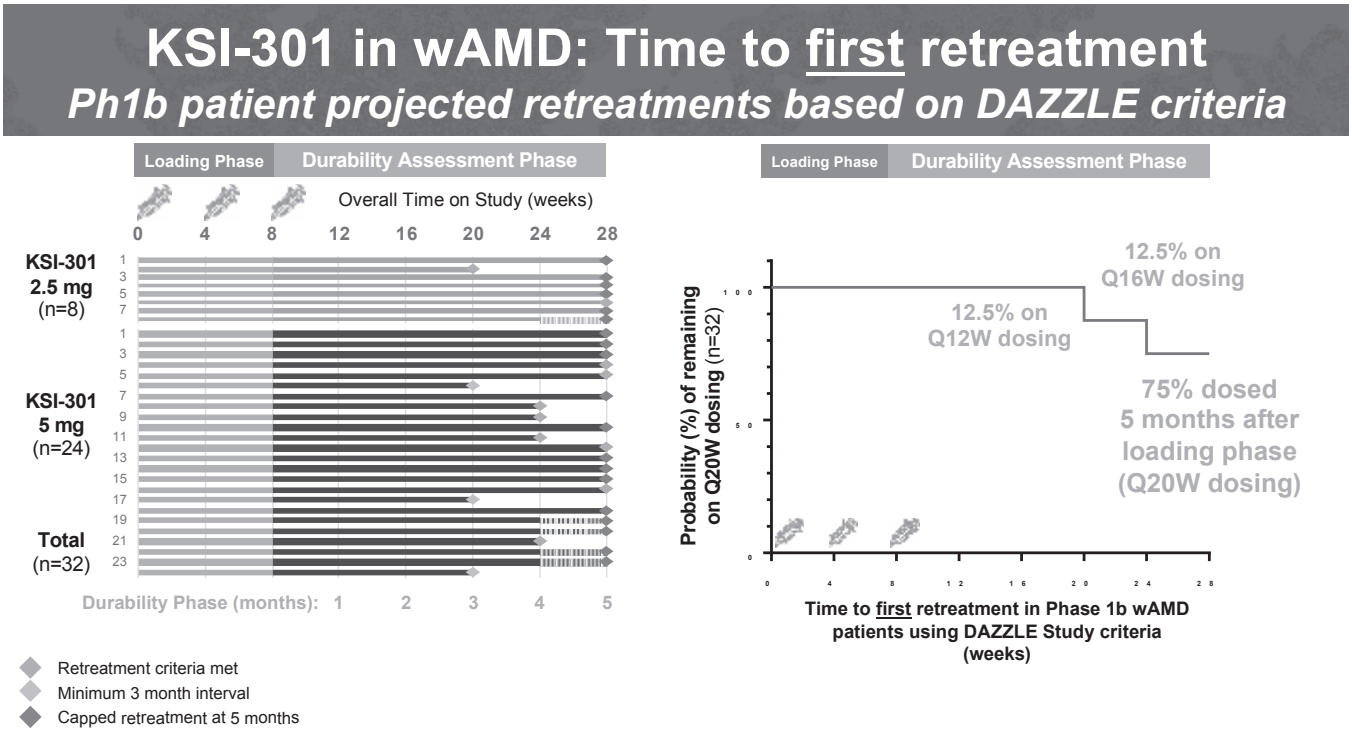
Visual acuity and retinal anatomy (OCT CST) improvements continue to be durable in the follow-up data as well. In the following graphs, the 31 wet AMD patients (pooled 2.5 mg and 5 mg dose levels) who reached the week 24 visit prior to the data cutoff date of January 21, 2020 are included. In the period between week 12 and week 24 (that is, months 1 to 3 after the loading phase), the treatment effect is maintained with only an average of 0.16 injections, with only a small (29.8 micron) change in average central subfield thickness on OCT was observed over the entire period from week 12 to week 24; from week 12 to 16 the change was 8.6 microns, from weeks 16 to 20 it was 9.1 microns, and between weeks 20 and 24 it was 12.1 microns. These data are consistent with an extended durability effect of KSI-301 and compare favorably to the OCT fluctuations observed with existing anti-VEGF agents despite those agents being given on shorter dosing intervals. Similarly, BCVA was also generally stable over these intervals, consistent with a prolonged duration of effect of KSI-301. BCVA tends to fluctuate by a small amount on a month-to-month basis in clinical trials.




In the Phase 1b study, the average retinal thickness (OCT CST) data as reported by our clinical investigators includes the height of pigment epithelial detachments (PEDs). PEDs are an anatomic feature in some patients with wet AMD; treatment success in subjects with PEDs does not necessarily imply complete flattening of the PED, but rather eliminating the intraretinal and subretinal fluid, particularly when the PED is very high prior to anti-VEGF treatment. Additionally, comparison across studies of OCT mean CST values is difficult because it is often not clear or not disclosed in presentations and publications whether the data include or exclude the height of the PED, among other reasons.

These data collectively demonstrate that KSI-301 has a potent anti-VEGF effect both on BCVA improvement and retinal drying in wet AMD patients. The clinical benefit appears in line with existing anti-VEGF agents (especially when considering differences in baseline characteristics), and we are observing longer durability of clinical effect with KSI-301 than is expected from existing agents.

Although the Phase 1b study is open-label, we believe these results are representative both because patients in the study are randomized to two dose levels and because the key assessments (visual acuity and OCT) are measured objectively and in a standardized, reproducible manner. The very high proportion of Phase 1b patients who have been extended to 4, 5, or even 6 months without receiving retreatment also supports the design of our ongoing pivotal study, DAZZLE, in which KSI-301 is administered to treatment-naïve wet AMD patients on an every 3, 4 or 5 month dosing regimen, as compared to aflibercept on an every 2 month regimen, each after three monthly loading doses. In DAZZLE, the criteria for assigning a patient to 3, 4, or 5-month dosing on KSI-301 are slightly stricter than the retreatment criteria in the Phase 1b. Applying the DAZZLE retreatment criteria to the wet AMD patients in the Phase 1b study who have reached week 20 or later, we observe that 75% would have a time to first retreatment in DAZZLE of five months, 12.5% at four months, and 12.5% at three months, further supporting the design of the DAZZLE study.

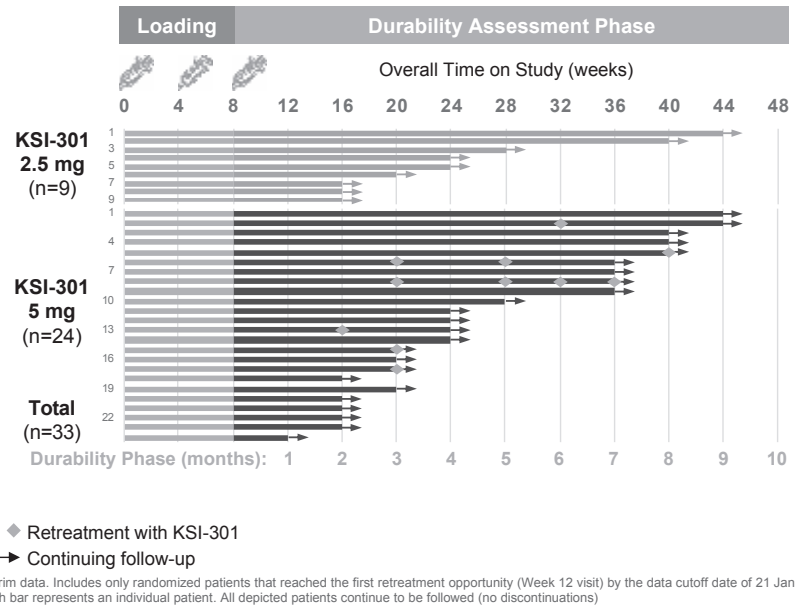



Interim data. Includes only randomized patients that would have met retreatment criteria before or at Week 28 by the data cutoff date of 21 Jan 2020. Each bar represents an individual patient.

***Diabetic macular edema***

In DME, currently-approved anti-VEGF medicines are labeled for either monthly or every other month dosing after 5 monthly loading doses, and in a National Eye Institute-funded DRCR.net collaborative group study of DME patients, almost all patients required 6 initial monthly loading doses and a median of 9-10 doses were administered in the first year of therapy for all of the tested agents (aflibercept, bevacizumab, and ranibizumab). Our objective with KSI-301 in DME is thus twofold: first, to reduce the number of initiating or loading doses, and second to extend the treatment interval in the maintenance phase to 3 months and beyond. In our Phase 1b study, we have observed that 76% of DME treated eyes have been extended to four months or longer after the 3 loading doses of KSI-301 without receiving retreatment, with most patients not yet receiving any retreatment, including patients followed for as long as 5 to 7 months after the initiating doses. 96.7% of patients have been extended to 3 months or longer after the last loading dose. The following results have been observed as of January 21, 2020:

## KSI-301 in DME: *3 loading doses can provide sustained disease control of 3 to 6+ months*

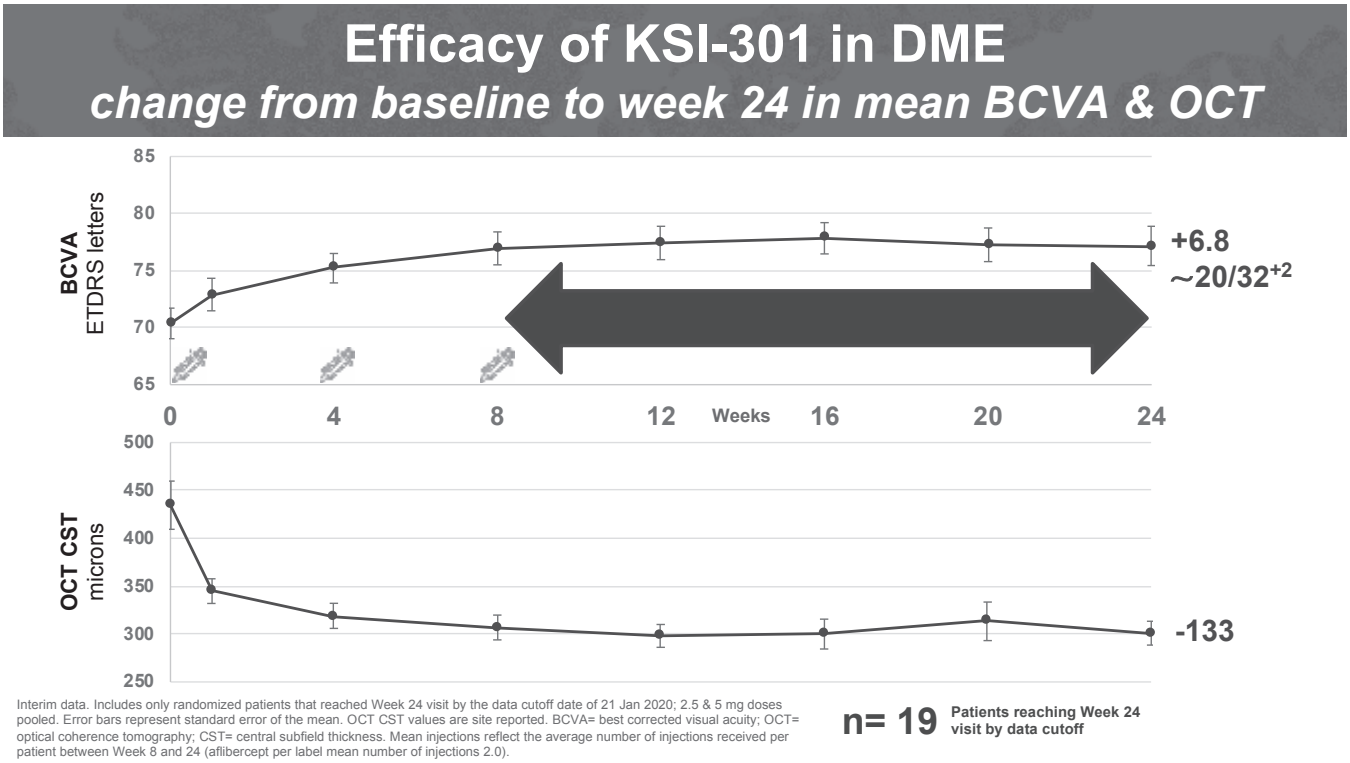



| First Retreatment | Percentage |
|---|---|
| At or before 3 months | 20% (5/24) |
| 4 months or longer | 76% (16/21) |
| 5 months or longer | 68% (11/16) |
| 6 months or longer | 64% (9/14) |

**64% (9/14) have reached 6 months or longer without retreatment**

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 21 Jan 2020.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

Visual acuity and optical coherence tomography improvements continue to be durable in the follow-up data as well. In the following Figure, the 19 DME patients (pooled 2.5 mg and 5 mg dose levels) who reached the week 24 visit prior to the data cutoff date of January 21, 2020 are included. In the period between week 12 and week 24 (that is, months 1 to 4 after the loading phase), the treatment effect is maintained, with only a 2.8 micron change in average central subfield thickness on OCT observed. This is consistent with the extended durability effect of KSI-301 and compares very favorably to existing anti-VEGF agents, particularly with a reduced number of loading doses. The change in OCT between weeks 16 and 20 appeared largely driven by the DME patients who required and received retreatment at week 20 under the protocol. Similarly, BCVA was also stable over these intervals, consistent with a prolonged duration of effect of KSI-301.



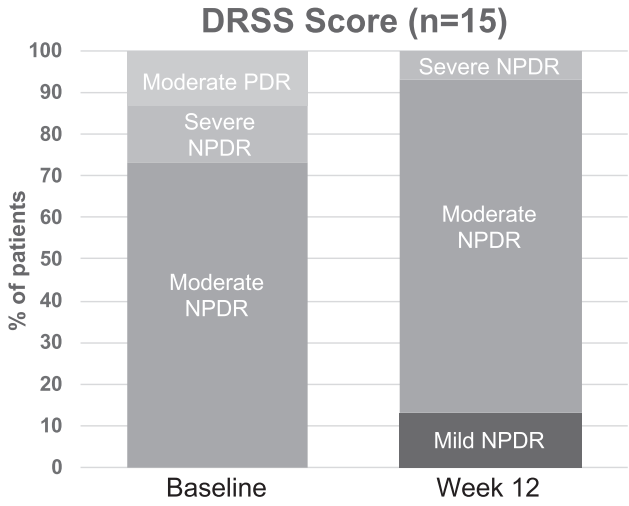

These data demonstrate that KSI-301 has a potent anti-VEGF effect both on BCVA improvement and retinal drying in DME patients. The clinical benefit appears in line with existing anti-VEGF agents (especially when considering differences in baseline characteristics) and we are observing longer durability of clinical effect with KSI-301 than with existing agents. Moreover, these results were achieved with fewer loading doses. These data support a pivotal study design where KSI-301 would be given on an every two- to six-month interval after three loading doses, compared to standard of care aflibercept on its approved every other month regimen after five loading doses.

***Diabetic retinopathy***

In DR, currently approved medicines are labeled for either monthly or every other month dosing after five monthly loading doses. Use of anti-VEGF therapy in non-proliferative DR patients can significantly reduce the risk of developing sight-threatening complications, such as DME and proliferative DR. Because patients with non-proliferative DR without DME have not yet lost vision, an important benefit-risk consideration is the intensity of treatment required. We believe that the treatment burden required with currently approved anti-VEGFs for DR is limiting the adoption of anti-VEGF therapy despite the demonstrated treatment benefits. Our objective with KSI-301 in NPDR is to develop a therapy that could be given on an infrequent basis, such as an every four- or even every six-month interval, and without the monthly loading doses required in the labeling of the currently approved medicines.

In our Phase 1b study, we have observed early signs of improvement in diabetic retinopathy in the eyes of patients with concomitant DME: as of October 10, 2019, the latest timepoint for which photographic grading data are currently available, 40% of patients improved in DR severity level within the first 12 weeks of treatment and no patient worsened in DR severity level.

## KSI-301 in DR: *signs of disease modification are seen within 12 weeks*

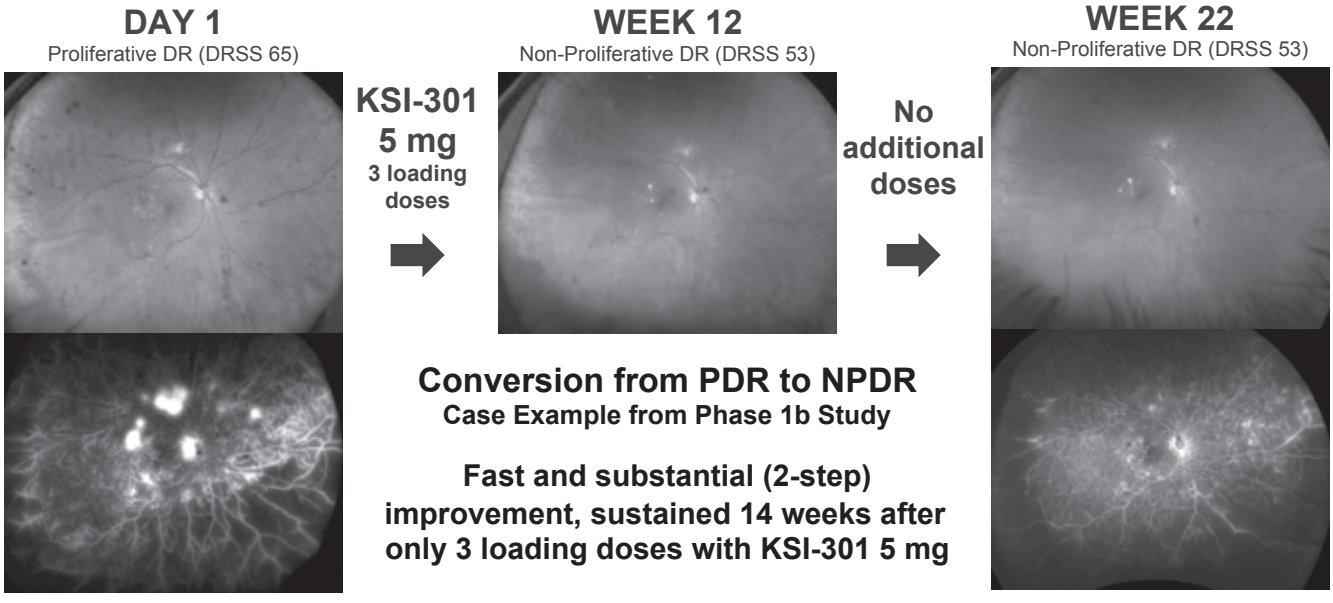



**All patients improved or maintained their DRSS Score**

| Change from Baseline in DRSS at Week 12 (n=15) | N (%) |
|---|---|
| Maintained | 9 (60) |
| 1-step improvement | 2 (13) |
| ≥2-step improvement | 4 (27) |

Includes only randomized patients that reached Week 12 and have gradable color fundus photos by the data cutoff date of 10 Oct 2019 DR= Diabetic Retinopathy; PDR= Proliferative DR; NPDR= Non-Proliferative DR; DRSS = DR Severity Scale. Vision-threatening PDR defined as PDR, need for panretinal photocoagulation or vitrectomy

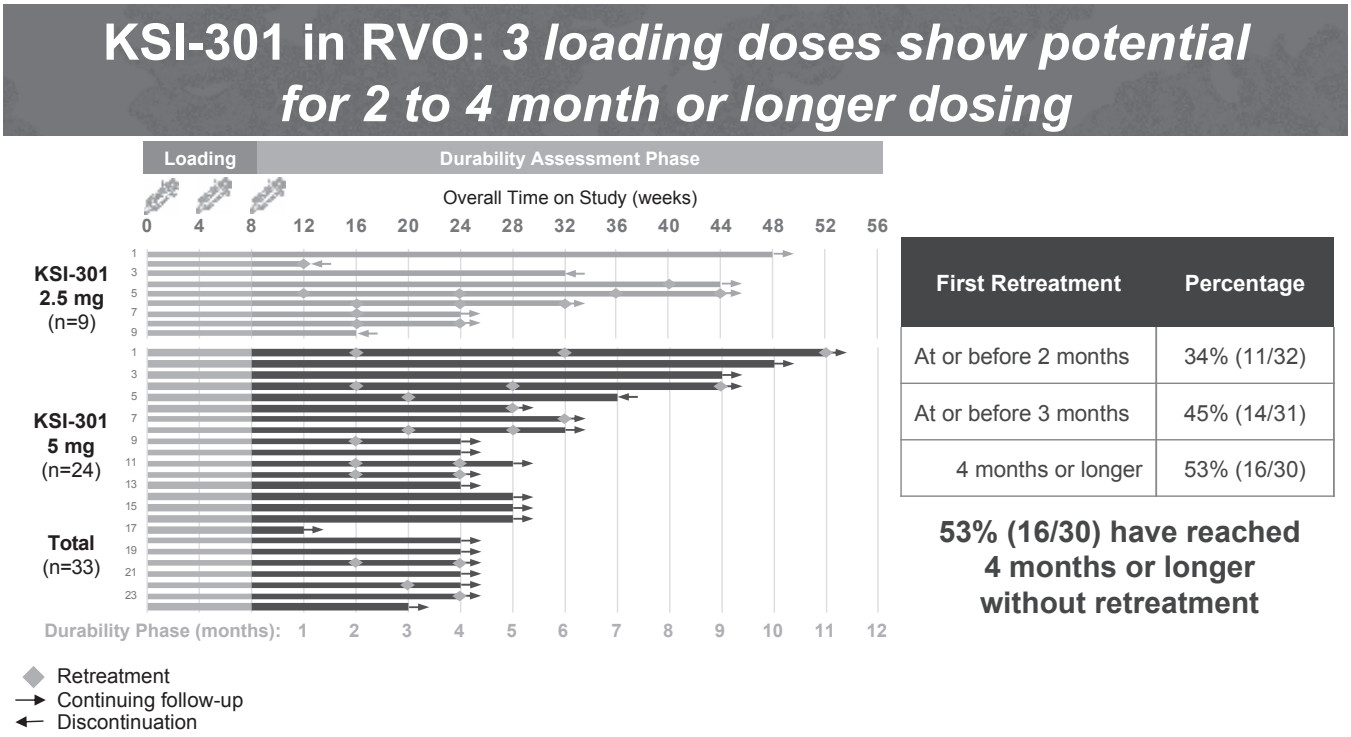
## The sustained disease control of only 3 loading doses of KSI-301 is also seen in proliferative diabetic retinopathy




DR= Diabetic Retinopathy; PDR= Proliferative DR; NPDR= Non-Proliferative DR; DRSS = DR Severity Scale; DRSS 53 = Severe NPDR; DRSS 65 = Moderate PDR

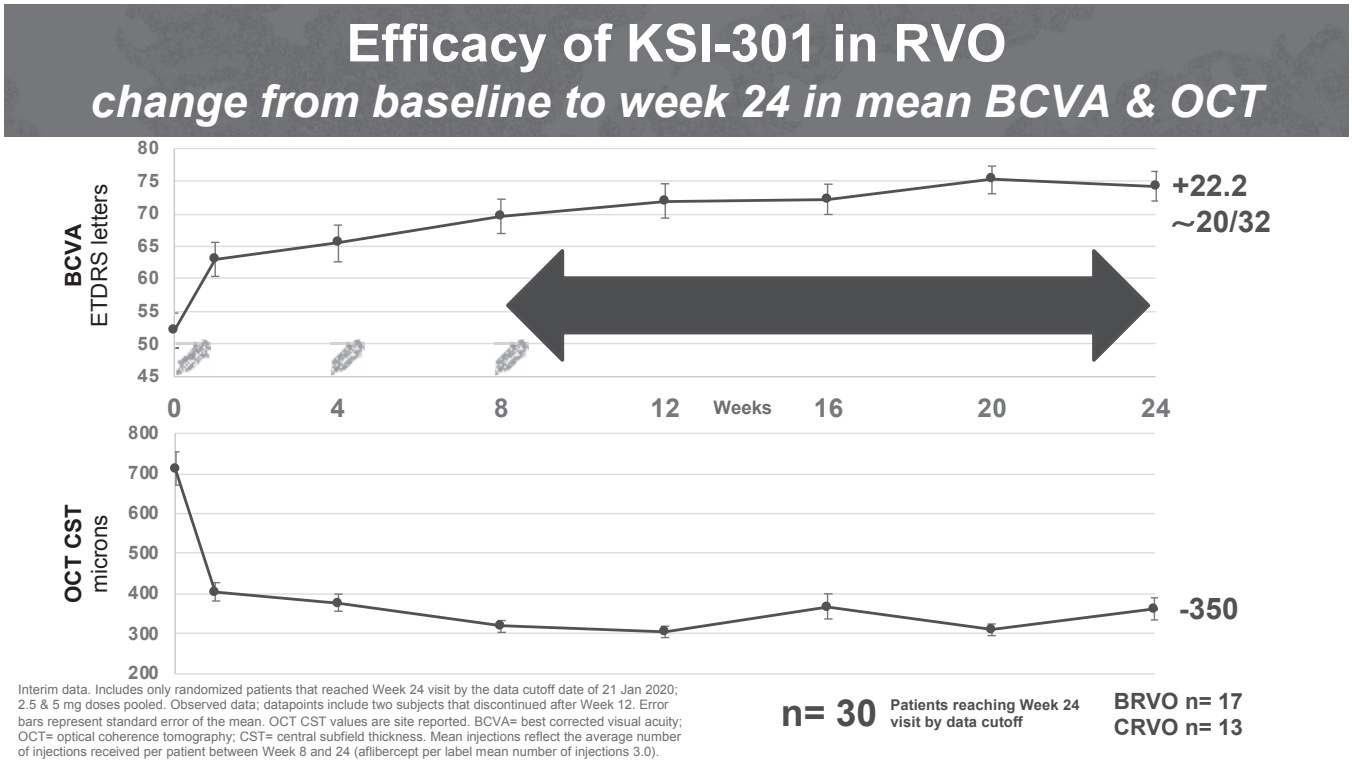
***Retinal vein occlusion***

In RVO, a disease which has higher levels of intraocular VEGF on average than wet AMD and DME, the currently-approved medicines are labeled for monthly dosing. Our objective with KSI-301 in RVO is thus twofold: first, to reduce the number of initiating or loading doses, and second, to extend the treatment interval to 2 months and beyond for BRVO patients, recognizing BRVO is approximately five times more common than CRVO. In our Phase 1b study, we have observed thus far that all RVO eyes treated with 5 mg KSI-301 have been extended to 2 months or longer after the last loading dose of KSI-301, with 45% of patients extended to 3 months or longer. The following results have been observed as of January 21, 2020:




Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 21 Jan 2020. Each bar represents an individual patient.

Visual acuity and optical coherence tomography improvements continue to be durable in the follow-up data as well. In the following Figure, the 30 RVO patients (pooled 2.5 mg and 5 mg dose levels) who reached the week 24 visit prior to the data cutoff date of January 21, 2020 are included. 17 of the patients had a branch RVO and 13 had a central RVO. In the period between week 12 and week 24 (that is, months 1 to 3 after the loading phase), the treatment effect is maintained, with only small fluctuations in average central subfield thickness on OCT observed, consistent with the observation that some patients required and received retreatment at week 16 and week 24. This is consistent with the extended durability effect of KSI-301 and compares favorably existing anti-VEGF agents. Similarly, BCVA was also markedly improved and stable over these intervals, consistent with a potent and prolonged duration of effect of KSI-301. An average improvement from baseline of +22.2 eye chart letters, which is over four eye chart lines, was observed at week 24.




These data collectively demonstrate that KSI-301 has a potent anti-VEGF effect both on BCVA improvement and retinal drying in RVO patients. The clinical benefit appears in line with existing anti-VEGF agents (especially when considering differences in baseline characteristics), with longer durability than with existing agents, and the effects were achieved with fewer loading doses. These data support a pivotal study design where KSI-301 would be given on an every two month or longer interval, compared to standard of care aflibercept on its monthly regimen. Having said that, we are considering different pivotal study designs for each of CRVO and BRVO which would reflect the different nature of the two diseases. Specifically, for CRVO we are considering a pivotal study design in which KSI-301 is dosed on a monthly basis during the first six months followed by extended-interval dosing in the year thereafter, and for BRVO we are considering a pivotal study design in which KSI-301 is dosed on an every-other month interval after two loading doses for the first six months, followed by extended-interval dosing in the year thereafter.

**Safety of KSI-301 injections**

As previously disclosed, a data cutoff of January 21, 2020 was selected to prepare data for presentation at the Angiogenesis, Exudation, and Degeneration 2020 Annual Meeting. Through this data cutoff, more than 500+ doses of KSI-301 were administered with no intraocular inflammation or study eye ocular serious adverse events reported. This number represents more than 415+ KSI-301 administrations in the Phase 1a/1b program and an estimated more than 85+ KSI-301 administrations in the DAZZLE wet AMD pivotal study (per review of the masked safety data as described below). This record of no drug-related ocular adverse events and no drug-related systemic adverse events continues to demonstrate a favorable safety profile for KSI-301 as a therapeutic candidate.

A more detailed look at Phase 1a and Phase 1b safety across all patients randomized as of January 21, 2020 and all doses administered across all cohorts includes:

- No drug-related adverse events, or AEs, and no drug-related serious adverse events, or SAEs;
- Most AEs were assessed as mild and are consistent with the profile of intravitreal anti-VEGFs;
- 17 non-ocular SAEs that were not drug-related were reported in 11 subjects:
- One 92 y/o RVO subject with hospitalization related to a pre-existing medical condition that resulted in death;
- Seven (43, 56, 62, 66, 67, 70 and 72 y/o, respectively) DME subjects with hospitalization related to a pre-existing medical condition;
- One 66 y/o RVO subject with hospitalization related to dizziness;
- One 43 y/o RVO subject with a broken leg related to a motorcycle accident; and
- One 85 y/o RVO subject with hospitalization related to a pre-existing medical condition.

As of March 6, 2020, in the Phase 1a/1b study, 130 patients have been enrolled and no drug-related serious adverse events have been reported. Two ocular adverse events of vitreous cell have been reported from a single site in two RVO patients. In the first patient, trace vitreous cell was noted at a routine study visit, and in a second patient, 1+ vitreous cell (on a scale of 0 to 4+ with 0 being none) was noted at a routine study visit. In both patients, the vitreous cells resolved and/or improved towards resolution with topical steroid eye drops. The patients had received 5 and 6 injections of KSI-301 and had been followed for 229 and 441 days, and the time from the last injection to the time the vitreous cells were noted was 49 and 23 days. Neither patient lost any vision, and at the time of their most recent visits, the two patients have gained +35 and +42 letters from baseline to a Snellen visual acuity of 20/25 and 20/32, respectively. Ophthalmic evaluations demonstrated no vasculitis and no retinitis in either patient.

As of March 6, 2020, in the DAZZLE study, over 175 patients have been enrolled and randomized 1:1 to KSI-301 5mg or aflibercept 2mg. All patients receive three loading doses with subsequent dosing for KSI-301 treated patients based on disease activity assessments and subsequent dosing for Eylea on an every-other-month fixed interval. No adverse event reports of intraocular inflammation have been reported in the masked database.

Additionally, we have continued to evaluate anti-drug antibody (ADA) status in the Phase 1a/1b program. A validated ECL bridging ADA assay is being utilized to analyze samples. Analysis is on-going. As of January 21, 2020, a total of 702 samples from 117 subjects were tested for the presence of anti-drug antibodies in the Phase 1a and 1b study. The number of samples and the last timepoint tested for each subject varies depending on the enrollment duration. No pre-treatment samples tested positive for ADA in any subject. To date, treatment emergent data show very low numbers of samples/subjects testing positive for ADAs, and these rare positive ADAs are at very low titer. Although we will continue to update these data as the study progresses, these data provide an additional and encouraging window into the safety of KSI-301.

**Phase 1b study ongoing status**

We extended the planned follow-up period of patients in the Phase 1b study from nine months to 18 months so that additional long-term durability and safety outcomes can be collected, and we intend to further increase the follow-up duration beyond 18 months. We intend to continue to present ongoing safety, efficacy and durability data from the Phase 1b study at medical and investor meetings in 2020.

**Accelerated clinical development strategy for KSI-301**

Based on the promising safety, efficacy and durability data observed to date in the Phase 1b study, we are accelerating the clinical development of KSI-301.

In the third quarter of 2019, we initiated enrollment in our pivotal DAZZLE clinical trial of KSI-301 in patients with treatment-naïve wet AMD. The DAZZLE study is recruiting well, and over 175 patients have been recruited as of March 6, 2020. In this study, all patients will receive KSI-301 on an every three-, four- or five- month dosing interval or standard-care aflibercept on an every two-month dosing interval, each after three initial monthly doses. We believe that an every three- to five- month dosing regimen with KSI-301 would represent a clinically meaningful improvement compared to the currently available standard of care for patients needing intraocular anti-VEGF therapy. A primary data readout is anticipated in 2021 depending on enrollment rates. We have increased the anticipated sample size from 368 patients to ~550 patients to ensure adequate statistical power consistent with the registrational nature of the study. This trial is currently recruiting patients in the United States and is additionally planned to enroll patients in several countries of the European Union as well as in Israel.

In October 2019, we announced our intention to initiate, in mid-2020, two Phase 3 studies of KSI-301 in RVO– one study in central RVO and one study in branch RVO. These two studies could support an initial BLA for KSI-301 and could result in our achieving rapid market entry, because the primary endpoint for RVO studies is evaluated at six months.

Subsequently, in the fourth quarter of 2019, we held a Type B (EOP) meeting with the FDA where we discussed the recommended clinical, non-clinical, and manufacturing activities to support the future licensure of KSI-301 in wet AMD, DME, RVO and DR. In particular, we discussed and agreed with FDA on the sequence and number of clinical studies required to support an initial BLA and sBLA to achieve approval in these four retinal diseases. FDA has indicated that approval in the four diseases of AMD, DME, RVO and DR without DME could be supported with a total of five pivotal trials – two in RVO, one in wet AMD, one in DME, and one in DR without DME. We also discussed with and received feedback from FDA on the designs of the proposed studies.

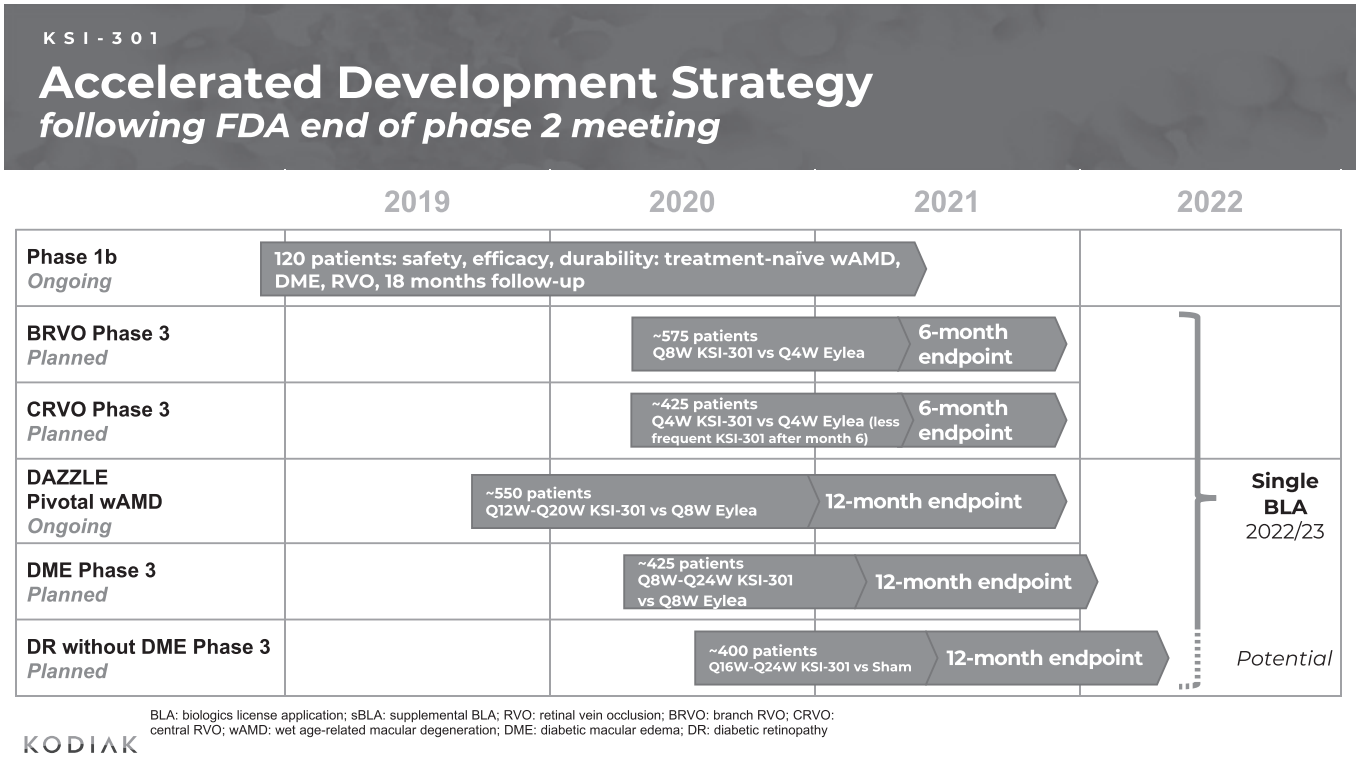
As a result of the supportive discussions with FDA, we now intend to initiate at least four US/EU-based pivotal trials in mid-2020: one in central RVO (CRVO), one in branch RVO (BRVO), one in DME, and one in DR without DME. These studies, together with our ongoing DAZZLE pivotal study in wet AMD, will be the basis of our intended BLA submissions. Each study will compare a differentiated KSI-301 dosing regimen head-to-head against standard of care: intravitreal anti-VEGF treatment in the case of wet AMD, DME, and RVO, and observation/sham injections for DR.

We believe the KSI-301 pivotal program can achieve primary data readouts in late 2021 or early 2022. Based on evolving expectations of individual study enrollment rates, we currently expect to submit the wet AMD, DME, and RVO indications in a single initial BLA for KSI-301 in 2022. Likewise, we believe the DR study could achieve primary data readout in 2022 and support a sBLA submission for DR in 2022 or 2023.

We are currently preparing to initiate the DME and RVO Phase 3 studies globally, following the discussions that we held with the FDA, and we intend to begin recruiting patients in those studies in mid-2020. For patients with branch RVO (the more common subtype), we believe an every-other month or longer dose regimen for KSI-301, following two loading doses, can be meaningfully differentiated from that of other marketed and in-development anti-VEGF biologics that require monthly dosing in this disease. For patients with DME, we are planning a DAZZLE-like design, with all patients on an every 2- to 6-month regimen after 3 monthly loading doses, compared to standard of care aflibercept dosed every 2 months (after 5 monthly loading doses). We believe this profile, in which we expect almost all patients will be on an every 3- month or longer dose regimen, and the majority expected to be on a 4-month or longer interval, can be meaningfully differentiated from that of other marketed and in-development anti-VEGF biologics.

We also expect to begin recruiting patients in the DR study in the second half of 2020. For DR patients, we believe that an every 4-, or 6- month regimen could offer an important and meaningfully differentiated benefit for patients. Although anti-VEGF therapy is now approved in the United States for DR, it is not standard of care for non-proliferative DR in most cases. Thus, a study of KSI-301 could compare against either placebo (sham injections) or anti-VEGF treatment.

Our anticipated US/EU clinical studies for KSI-301 are therefore as follows:




We additionally plan to initiate one or more clinical studies in China, and we are also evaluating the potential to include patients from China in selected global Phase 3 studies. We held our China pre-investigational new drug, or IND, meeting for KSI-301 with the China Center for Drug Evaluation, or CDE, in the second quarter of 2019. Based on this supportive meeting, as well as the progress with our clinical development of KSI-301 and the recent FDA feedback, we intend to submit one or more INDs for KSI-301 in China in the first half of 2020. Our thinking on the timing of our China IND submission(s) is impacted by the novel strain of coronavirus, COVID-19, as well as our evolving views about which indications from the global pivotal studies program should include patients from China and which indications to develop via China-specific pivotal studies.

**Our Strategy**

Our goal is to become a leading biopharmaceutical company focused on developing and commercializing therapeutics for the treatment of ophthalmic diseases. The key elements of our strategy are:

- *Complete clinical development of KSI-301 for wet AMD, DME, RVO, and DR.* We are devoting a significant portion of our resources and business efforts to the manufacture and clinical development of KSI-301 for retinal vascular diseases.
- *Establish market acceptance of KSI-301 in wet AMD, diabetic eye disease, and RVO.* We believe that if KSI-301 is approved and is shown to have comparable efficacy and improved durability to other anti-VEGF therapies, it will compete favorably with other marketed products for retinal vascular disease. In addition, we believe KSI-301 may potentially expand the market reach to patients not currently on approved standard of care therapies or not currently on therapy at all.
- *Seek to expand the use of KSI-301 in DR beyond DME.* We intend to explore the use of KSI-301 in the treatment of all subtypes of DR patients. Currently-marketed anti-VEGFs are used primarily to treat late and advanced manifestations of DR, particularly DME. We believe that the potential for improved durability of KSI-301 could not only improve the standard of care but also expand the patient population that receives anti-VEGF therapy to include patients with less severe forms of DR for whom frequent injections may be a barrier to adoption.

- *Commercialize KSI-301 with our own specialty sales force.* KSI-301 is wholly owned by us, subject only to the capped, pre-payable royalty payment obligations described in the section titled "—Funding Agreement" below. If KSI-301 receives marketing approval, we plan to commercialize it in the United States with our own focused, specialty sales force. We believe that retinal specialists in the United States, who perform most of the medical procedures involving retinal diseases, are sufficiently concentrated that we will be able to effectively promote KSI-301 with a sales and marketing group of fewer than 200 people. We expect to explore collaboration, distribution or other marketing arrangements with one or more third parties to commercialize KSI-301 in markets outside the United States.
- *Advance the development of our other ABC product candidates.* We intend to continue deploying capital to selectively develop our own portfolio of product candidates based on our ABC Platform (including bispecific inhibitors such as KSI-501). We may partner with biotechnology and pharmaceutical companies to further develop our ABC Platform and product candidates.
- *Discover and develop future product candidates for areas of unmet need.* We intend to continue our discovery efforts and deepen our pipeline of medicines for high-prevalence ophthalmic diseases. We may opportunistically in-license or acquire the rights to complementary products, other product candidates and technologies to aid in the treatment of a range of ophthalmic diseases, principally diseases of the retina.

***Current Standard of Care for Wet AMD, DME/DR, and RVO***

Overexpression of vascular endothelial growth factor, or VEGF, in ocular tissues is central to the pathogenesis and clinical manifestations of wet AMD, DME/DR, and RVO. VEGF is a protein produced by cells that stimulates the formation of new blood vessels, a process called neovascularization, and induces vascular permeability. In wet AMD, DME, and RVO fluid that exits from blood vessels causes swelling, or edema, of the retina and loss of vision. This loss of vision can be reversed if treated early with an anti-VEGF agent to suppress VEGF signaling. Delayed treatment or undertreatment can result in permanent retinal damage and blindness. To reach effective ocular tissue concentrations, these agents must be injected into the vitreous humor, the jelly-like substance that fills the area between the lens and retina. These injections must occur at regular intervals in order to maintain anti-VEGF effects.

Lucentis (ranibizumab), marketed by Genentech, Inc., a subsidiary of the Roche Group, in the United States and by Novartis AG outside the United States, and Eylea (aflibercept), marketed by Regeneron Pharmaceuticals, Inc. in the United States and by Bayer HealthCare LLC outside the United States, are anti-VEGF therapies that have become the standard of care for treating wet AMD and severe forms of DR based on pivotal clinical studies in which Lucentis was injected every four weeks and Eylea was injected every eight weeks (after three initial monthly doses in the case of wet AMD and after five initial monthly doses in the case of DR with DME). BeoVu (brolucizumab), marketed worldwide by Novartis, was approved in late 2019 in the United States and early 2020 in Europe for the treatment of wet AMD and is injected every eight to 12 weeks after three initial monthly doses. Avastin (bevacizumab), marketed for non-ocular indications by Genentech in the United States and by Roche outside of the United States, is an anti-VEGF cancer therapy that shares structural characteristics with Lucentis and is commonly used off-label to treat wet AMD, DME, and RVO through intravitreal injection dosed every four weeks.

Annual worldwide sales of Lucentis and Eylea for all indications totaled approximately $11.5 billion in 2019. We believe that a substantial majority of these sales were in connection with the treatment of wet AMD and DME. Avastin, which is currently approved and marketed for the treatment of cancer, is also used off-label to treat wet AMD, DME, and RVO. We estimate that off-label Avastin represents approximately 60% of the U.S. wet AMD market by volume. We believe that an improved anti-VEGF therapy could further increase both adoption of approved therapies and extend the duration patients remain on treatment, and thus the total addressable market opportunity in wet AMD, DME/DR, and RVO could be substantial.

***Limitations of Current Anti-VEGF Therapies***

The limitations of current anti-VEGF therapies include:

- *Existing anti-VEGF therapies block VEGF activity effectively but have limited durability.* We believe current anti-VEGF therapies maintain potent and effective drug levels in ocular tissues for three to six weeks after injection on average. But typical treatment intervals in real-world clinical practice are longer. When a patient's dosing cycle is extended beyond the durability of the anti-VEGF agent, and the amount of drug remaining in the eye falls below therapeutic levels, the disease can progress and cause cumulative and permanent retinal damage. Most wet AMD, DME, RVO and DR patients will require protracted anti-VEGF therapy, possibly for life. Under these circumstances, strict adherence to the manufacturer's labeled treatment regimen of every four weeks for Lucentis and every eight weeks for Eylea is challenging.

- *Real-world utilization of current anti-VEGFs results in undertreatment, which diminishes effectiveness.* A divergence between the efficacy of Lucentis and Eylea in pivotal clinical trials and in the real world is evidenced in multiple studies and is increasingly recognized as an important unmet medical need. A 2017 report by the Angiogenesis Foundation suggested that the burden involved in monthly visits for evaluation and treatment causes patients and physicians to extend treatment intervals, which in turn results in undertreatment and visual outcomes that fall short of the results seen in clinical trials. For example, Lucentis was tested and failed to successfully extend the treatment interval to 12-week dosing, with patients going back to pre-treatment baseline or even losing vision at the end of the first year of treatment, on average. The Lucentis U.S. product labeling refers to this regimen as an option which is "not as effective" as monthly dosing. The FDA allowed an update to Eylea's labeling to allow 12-week dosing, but only in the second year of treatment (after one full year of intensive treatment). The labeling refers to it as "not as effective as the recommended every 8-week dosing." Even a small deviation from per label dosing can be devastating for vision. Missing as few as one or two injections in a year from Eylea's recommended dosing, results in almost one line of vision lost.
- *Patients are not sustaining visual acuity gains over the long term.* Following exit from tightly controlled clinical trials into the real-world environment, patients, on average, lose all the gains in visual acuity that had been previously achieved.
- *Damage caused by these retinal diseases may be irreversible if anti-VEGF therapy is not initiated early in the disease progression.* A study in patients with diabetic macular edema, or DME, a severe form of DR, found that undertreatment in the early course of patients' disease may reduce the patients' ability to respond to anti-VEGF therapies.

**Market Opportunity**

***Wet AMD***

*Overview of Wet AMD*

AMD is a common eye condition affecting people of age 55 years and older with a reported prevalence of approximately 11 million people in the United States and 170 million people globally. It is a progressive disease affecting the central portion of the retina, known as the macula, which is the region of the eye responsible for sharp, central vision and color perception. The likelihood of AMD progression and associated vision loss increases with age.

Wet AMD is an advanced form of AMD characterized by neovascularization and fluid leakage under the retina. It is the leading cause of severe vision loss in patients over the age of 50 in the United States and the EU, with a reported prevalence of approximately 1.25 million people and an annual incidence of approximately 200,000 people in the United States. The likelihood of disease progression increases with age, so the prevalence and incidence of wet AMD is projected to accelerate in countries with aging populations. It has additionally been observed that approximately 50% of patients presenting with wet AMD in one eye will develop wet AMD in the other eye within five years, leading to a relatively significant number of patients requiring treatment in both eyes. While wet AMD represents only 10% of the number of cases of AMD overall, it is responsible for 90% of AMD-related severe vision loss. In many eyes with wet AMD, the disease can progress quickly with rapid loss of central vision needed for activities such as reading and driving. Untreated or undertreated wet AMD results in blood vessel leakage, fluid in the macula, and ultimately scar tissue formation, which can lead to permanent vision loss, or even blindness, as a result of the scarring and retinal deformation that occur during periods of non-treatment or undertreatment.

*Current Therapies for Wet AMD*

The standard of care treatments for wet AMD are two anti-VEGF drugs, Lucentis (ranibizumab) and Eylea (aflibercept). Lucentis (ranibizumab), marketed by Genentech, Inc., a subsidiary of the Roche Group, in the United States and by Novartis AG outside the United States, is a recombinant humanized monoclonal antibody fragment that binds to and inhibits VEGF proteins in the eye and was approved in the United States in 2006 and in Europe in 2007. Eylea (aflibercept), marketed by Regeneron Pharmaceuticals, Inc. in the United States and by Bayer HealthCare LLC outside the United States, is a recombinant fusion protein containing portions of the human VEGF receptor that binds to soluble VEGF and was approved in the United States in 2011 and in Europe in 2012. These drugs became the standard of care for treating wet AMD based on pivotal clinical trials in which Lucentis was injected every four weeks and Eylea was injected every eight weeks (after three initial monthly loading doses). Since its approval, Eylea has been widely adopted largely due to a durability advantage compared to Lucentis, but both agents were effective in improving visual acuity in the first months of the treatment period and sustaining this gain throughout the duration of their respective clinical trials. Avastin (bevacizumab), marketed for non-ocular indications by Genentech in the United States and by Roche outside of the United States, is an anti-VEGF cancer therapy that shares structural characteristics with Lucentis and is commonly used off-label as a monthly, intravitreal injection for wet AMD. BeoVu (brolucizumab), marketed worldwide by Novartis, was approved in late 2019 in the United States and early 2020 in Europe for the treatment of wet AMD and is injected every eight to 12 weeks after three initial monthly doses. Its competitiveness with Lucentis and Eylea in the commercial marketplace has yet to be observed.

*Total Market for Wet AMD*

Annual worldwide sales of Lucentis and Eylea for all indications totaled approximately $11.5 billion in 2019. We believe a substantial majority of these sales were in connection with the treatment of wet AMD, DME, and RVO. Avastin, which is currently approved and marketed for the treatment of cancer, is also used off-label to treat wet AMD, DME, RVO, and DR. We estimate that off-label Avastin represents approximately 60% of the U.S. wet AMD market by volume. We believe that an improved anti-VEGF therapy could further increase both adoption of approved therapies and extend the duration patients remain on treatment, and thus the total addressable market opportunity in wet AMD and DR could be substantial.

With an improved anti-VEGF therapy, we believe the total addressable market opportunity in wet AMD could be substantially greater than sales of Lucentis and Eylea in wet AMD, DME and RVO. A clinically meaningful durability advantage over existing treatments could increase long-term compliance rates and maintain patients on a consistent and FDA approved treatment regimen for this chronic condition. Furthermore, we believe that an anti-VEGF therapy that is more durable than Avastin may reduce the relative weight of cost as a deciding factor for patients and providers who currently favor Avastin and expand the market for “branded” treatments.

***Diabetic Retinopathy***

*Overview of Diabetic Retinopathy*

DR is an eye disease resulting from diabetes, in which chronically elevated blood sugar levels cause damage to blood vessels in the retina. There are two major types of DR:

- *Non-proliferative DR, or NPDR*. NPDR is an earlier, more typical stage of DR and can progress into more severe forms of DR over time if untreated and if exposure to elevated blood sugar levels persists.
- *Proliferative DR, or PDR*. PDR is a more advanced stage of DR than NPDR. It is characterized by retinal neovascularization and, if left untreated, leads to permanent damage and blindness.

DME, which occurs when fluid accumulates in the macula due to leaking blood vessels, can develop at any stage of DR. PDR, together with DME, are the primary causes of vision-threatening DR, or VTDR. VTDR is the leading cause of blindness among people with diabetes and the leading cause of blindness among working age adults in the United States and the EU. Patients with mild or moderate NPDR who have not developed DME are characterized as patients with non-vision threatening DR, or NVTDR.

*Current Therapies for DR*

PDR has historically been treated with laser therapy. In recent years, use of anti-VEGF therapies has emerged as a complementary first-line treatment for PDR. Lucentis and Eylea are also approved for the treatment of DME with or without PDR. In April 2017, Lucentis' approval was expanded to include all forms of DR, whether or not the patient also has DME. The approval was based on the demonstration that treatment with Lucentis results in more patients experiencing improvement of their diabetic retinopathy severity (disease regression). In March 2018, Regeneron announced results from its study in which Eylea demonstrated it can reverse disease progression in patients with moderately severe to severe NPDR when administered on average 4.4 times over 24 weeks. In 2019, Eylea received FDA approval as a treatment for DR without DME. For DR without DME, the recommended Lucentis regimen is monthly and the recommend Eylea regimen is every 8 weeks after 5 initial monthly injections.

The first-line interventions for non-vision threatening DR are observation, lifestyle changes and treatment of underlying diabetes. In practice, anti-VEGF therapies are not commonly prescribed for patients with NVTDR. However, results from the RISE and RIDE trials for Lucentis as well as the PANORAMA study for Eylea showed that anti-VEGF therapies can slow disease progression in patients with NPDR as well as induce regression.

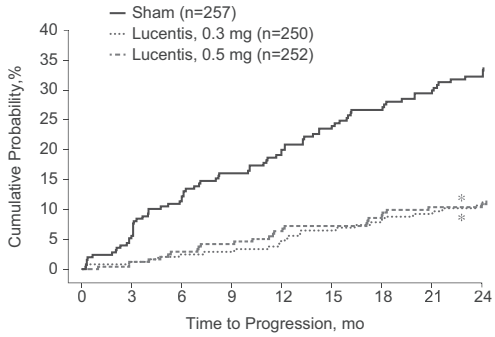



**Figure: Time to disease worsening (DR progression as defined by a composite endpoint) from baseline in DME patients with NPDR treated with sham procedures vs. Lucentis.**

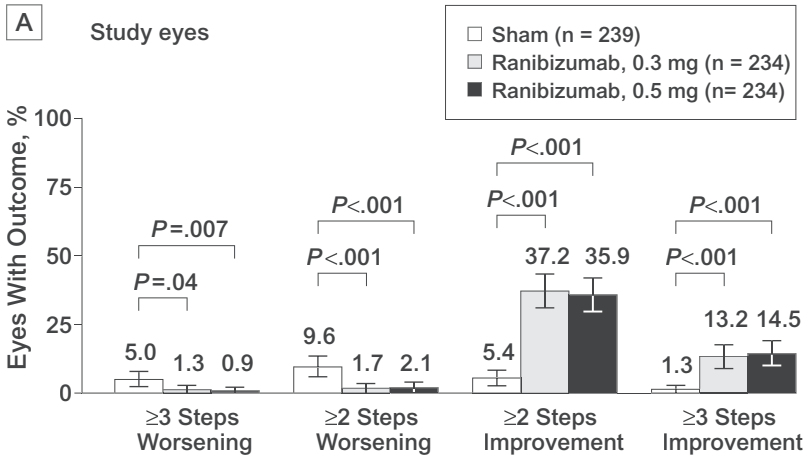



**Figure: Proportion of subjects improving or worsening per treatment arm.**

*Total Market for DR*

According to the Center for Disease Control, or CDC, and National Institutes of Health, or NIH, (1) an estimated 30 million people in the United States have diabetes, with approximately 1.5 million additional people in the United States diagnosed with diabetes each year, and (2) 285 million people worldwide have diabetes. We estimate that the number of people in the United States and the EU with DR in 2015 was approximately 28.5 million. According to the NIH, the number of Americans with DR is expected to nearly double from 2010 to 2050. The CDC estimates that approximately 900,000 Americans are affected by VTDR. We believe a substantial majority of the $11.5 billion in global sales of Lucentis and Eylea in 2019 were for the treatment of wet AMD, DME and RVO, with only a small proportion of sales for the treatment of NPDR without DME. Furthermore, we believe that the frequent injections required by current anti-VEGF therapies may dissuade patients with mild or asymptomatic forms of DR from accepting treatment. A more durable agent such as KSI-301 could be attractive for these untreated patients and extend the anti-VEGF market to include patients with NVTDR.

**Limitations of Current Anti-VEGF Therapies**

The underlying pathophysiologies of wet AMD, DME, DR and RVO are responsive to anti-VEGF drugs. Both conditions suffer from the limitations of current anti-VEGF therapies such as limited on-mechanism durability and frequent dosing intervals. On-mechanism durability is a function of the time that therapeutic levels are sustained in the ocular tissues. Data suggest that the effectiveness of Lucentis and Eylea in clinical practice is inferior to the results seen in well-controlled clinical studies, an observation attributed to insufficiently frequent dosing and resulting undertreatment even, in the case of Eylea, with its labeled eight-week regimen. Other studies show that while patients may benefit from anti-VEGF therapies in the early treatment phase, they may fail to sustain their visual acuity gains over the long term. Clinical studies have also shown that non-treatment or undertreatment with anti-VEGF agents in the months or years after disease onset may reduce the benefit of anti-VEGF therapies once therapy is initiated. These factors contribute to permanent and unnecessary vision loss for many patients.

***Existing anti-VEGF therapies block VEGF activity effectively but have limited durability.***

Wet AMD, DME, and DR are chronic and progressive diseases that require protracted treatment, possibly for life. Currently available anti-VEGF agents have relatively short durability. To maintain effective drug levels in the eye, existing anti-VEGF treatments must be administered on a frequent and sustained schedule. Lucentis was approved based on a monthly dosing interval. For wet AMD and DME, Eylea was approved based on a dosing interval of every eight weeks (following three initial, monthly loading doses for wet AMD, and five for DME). The most accepted sign of disease activity in wet AMD for retina specialists worldwide is recurrent accumulation of fluid in the macula, as determined by evaluating the retinal thickness and anatomic appearance with OCT. As can be seen in the figure below, when Eylea or Lucentis are dosed on a Q4W (once every four weeks) regimen, the retinal thickness remains stable between doses, as measured on OCT. However, when Eylea dosing is shifted to its Q8W (once every eight weeks) labeled regimen, the retina expands and contracts as it begins to swell with fluid before its next retreatment, exhibiting a seesaw pattern that we refer to as OCT flutter. This suggests that, although vision outcomes are comparable on average between fixed-interval 4-weekly and 8-weekly dosing, Eylea's durability and ability to maintain disease control as measured by OCT is less than the approved 8-week per-label dosing.

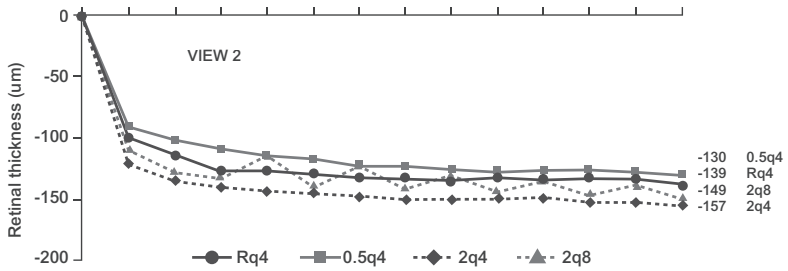



**Figure: Retinal thickness (y-axis), measured in microns, decreases upon treatment with Eylea. Rq4 = Lucentis every four weeks; 0.5q4 = Eylea 0.5mg every four weeks; 2q4 = Eylea 2mg every four weeks; 2q8 = Eylea 2mg every eight weeks.**

The clinical implication is that when a patient's dosing cycle is extended beyond the durability of the anti-VEGF agent and the amount of drug remaining in the eye falls below therapeutic levels, disease activity can recur. At this point, the disease can progress and begin to cause cumulative and possibly permanent retinal damage. To this point, the Eylea product labeling in the United States notes that "some patients may need every 4-week (monthly) dosing after the first 12 weeks (3 months)."

Additional evidence of the recognition of limited durability is seen in the FDA's evaluation of both Lucentis and Eylea. Lucentis was tested for its potential to reach quarterly dosing in a Phase 3b study; it failed to successfully deliver the same efficacy results as monthly dosing. The FDA did accept dosing every three months after three initial monthly loading doses in the Lucentis product labeling, with the following wording: "Although not as effective, patients may be treated with 3 monthly doses followed by less frequent dosing with regular assessment. In the 9 months after three initial monthly doses, less frequent dosing with 4-5 doses on average is expected to maintain visual acuity while monthly dosing may be expected to result in an additional average 1-2 letter gain. Patients should be assessed regularly." The loss of one line of vision translates into patients going back to baseline or even losing vision at the end of the first year of treatment, on average. Furthermore, the required wording of regular assessments means that the high burden of frequent office visits remains. For Eylea, recently, the FDA updated the product labeling to allow 12-week dosing but only in the second year of treatment, after one full year of intensive treatment. The labeling refers to it as "not as effective as the recommended every 8-week dosing." For both Lucentis and Eylea, the recommended fixed interval dosing of monthly and bimonthly, respectively, appear to result in the best and most consistent visual acuity results, with all flexible or less-frequent dosing intervals labeled by FDA as "not as effective."

***Real-world utilization of current anti-VEGF therapies results in undertreatment which diminishes effectiveness.***

Extended treatment intervals caused by the burden of frequent treatments causes undertreatment and visual outcomes that fall short of the results seen in pivotal clinical trials.

Compared to Lucentis' pivotal trials in wet AMD, ANCHOR and MARINA, where initial vision gains are maintained with monthly dosing over two years, a variety of studies have shown that the initial gains (if achieved) are not maintained, on average, after the initial loading phase.

This is clearly seen in AURA, a multi-country real-world practice study of Lucentis. The visual acuity improvement seen in AURA falls significantly short of the visual acuity improvement that patients showed in MARINA and ANCHOR. A gradual loss of the initial vision gains can be seen as early as three months after initiation of treatment as depicted in the graph below. A key finding in AURA is that populations that received less frequent anti-VEGF treatment tended to experience less improvement in visual acuity, on average, as illustrated in the table below.

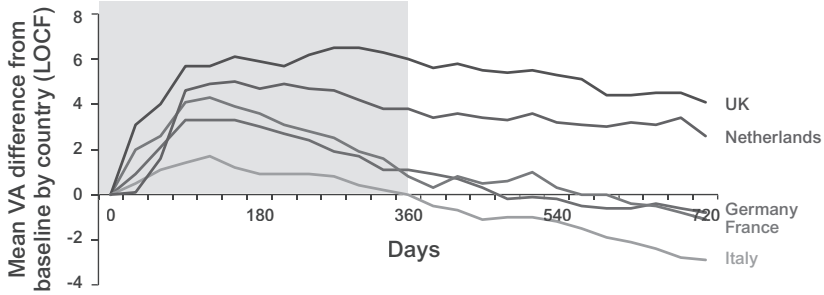



**Figure: Vision gains seen in the AURA study over time for all patients by country (adapted from Holz et al).**
***Last observation carried forward analysis.**

| Country | N | Mean injections in full 2 years | Change in VA score to day 90* | Change in VA score to year 1* | Change in VA score to year 2* | Mean VA score at year 2* |
|---|---|---|---|---|---|---|
| UK | 410 | 9.0 | 5.7 | 6.0 | 4.1 | 59.0 |
| The Netherlands | 350 | 8.7 | 4.6 | 3.8 | 2.6 | 52.4 |
| France | 398 | 6.3 | 4.1 | 0.8 | -1.1 | 54.4 |
| Germany | 420 | 5.6 | 3.3 | 1.1 | -0.8 | 51.9 |
| Italy | 365 | 5.2 | 1.4 | 0 | -2.9 | 62.7 |

**Table: Summary of changes in visual acuity (VA) score from baseline and number of injections over two years, per country.**
***Last observation carried forward analysis.**

Consistent with the AURA study, an observational study following patients who completed the SEVEN UP and HORIZON trials for Lucentis in wet AMD showed a correlation between the number of injections and level of visual acuity benefit. Patients who received 11 or more injections during the period from four to eight years after they exited the pivotal clinical trial were more likely to experience improved vision (average gain of 3.9 letters) than patients who received six to ten injections during the same period (average loss of 6.9 letters).

| | No injections (n=26) | 1-5 injections (n=11) | 6-10 injections (n=11) | ≥11 injections (n=14) |
|---|---|---|---|---|
| Letter change: | | | | |
| SEVEN UP vs HORIZON exit | -8.7 | -10.8 | -6.9 | +3.9 [1] |

[1] $p<0.05$

**Table: Mean letter change from HORIZON to SEVEN UP by total number of anti-VEGF treatments.**

The implication of these data is that in clinical practice and outside of clinical studies, patients are receiving fewer injections than the labeled regimens for Lucentis (12 per year) and Eylea (seven to eight in the first year and six in subsequent years). In 2017, the Angiogenesis Foundation reported that in routine clinical practice, 65% of wet AMD patients receive six or fewer injections during the first year of treatment. Likewise, a recent publication from the American Academy of Ophthalmology's IRIS (Intelligent Research In Sight) patient registry showed that, in 13,859 U.S. patients with wet AMD, the average number of injections in the first year of treatment was approximately six.

As illustrated in the top right of the figure below, data regarding long-term anti-VEGF treatment show that visual acuity outcomes are positively correlated with number of injections, with the greatest benefit seen when therapies are used at 10.5 or more injections per year reflecting high intensity, fixed Q4W or Q8W dosing.

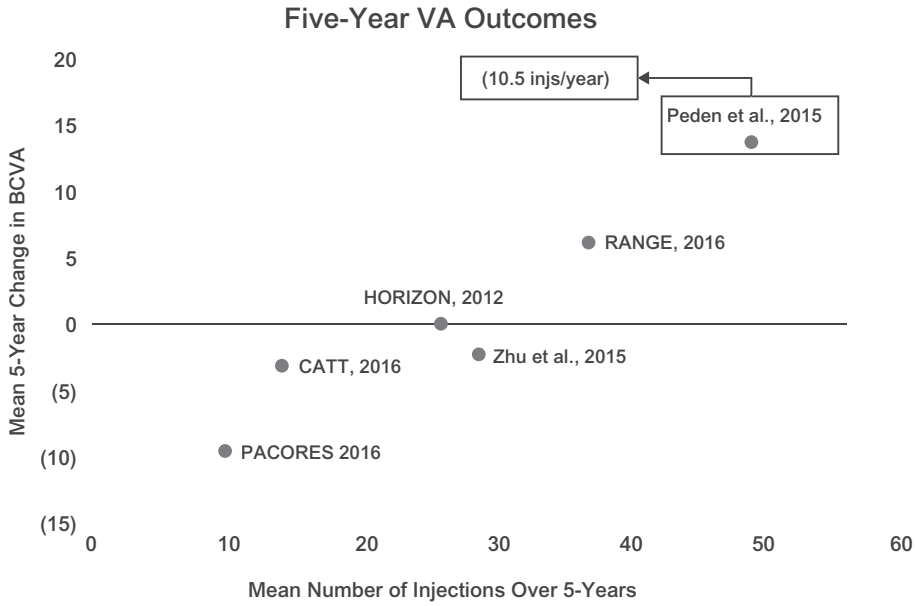



**Figure: Five-year visual acuity outcomes versus injection frequency for three or more years in AMD.**

In real-world practice, even a small deviation from per-labeled dosing can result in significant vision loss. In the PERSEUS Study, the real-world effectiveness of Eylea was evaluated in patients treated per-label (regular treatment) compared to patients treated irregularly. Patients treated regularly received a mean of 7.4 injections compared to 5.2 in the irregular treatment group. The initial vision gains seen after the loading doses started to decrease at month four, with vision returning, on average, to almost baseline in the irregularly treated patients, as shown in the graph below. The difference in vision of 4.6 letters gained between the two groups is statistically significant, and, more importantly represents almost a line (five eye chart letters) of vision difference on average, which is recognized in the field as clinically meaningful. Additionally, in this study, the majority of patients (70.5%) did not receive regular treatment.

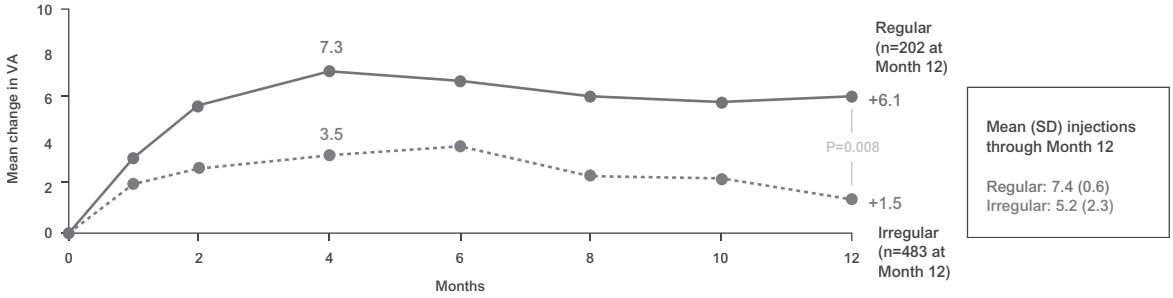



**Figure: mean change in visual acuity for regularly and irregularly treated patients in the PERSEUS Study (effectiveness set)**

Real-world outcomes of anti-VEGF treatment in patients with DME show similar patterns to wet AMD. For instance, a recently published report of electronic health records real-world data from 15,608 DME patient eyes showed that patients on average receive fewer injections over 12 months and have meaningfully worse visual acuity outcomes compared to randomized controlled trials.

***Patients are not sustaining visual acuity gains over the long term.***

Patients treated with anti-VEGF agents can sustain visual acuity gains over time if they adhere to a tighter dose frequency. Results from the VIEW 1 extension study demonstrate that it is possible for patients treated with anti-VEGF agents to sustain visual acuity gains over time, as long as patients adhere to a tighter dose frequency that is closer to the labeled regimen. In the early intensive treatment phase, patients in VIEW 1 achieved a ten-letter visual acuity gain, which they then maintained over two years on a Q8W regimen. At the end of two years, patients shifted into a less-intensive clinical monitoring regimen and into a more flexible dosing regimen in which they were required to maintain at least Q12W dosing. In this hybrid setting, patients showed a slow but steady decrease in average visual acuity from ten letters to seven letters; however, their average visual acuity did not drop to pretreatment levels or below.

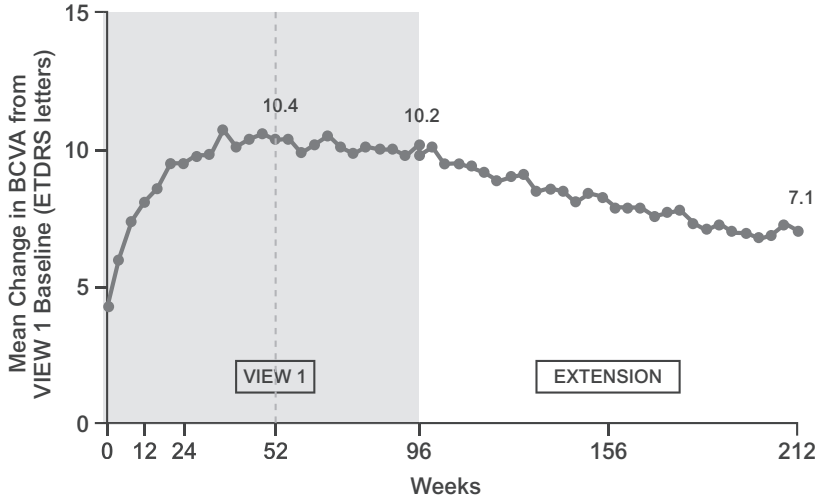



**Figure: Mean visual acuity and 95% confidence interval for 647 patients in the Comparison of Age-Related Macular Degeneration Treatments Trials Follow-up Study: (A) overall and by drug assigned in the clinical trial and (B) overall and by dosing regimen assigned in the clinical trial. PRN = "as needed."**

As mentioned above, AURA and many other real-world practice studies show that the vision gains seen in tightly controlled clinical trials are not transferrable to clinical practice. A United Kingdom study of approximately 93,000 Lucentis injections reviewed EMRs of thousands of patients treated outside the context of clinical trials. On average, patients received a median of 5, 4, and 4 injections of Lucentis over years one, two and three, respectively. The study found that although patients showed early improvement, they regressed, on average, to pretreatment levels by the end of year two with continued deterioration below their starting visual acuity by year three, as shown in the chart below.

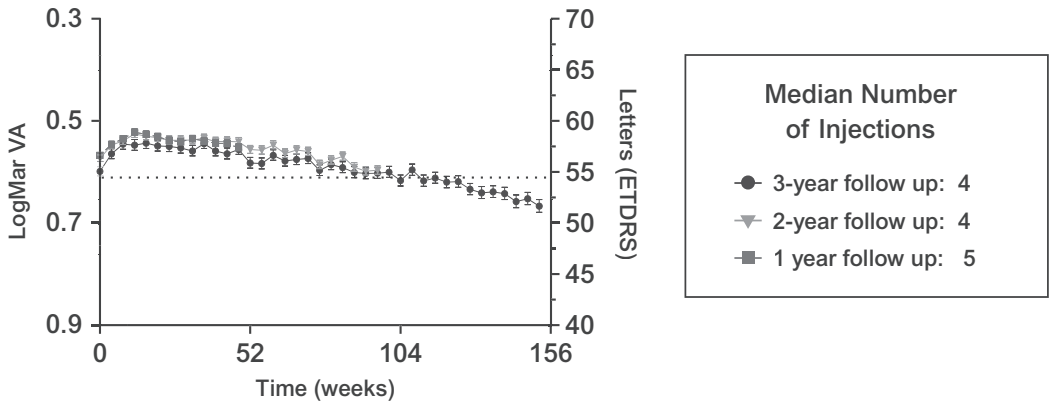



**Figure: Mean visual acuity (VA), as measured by letter score, over time comparing patients with follow-up of at least 1, 2 or 3 years.**

More importantly, with many patients losing vision, during the study follow-up many patients experienced new sight impairment (29.6%, 41%, 48.7% and 53.7% in years one, two, three and four, respectively) and even new cases of blindness (5.1%, 8.6%, 12% and 15.6% in years one through four, respectively).

In the United States, an EMR study of 7,650 eyes treated with Lucentis and Eylea outside of the clinical trial setting showed that these therapies improved patients' visual acuity less in practice than they do in clinical trials. Further, by the end of the first year of treatment, patients' average visual acuity had deteriorated below their pretreatment levels.

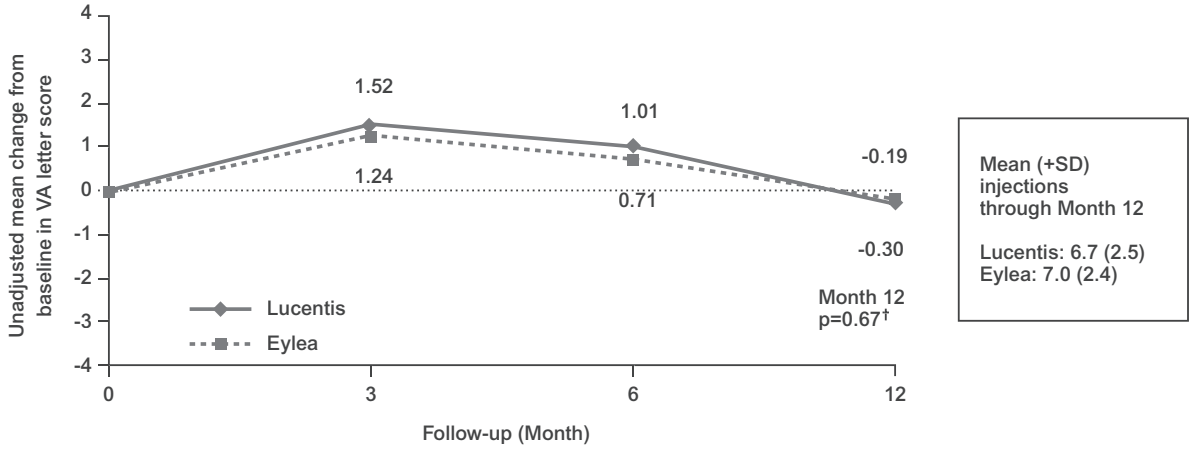



**Figure: Mean change in visual acuity (VA) letter score at 3, 6 and 12 months in the first year of treatment. VA was lower at 12 months than at the beginning of treatment.**

When patients leave the tightly controlled clinical trial environment, their eyesight, on average, falls to pretreatment levels. In practice, anti-VEGF therapies are not delivering the level of benefit that their pivotal clinical trials suggested. In the pivotal Lucentis trials MARINA and ANCHOR, patients were able to gain and maintain vision gains with monthly dosing over two years. After exiting the clinical trials, patients were followed in the HORIZON study with as needed dosing (Pro Re Nata or PRN) for three more years. Gradual vision decline can be seen immediately after exiting the trials, returning to pre-treatment baseline vision before the end of the third year of follow-up in HORIZON.

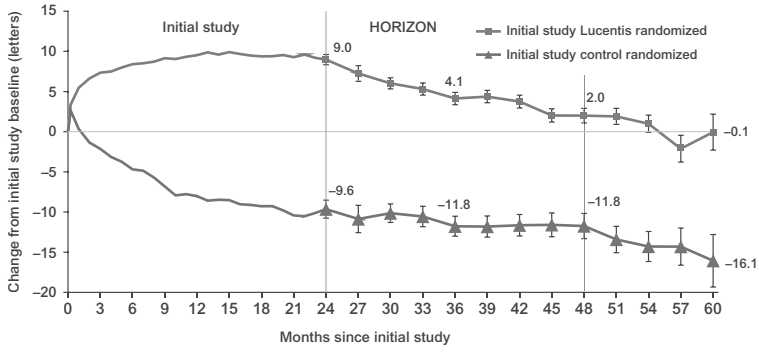
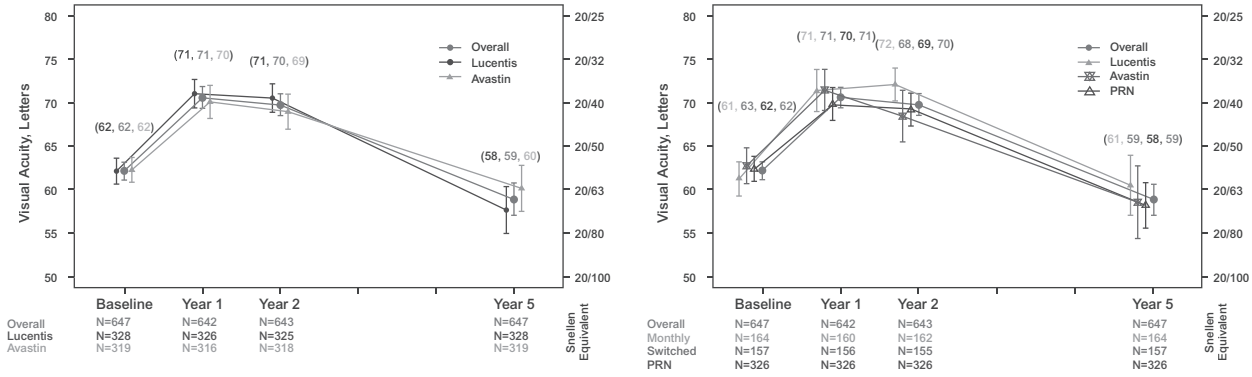



**Figure: Mean change in visual acuity (VA) letter score in MARINA and ANCHOR (years one and two) and in HORIZON (years three to five). VA gradually decreased immediately after the patients exited monthly dosing in a clinical trial setting.**

A study funded by the National Eye Institute followed patients who left the tightly controlled clinical trial environment into clinical practice and showed that these patients, on average, lost all the gains in visual acuity that they obtained while enrolled in the trial.



***Undertreatment in the early course of patients' disease risks the patients' ability to benefit from anti-VEGF therapies after the passage of time.***

After disease onset, how soon patients receive appropriate treatment is important to whether they can respond to treatment. Failure to appropriately treat neovascularization in the early period may reduce patients' ability to respond to anti-VEGF therapies as the disease progresses, possibly leading to irreversible damage. In the RIDE/RISE clinical studies of Lucentis in DR, patients who received Lucentis saw an increase in visual acuity of 10 to 12 letters at month 24. Patients who received sham treatment (a procedure that is intended to mimic a therapy in a clinical trial as closely as possible without having any actual efficacy) for 24 months saw no benefit. At the 24-month mark, the patient arms were crossed over, such that the patients who had initially received sham treatment now began to receive Lucentis. These patients were only able to improve by four letters by year three. The interpretation is that the unchecked disease progression in the initial period damaged the retina to such an extent that patients were subsequently unable to respond to Lucentis to the same degree as patients treated with Lucentis earlier in their disease process.

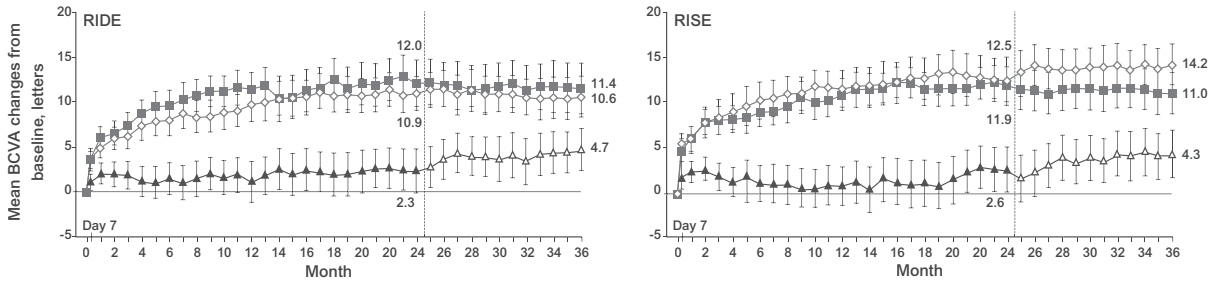



**Figure: At 36 months, patients who received Lucentis 0.5mg experienced a mean BCVA change from baseline of 11.4 letters and 11.0 letters in RIDE and RISE, respectively. Patients who received sham treatment for 24 months and then crossed over to Lucentis 0.5mg experienced a diminished benefit in mean best corrected visual acuity change from baseline at 36 months of 4.7 letters and 4.3 letters in RIDE and RISE, respectively.**

***Conclusions***

There is a significant and urgent unmet medical need to find better therapeutic options for patients with neovascular diseases of the retina that can:

- keep patients on mechanism for longer than currently available anti-VEGF therapies, thereby preventing repeated undertreatment by overextending treatment intervals and thus avoiding latent recurrence of retinal edema;
- match the required frequency of injections to keep the patient's disease quiescent with the frequency of visits that patient and physician behavior suggest is achievable in practice;
- sustain the strong visual acuity gains of the early intensive treatment phase over the long term and outside of clinical trial contexts; and
- provide a tolerable treatment regimen even for patients who are early in the course of their disease, so they can achieve the maximal benefit of anti-VEGF therapy.

In the 2018 Preferences and Trends Survey conducted by the American Society of Retina Specialists, retina specialists worldwide cited both reduced treatment burden and long-acting durability as the greatest unmet needs regarding wet AMD treatment, and in the 2019 Survey, the majority of retina specialists believed that wet AMD patients are being undertreated.

**Our Lead Product Candidate: KSI-301**

Our lead product candidate, KSI-301, is a novel, clinical-stage anti-VEGF biological agent that combines inhibition of a known pathway with a potentially superior on-mechanism durability profile compared to currently marketed drugs for wet AMD, DME, DR and RVO. By addressing the primary causes of undertreatment, KSI-301 has the potential to improve and sustain visual acuity outcomes in patients with retinal vascular and exudative diseases.

***Components of KSI-301***

KSI-301 is a bioconjugate comprised of two novel components. The first component is a recombinant, full-length humanized anti-VEGF monoclonal antibody. The second component is a branched, optically clear phosphorylcholine biopolymer. The antibody is conjugated to the biopolymer in a one-to-one ratio through a stable and site-specific chemical linkage to form the antibody biopolymer conjugate. The molecular weight of KSI-301 is approximately 950,000 Daltons (Dalton is a standard measure of molecular weight), of which approximately 150,000 Daltons are attributable to the antibody component and 800,000 Daltons are attributable to the biopolymer component. It is well-established that substances, when injected intravitreally, with a smaller molecular weight will be cleared from ocular tissues more quickly than larger substances.

**Figure: Functional structure of the KSI-301 antibody biopolymer conjugate.**

*Antibody Intermediate*

The antibody intermediate of KSI-301 consists of a humanized anti-VEGF antibody. KSI-301 behaves pharmacologically similar to Lucentis by inhibiting VEGF-mediated neovascularization and vascular permeability.

*Biopolymer Intermediate*

The biopolymer component is a branched, optically clear phosphorylcholine biopolymer. Phosphorylcholine is a naturally occurring phospholipid head group present on the external surface of mammalian cellular membranes. Phosphorylcholine demonstrates physiological inertness that has been attributed to its molecular structure, where a permanent positive charge on the nitrogen group is equally balanced by a negative charge on the phosphate, yielding a net neutral charge over a wide range of conditions. Because of these biophysical properties, phosphorylcholine-based materials demonstrate super-hydrophilic properties in which they bind large amounts of water molecules very tightly, to create what we call "structured water." Phosphorylcholine is used successfully in marketed medical materials as the key water control monomer, in particular as a hydrogel in certain contact lenses and as a polymeric surface coating in certain cardiac drug-eluting stents. In these applications, phosphorylcholine containing monomers are polymerized via "uncontrolled" free radical polymerization. For an external hydrogel application (contact lens) and an internal surface coating application (drug eluting stent), control of molecular weight and architecture are not important performance attributes. Kodiak's objective was to incorporate phosphorylcholine into well-controlled biomaterials to use as conjugates for soluble, injectable medicines such as biopharmaceuticals. In such an application, control of molecular weight and architecture are important manufacturing and performance parameters. Therefore, we used controlled "living" polymerization techniques to build precise, star-shaped, high molecular weight, well-characterized phosphorylcholine-based biopolymers that preserve functional chemistry for subsequent conjugation to biologically active proteins and, once conjugated, bring a highly structured water environment into close proximity with the bioactive antibody's target binding regions. We are also applying these controlled "living" polymerization techniques to develop phosphorylcholine-based biopolymers as copolymers of phosphorylcholine-containing and drug-containing comonomers to build chemistry-based product candidates that we believe may demonstrate high biocompatibility, high drug loading and sustained release of small molecule drugs for ophthalmology applications.

***Characteristics of KSI-301***

We believe that KSI-301 can be a highly differentiated treatment with an improved durability and bioavailability profile compared to current anti-VEGF therapies due to the following design features and resulting performance benefits we have observed with KSI-301 in our preclinical development:

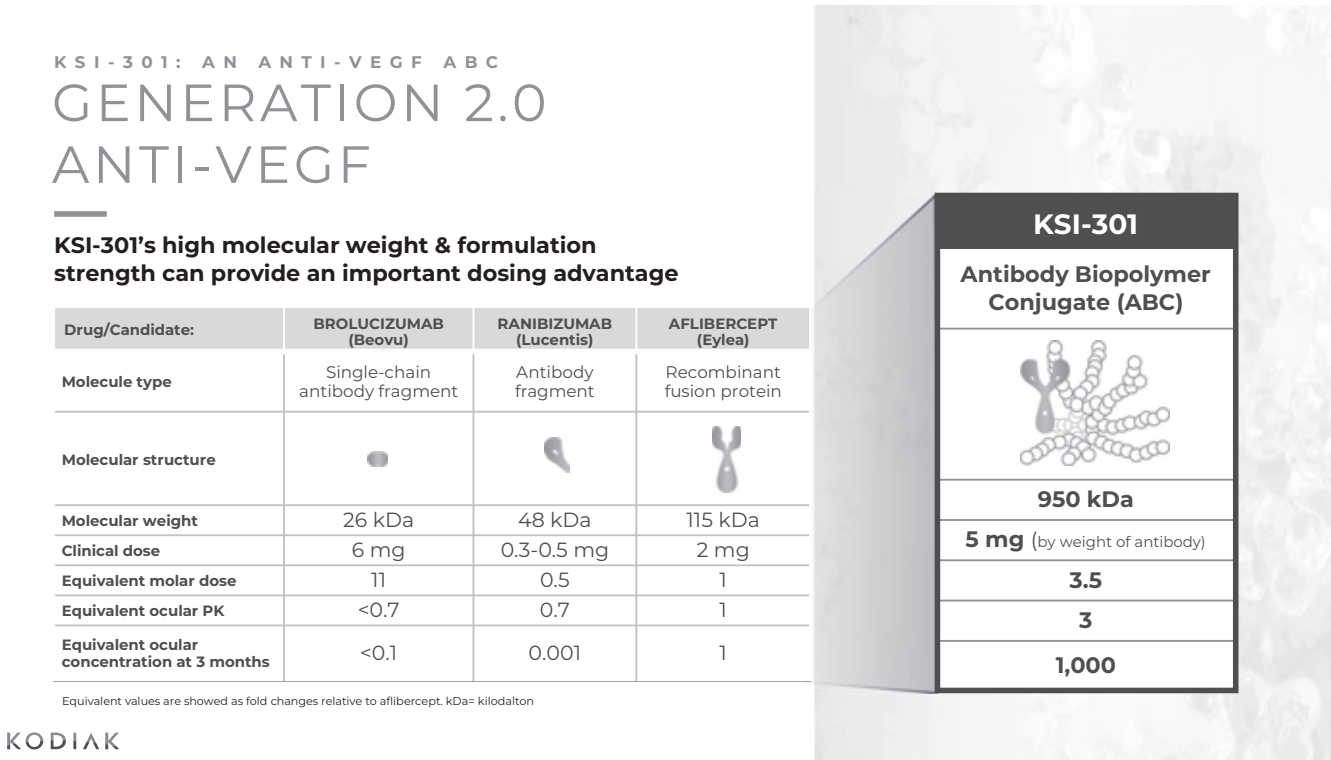
- Design feature: KSI-301's ultra-high molecular weight of 950,000 Daltons as compared to 115,000 for Eylea, 48,000 for Lucentis and 27,000 for brolucizumab
    - Associated performance benefits:
        - 3x improvement in key ocular pharmacokinetic parameters of KSI-301, as compared to Eylea
        - ~1000x ocular concentration advantage at three months post-dosing of KSI-301, as compared to Eylea
- Design feature: KSI-301's phosphorylcholine-based ABC Platform
    - Associated performance benefits:
        - 4x increase in key target ocular tissue bioavailability, as compared to Eylea
        - Same or increased bioactivity, as compared to the standard of care anti-VEGF agents
        - Increased stability and resistance to degradation of bioconjugates compared to therapeutic proteins
- Design feature: KSI-301's increased formulation strength of 50 mg/mL as compared to 40 mg/mL for Eylea and 10 mg/mL for Lucentis, as measured by weight of protein moiety
    - Associated performance benefits:
        - 3.5x and 7x higher number of anti-VEGF binding sites per dose, as compared with Eylea and Lucentis, respectively

We believe that the aggregated effects of these properties could afford KSI-301 a longer on-mechanism durability that will more closely match the frequency of physician visits that is realistic for patients in clinical practice.

We also believe that these properties along with KSI-301's delivery by intravitreal injection position it favorably compared to other therapies being studied in the clinic with the aim of long-interval dosing in retinal vascular disease. For example, both subretinal gene therapy and an implantable drug reservoir require the patient to undergo surgery, which is generally riskier than an intravitreal injection. This need for surgery may reduce the likelihood that those technologies could be useful for or adopted by a broad range of physicians and patients, especially those patients with earlier-stage disease. An implantable drug reservoir also leaves a foreign body permanently in the eye, with an attendant increased risk of infection. Coated microsphere drug depots that deliver small-molecule receptor tyrosine kinase inhibitor drugs into the eye may leave a foreign residual material, which may cause visual symptoms and/or other safety problems. Additionally, receptor tyrosine kinase inhibitor drugs affect signaling through additional receptors other than VEGF receptor; the effects on the eye of this additional receptor inhibition, either good or bad, are not yet known. Likewise, intravitreally-administered gene therapy vectors have been associated with chronic intraocular inflammation in a high percentage of treated patients, which may limit the efficacy of these treatments, the ability to retreat the first eye or treat the second eye over time, and the overall adoption of these approaches if they are successful. Finally, bispecific antibodies that target VEGF as well as other angiogenic signaling pathways are attempting to increase durability of treatment effect through targeting of yet-unvalidated biologic pathways, but the antibodies being used are the same size as typical monoclonal antibodies (~150 kDa) and we believe they do not have any unique size or half-life extending properties.

***Trajectories in Field of Medicines Development for Retinal (Intravitreal) Therapies***

Since the initial FDA approval of Lucentis in 2006 as a monthly therapy for wet AMD, efforts have been made to improve the durability of intravitreal anti-VEGF therapy. Primarily, two parameters have been varied: size of molecule and amount of injected dose. First, increasing molecular weight, which can increase durability or ocular pharmacokinetics, or PK, in the eye because a larger molecule can lead to a slower exit from the eye. For example, Lucentis has a molecular weight of 48 kDa whereas Eylea, approved in 2011, has a molecular weight of 115 kDa. The second parameter is increasing the formulation strength (concentration) to increase the effective dose of anti-VEGF, given the limited volume of medicine that can be injected intravitreally in a single administration. This increases effective durability by keeping drug concentrations in the eye above a minimal threshold for longer periods of time. For example, Eylea has a 2x molar equivalence to Lucentis. In designing KSI-301, we addressed both parameters: first, increasing the molecular weight to 950 kDa through our ABC approach, and second, increasing the molar strength through a high concentration formulation of 50 mg/mL (by weight of protein). Of note, some recently developed therapeutic candidates have leveraged one parameter at the expense of the other. For example, brolucizumab was tested in Phase 3 (data available in 2017) at a high concentration and thus high injected dose level, giving it a high molar strength (22x of Lucentis), but with a molecular weight of only 27 kDa the duration of each molecule in the eye is less than that of Lucentis. Clinically, the Phase 3 result was that roughly half of patients were able to be maintained on 12-week dosing, and the remainder required 8 week (or more frequent) dosing. We believe our design decisions for KSI-301 may provide increased durability. The following figure illustrates these concepts.



*Affinity for and Inhibition of VEGF*

The therapeutic activity of KSI-301 is driven by its antibody component, OG1950, which (1) binds to VEGF and (2) prevents VEGF from carrying out its functions that promote neovascularization and increase vascular permeability. Our preclinical tests have demonstrated that OG1950 and KSI-301 bind to VEGF with similar affinity, which indicates that, despite the size and complex architecture of the biopolymer intermediate, the biopolymer does not interfere with antibody binding.

**Table: Binding kinetics of OG1950 and KSI-301 to huVEGF-A165 by SPR or KinExA analysis.**

| Molecule | Platform (°C) | $K_{on}$ (M) | $K_{off}$ (M) | $K_D$ (pM) |
|---|---|---|---|---|
| OG1950 | Biacore(25°) | $5.31x10^6$ | $4.48x10^{-5}$ | 9.02 |
| | KinExA(37°) | $5.09x10^5$ | $1.75x10^{-6}$ | 3.43 |
| KSI-301 | Biacore(25°) | $3.19x10^6$ | $5.33x10^{-5}$ | 17.0 |
| | KinExA(37°) | $2.69x10^5$ | $1.82x10^{-6}$ | 6.75 |

*°C = degrees Celsius; $K_D$ = dissociation constant*

We have also tested OG1950 and KSI-301 in vitro alongside other anti-VEGF biologics to test their respective abilities to inhibit VEGF from binding to VEGF receptors. As shown in the figure and table below, while KSI-301 and OG1950 have similar IC50 (the concentration at which binding is reduced by half) compared to Eylea, KSI-301 consistently demonstrates a higher maximal inhibition than Eylea or Lucentis. Of note, KSI-301 improved maximal inhibition more than OG1950, suggesting that the special nature of our antibody biopolymer conjugate synergistically improves the bioactivity of the antibody intermediate acting alone.

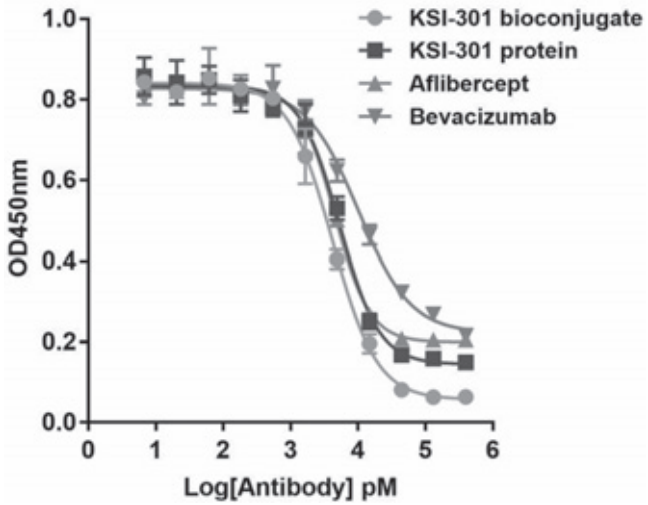



**Figure: Inhibition of VEGF binding to VEGF receptors by anti-VEGF agents.**

| Molecule | $IC_{50}$ (nM) | Maximal inhibition (%) |
|---|---|---|
| KSI-301 | 3.72±0.74 | 93.89±1.41 |
| OG1950 | 3.97±1.19 | 83.72±3.13 |
| Ranibizumab (Lucentis) | 8.60±1.29 | 70.67±2.36 |
| Aflibercept (Eylea) | 4.50±0.14 | 74.96±1.84 |
| Bevacizumab (Avastin) | 10.29±0.70 | 73.08±4.20 |

**Table: Average $IC_{50}$ and maximal inhibition of anti-VEGF agents. $IC_{50}$ values measured in nanomoles (nM) and calculated from concentration of anti-VEGF agents. All values shown as average with standard deviation.**

*Inhibition of VEGF-Mediated Processes*

Based on its ability to bind and inhibit VEGF, KSI-301 is expected to behave pharmacologically similar to Lucentis, Eylea and Avastin to decrease the leakage of blood proteins and fluid into the retina. In fact, *in vitro* testing of KSI-301 against Lucentis, Eylea and Avastin in their respective ability to inhibit VEGF-mediated endothelial cell proliferation (a key component of neovascularization) in primary human retina microvascular endothelial cells, or HRMVECs, showed that KSI-301 inhibited proliferation to approximately the same degree as Eylea and with greater potency than Lucentis or Avastin. In addition, KSI-301 displayed a superior maximal inhibition of VEGF-mediated proliferation relative to Eylea and Avastin.

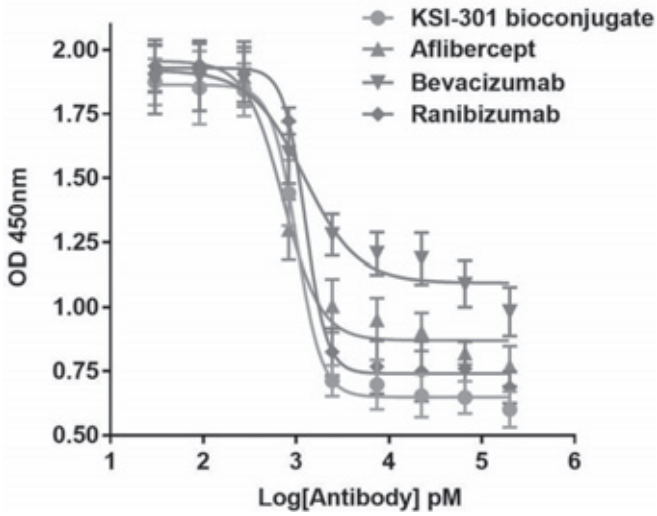



**Figure: Effects of KSI-301, Lucentis, Eylea and Avastin on HRMVEC proliferation.**

| Molecule | $IC_{50}$ (nM) | Maximal Inhibition (%) |
|---|---|---|
| KSI-301 | 0.96±0.18 | 64.74±2.36 |
| OG1950 | 0.85±0.07 | 58.92±5.30 |
| Ranibizumab (Lucentis) | 1.25±0.14 | 60.96±2.53 |
| Aflibercept (Eylea) | 0.74±0.10 | 53.93±4.91 |
| Bevacizumab (Avastin) | 1.25±0.36 | 38.98±6.18 |

**Table: IC50 Values and maximal inhibition of anti-VEGF agents on VEGF-mediated proliferation of HRMVECs. IC50 values were calculated from concentration of anti-VEGF agents. All values shown as average with standard deviation.**

To mimic *in vivo* conditions where endothelial cells and pericytes coexist in blood vessels, a three-dimensional co-culture of HRMVECs and human mesenchymal pericytes, or HMPs, grown on beads was established. This model was then used to test the ability of KSI-301 to inhibit VEGF-mediated vascular sprouting compared to Lucentis and Eylea. The average number of sprouts per bead and the length per sprout were analyzed under each treatment condition.

As shown in the figures below, at maximal anti-VEGF inhibition the average sprout length of cultures treated with KSI-301 was substantially less than that of the control (481 compared with 990 microns) and comparable to Lucentis and Eylea (505 and 428 microns respectively). The average number of sprouts per bead for cultures treated with KSI-301 was 11.5, which was comparable to 13.3 and 13.0 sprouts per bead observed for the cultures treated with Lucentis and Eylea, respectively.

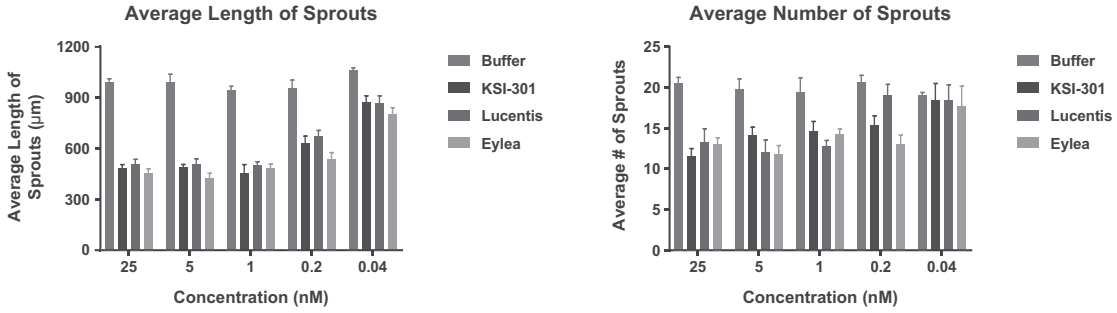


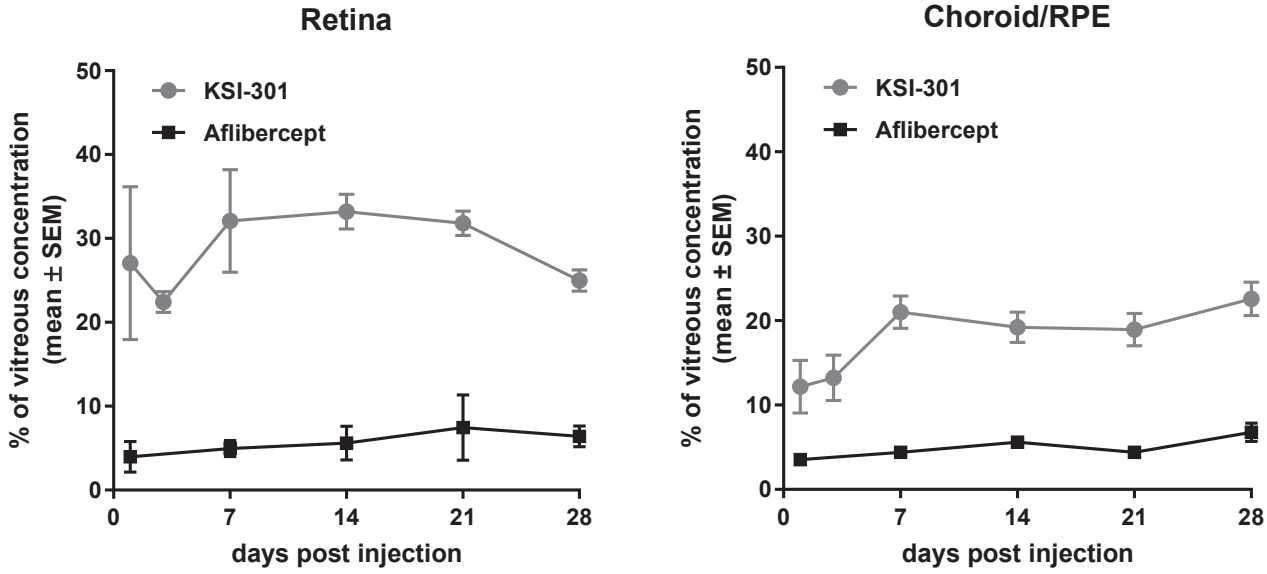

**Figure: Effects of KSI-301 and other anti-VEGF molecules on length and number of vascular sprouts in 3-dimensional culture.**

*Extended Ocular Half-Life versus Standard of Care Agents*

The addition of the biopolymer intermediate increases the size of the biologic, thereby extending the ocular half-life of the molecule beyond that of standard of care anti-VEGF agents. Preclinical studies with KSI-301 in the well-established rabbit ocular pharmacokinetics model have demonstrated that KSI-301 has ocular tissue half-lives of 10+ days in the retina and 12.5+ days in the choroid. This is in comparison to published data for ocular tissue half-lives for Lucentis of 2.9 days and Eylea of 4-5 days.

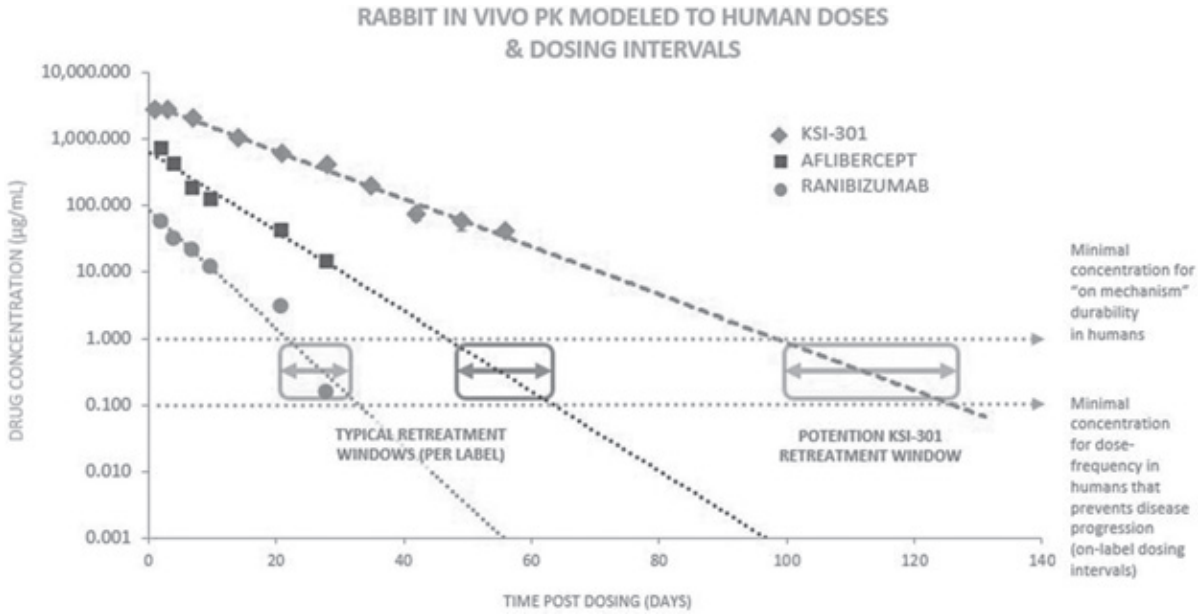
*Enhanced Ocular Tissue Bioavailability versus Eylea*

The data also show that KSI-301, despite its large size, penetrates ocular tissues well and has a retina and choroid ocular tissue biodistribution that is more than four-fold higher than Eylea.



*Modeling On-Mechanism Durability and Human Dose Frequency*

In order to estimate the impact of high potency and extended ocular half-life on durability of effect, we used a pharmacokinetic and pharmacodynamic model that overlays rabbit ocular tissue pharmacokinetic profiles of intravitreally injected anti-VEGF therapeutics and correlates the drug levels with (1) human OCT data to define a rabbit minimal inhibitory concentration to maintain human on-mechanism durability that corresponds with human OCT outcomes, and (2) human dose frequency to define a rabbit minimal inhibitory concentration to support a dose frequency in humans which corresponds to the ability to maintain visual acuity outcomes over the long-term. Specifically, we overlay the ocular tissue pharmacokinetic profiles of Lucentis at 0.5 mg dose (the marketed dose in wet AMD), Eylea at 2.0mg dose (the marketed dose), and bioconjugate KSI-301 at 5.0 mg dose (our selected dose), as separately tested.




Our modeling suggests a single dose of KSI-301 can stay above both on-mechanism and "dosing" minimal inhibitory concentrations for longer than 12 weeks in wet AMD patients. A minimal inhibitory concentration is the minimum concentration of a drug that still has the desired therapeutic effect. The implication is that KSI-301 may on average keep the retina dry for longer than 12 weeks after dosing, allowing patients to be dosed in regular 12-week intervals or less frequently and still maintain anti-VEGF mediated visual acuity gains over the long term. This contrasts with overextending the treatment interval beyond a point where retinal swelling recurs as observed in Eylea's VIEW 2 Phase 3 clinical trial (as described above).

***KSI-301 has demonstrated superior stability compared to typical protein therapeutics***

Stability studies have shown that KSI-301 bioconjugate is stable in ex vivo vitreous for at least 4 months at 37°C. Further, forced degradation studies at the extreme condition of 64°C have shown that KSI-301 bioconjugate remains in solution and is optically clear for at least 48 hours whereas the precursor antibody protein precipitated forming an opaque white suspension within several hours.

***Toxicology Profile***

KSI-301 has demonstrated an attractive safety profile. In all GLP monkey toxicology studies conducted through ocular or systemic administration, KSI-301 has been well tolerated. In ocular studies, KSI-301 was dosed bilaterally via intravitreal injection at 2.5 or 5.0 mg per eye every four weeks up to seven doses and evaluated through 40 weeks. Findings were limited to a dose-related anterior segment and posterior segment mild inflammatory response, which was not associated with other ocular abnormalities. The anterior segment response declined during the interval between doses and generally the finding was not present one-week post dose. The posterior segment response was attributed to a mild immune mediated response typically observed to a humanized therapeutic in monkeys. No drug related systemic toxicity was observed. Additionally, in a systemic administration study, KSI-301 was well tolerated up to the highest dose of 5 mg/kg when dosed intravenously every four weeks for ten weeks. In summary, the results of the toxicology studies strongly indicate that KSI-301's well tolerated safety profile in monkeys is favorable compared to that reported for Lucentis and Eylea.

**KSI-301 Commercialization**

We currently have no sales, marketing or commercial product distribution capabilities and have no experience as a company in marketing products. We intend to build our own commercialization capabilities over time.

If KSI-301 receives marketing approval, we plan to commercialize it in the United States with our own focused, specialty sales force. We believe that retinal specialists in the United States, who perform most of the medical procedures involving diseases of the back of the eye, are sufficiently concentrated that we will be able to effectively promote KSI-301 to these specialists with a sales and marketing group of fewer than 200 persons.

We expect to use a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize KSI-301 in markets outside the United States.

**KSI-301 Manufacturing**

We believe it is important to our business and success to have a reliable, high-quality clinical drug supply. As we mature as a company and approach commercial stage operations, securing reliable high-quality commercial drug supply will be critical.

We do not currently own or operate facilities for product manufacturing, storage, distribution or testing.

We rely on third-party contract manufacturers, or CMOs, to manufacture and supply our clinical materials to be used during the development of our product candidates. We have established relationships with several CMOs, including Lonza AG, or Lonza, for the manufacture of KSI-301, as well as certain of our other product candidates.

We currently do not need commercial manufacturing capacity. When and if this becomes relevant, we intend to evaluate both third-party manufacturers as well as building out internal capabilities and capacity. We may choose one or both options, or a combination of the two.

The process for manufacturing KSI-301 consists of conjugating our antibody intermediate with our biopolymer intermediate. Our antibody intermediate is produced in a recombinant GS-CHO (Glutamine Synthetase—Chinese Hamster Ovary) cell line in a protein-free and animal component-free medium. Our biopolymer intermediate is synthesized via a multi-step controlled “living” polymerization process, purified and formulated. Following conjugation of the intermediates, the bioconjugate drug substance is further purified, concentrated, and stored.

To date, we have relied primarily on Lonza for the manufacture of KSI-301. Notably, in the first quarter of 2020, we completed three successful re-supply batches of cGMP-manufactured KSI-301 drug substance. We believe that supply from these new batches, together with previously available KSI-301 supply from prior cGMP drug substance manufacturing, is sufficient to support our ongoing and planned clinical development activities.

The manufacture of KSI-301, like other biologic products, is complex and we have actively worked with Lonza to develop and refine our manufacturing process. As our need for KSI-301 increases in connection with pre-BLA manufacturing and validation activities and, if approved, commercial quantities, we anticipate continued collaboration with Lonza. We have also identified multiple other CMOs that we believe would be capable of implementing, validating and commercializing our manufacturing process for KSI-301 should the need arise.

**ABC Platform**

We believe that our ABC Platform is well suited to extend the durability of soluble, injectable retinal medicines, while at the same time providing for other useful benefits. We intend to develop additional drug candidates by applying our ABC Platform in other significant areas of unmet medical need in retina and ophthalmic disease.

We believe our ABC Platform differentiates us and has the potential to fuel a pipeline of differentiated product candidates in high-prevalence ophthalmic diseases. In addition to KSI-301, we have leveraged our ABC Platform to build a pipeline of potential product candidates, including KSI-501, a recombinant, mammalian cell expressed dual inhibitor antibody biopolymer conjugate, targeting both VEGF and IL-6 for the treatment of retinal diseases with an inflammatory component. The cGMP master cell bank for KSI-501 has been completed, and KSI-501 is being further developed towards an IND in 2021.

In addition, we have expanded our early research pipeline to include ABC Platform-based triplet inhibitors. In this approach, a bispecific or dual inhibitor antibody is conjugated to a phosphorylcholine biopolymer variant that is embedded with hundreds of copies of a small-molecule drug. As a result, multiple disease-related biologies - both intracellular and extracellular - can be targeted with a single medicine. This approach can be of particular relevance for common vision-threatening diseases that are more complex because of their multifactorial pathophysiology, such as dry AMD and glaucoma. KSI-601 is a triplet inhibitor for dry AMD, and we currently intend to submit an IND in 2022.

**Overview of KSI-501**

In addition to angiogenesis, inflammation has been implicated in the pathogenesis of a number of retinal diseases. Anti-inflammatory therapies such as steroids have been effective in treating both uveitis (a spectrum of diseases with intraocular inflammation as a defining characteristic) and DME. Similarly, genetically inherited variations in the interleukin 6, or IL-6, gene have been associated with higher PDR incidence in patients with type 2 diabetes. Moreover, disease progression in AMD, DR and RVO have been reported to be associated with increased serum and/or ocular levels of IL-6. Additionally, chronic inflammatory cells have been seen on the surface of the basement membrane behind the retina in eyes with wet AMD. Interestingly, IL-6 has been implicated in resistance to anti-VEGF treatments in DME patients. This in part is believed to be an indirect result of IL-6 mediated upregulation of VEGF expression as well as more direct VEGF-independent angiogenic functions mediated by IL-6 signaling that occur in the presence of VEGF inhibitors.

Our KSI-501 product candidate is a dual inhibitor Trap-Antibody-Fusion, or TAF, bioconjugate molecule designed to target concurrent inflammation and abnormal angiogenesis observed in the pathogenesis of retinal vascular diseases. KSI-501 acts through an anti-VEGF mechanism similar to Eylea and an anti-inflammatory mechanism that targets the potent cytokine IL-6. Similar to KSI-301, KSI-501 uses the ABC Platform and is a bioconjugate of the TAF protein conjugated to our phosphorylcholine-based biopolymer. Preclinical binding and functional studies demonstrate that the TAF protein binds specifically and simultaneously to its intended targets. We believe that this dual inhibition may provide a superior treatment option for patients with retinal vascular diseases and in particular those patients with diseases known to have a high inflammatory component such as DME, as well as in ocular inflammatory diseases such as uveitis.

KSI-501 is now in GMP manufacturing and we currently plan to submit an IND for KSI-501 in 2021.

***Components of KSI-501***

KSI-501 is a bioconjugate of a dual inhibitor TAF protein and a phosphorylcholine-based biopolymer. The protein portion of KSI-501 has two VEGF binding domains from human VEGF receptors which together act as a trap or soluble receptor decoy to bind the most abundant isoforms of VEGF. The anti-VEGF trap domains are fused to a high-affinity IgG1 antibody that binds with high specificity and affinity to IL-6 and disrupts the ligand's association with its cognate IL-6 receptor. Moreover, the Fc domain has been engineered to reduce immune effector function and facilitate site-specific conjugation to our phosphorylcholine-based biopolymer.

Notably, this IgG1 antibody sequence is identical to that from KSI-301, except for the six CDR regions that mediate target binding and which are specific for binding to the IL-6 target. Retaining the IgG1 frameworks across ABC Platform-derived product candidates enables "platform capability" which simplify manufacturing and product development. KSI-501, furthermore, uses the same cGMP biopolymer intermediate as KSI-301.

**Figure: Functional structure of the KSI-501 antibody biopolymer conjugate. CH – constant heavy, CL – constant light, VH – variable heavy, VL – variable light, – Complementarity Determining Regions (CDR).**

***Characteristics of KSI-501***

We believe that KSI-501 can be a highly differentiated treatment due to its dual mechanism of action, with an improved durability and bioavailability profile due to the ABC Platform component. In addition, there are currently no IL-6 inhibitors approved for use in the eye.

We incorporated the following design features into KSI-501:

- Binds with high affinity to the most abundant isoforms of VEGF
- Engineered to remove a protease hotspot to prevent cleavage in Chinese Hamster Ovary, or CHO, mammalian expression systems, which may improve potency and formulation stability

Design Feature: KSI-501's anti-IL-6 domain

- Affinity matured, humanized anti-IL-6 IgG1 that binds with high affinity to IL-6 and inhibits binding of IL-6 to its cognate receptor
- IgG1 Fc domain engineered to reduce immune effector functions

Design Feature: KSI-501's phosphorylcholine-based ABC Platform

- Ultra-high molecular weight of 1,000,000 Daltons for improved ocular pharmacokinetics
- Same IgG1 framework sequences and same phosphorylcholine-based biopolymer as KSI-301 and other ABC Platform-derived product candidates to simplify manufacturing and product development
- Other benefits of the ABC Platform such as enhanced tissue access to key ocular tissues and bioconjugate stability

Note that the in vitro data shown below are generated using the TAF (protein) of KSI-501, without conjugation to our ABC biopolymer. Results using KSI-501 may be different, but experience with a structurally similar prior molecule, KSI-201, has shown that these individual components, *i.e.,* trap antibody fusion protein and biopolymer, can function together simultaneously as a dual inhibitor bioconjugate. Prior experiences with bioconjugates KSI-201 and KSI-301 have also demonstrated that the biopolymer portion does not interfere with the bioactivity of the protein portion.

*Affinity and concurrent binding to VEGF and IL-6*

Preclinical studies indicate that the TAF portion of KSI-501 binds with high affinity to both VEGF and IL-6, as measured by SPR analysis (Table). Importantly, binding of each molecule has no effect on the binding of the other, and KSI-501 can bind to both molecules as shown below. Thus, we believe our dual inhibitor can simultaneously inhibit both of its targets with high potency.

**Table: Binding kinetics of TAF portion of KSI-501 to huVEGF-A165 or IL-6 by SPR analysis.**

| Molecule | $K_{on}$ (M) | $K_{off}$ (M) | $K_D$ (pM) |
|---|---|---|---|
| IL-6 | $3.72x10^{6}$ | $4.06x10^{-4}$ | 109 |
| VEGF-A165 | $1.07x10^{7}$ | $1.63x10^{-4}$ | 15.2 |

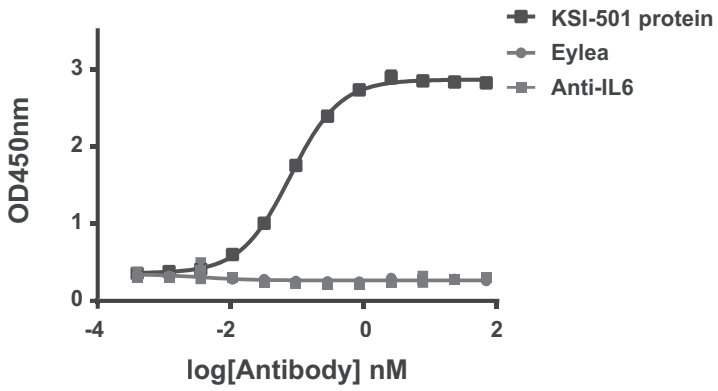



**Figure: TAF of KSI-501 simultaneously binds to IL-6 and VEGF by sandwich ELISA, which only shows a signal if a compound binds to both IL-6 and VEGF concurrently.**

*Inhibition of VEGF and IL-6*

KSI-501 was designed to inhibit both VEGF and IL-6 mediated signaling that occur after the ligands bind to their respective receptors. The figure below shows that the TAF protein of KSI-501 effectively prevents VEGF from stimulating downstream VEGFR2 signaling in a reporter assay in a comparable manner to Eylea, while anti-IL-6 alone served as a negative control.

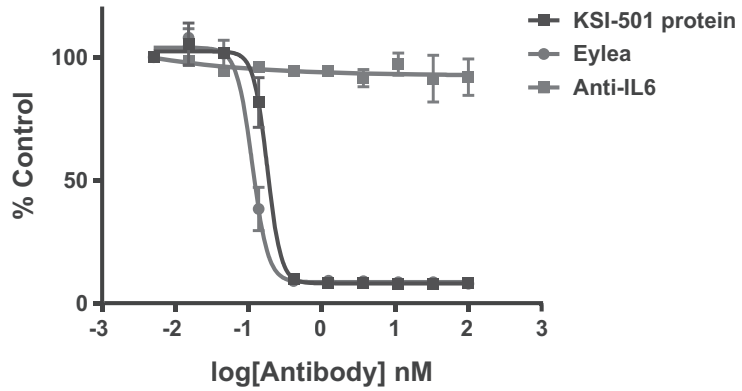



**Figure: VEGF stimulated reporter assay with increasing concentrations of anti-VEGF inhibitors**

The figure below shows that the control anti-IL-6 antibody and TAF protein of KSI-501 effectively compete with IL-6R for binding to plate-bound IL-6 and therefore inhibit this specific antigen-receptor interaction. The IC50 values for the control anti-IL-6 monoclonal antibody and the TAF protein are comparable (anti-IL-6 = 0.36 nM, KSI-501 = 0.47 nM), while Eylea had no effect.

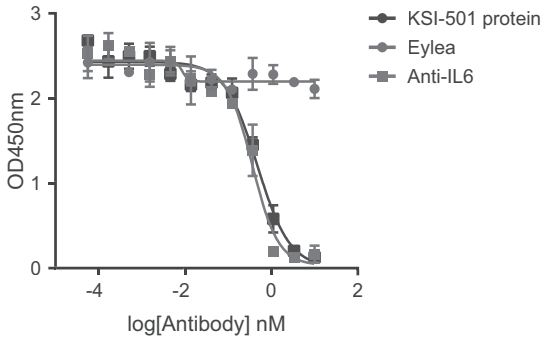



**Figure: ELISA measuring IL-6 binding to IL-6R in the presence of increasing concentrations of anti-IL-6 inhibitors**

Together, these data indicate that the TAF protein of KSI-501 inhibits both VEGF and IL-6 from binding their cognate receptors as effectively as the monotherapies. Importantly, these data also demonstrate that the TAF protein of KSI-501 can simultaneously block downstream signaling mediated by both VEGF and IL-6.

*IL-6 and VEGF mediated proliferation of HUVECs*

The ability of the TAF protein of KSI-501 to inhibit IL-6 and VEGF mediated angiogenic functions was tested in a Human Vascular Endothelial Cell, or HUVEC, proliferation assay as shown in the figure below. Importantly, the concentrations of VEGF and IL-6 used to stimulate proliferation were below the saturation point for each individual stimulant and under these conditions VEGF and IL-6 showed some synergy for growth. The presence of TAF protein significantly attenuated proliferation to approximately 50% of maximal growth, while neither Eylea nor control anti-IL-6 alone had quantifiable effects. These data provide supporting evidence that KSI-501 can synergistically abrogate endothelial cell proliferation that is driven by concurrent inflammatory and VEGF mediated signaling.

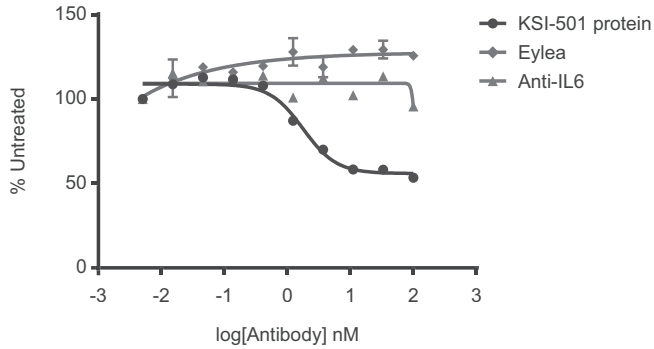



**Figure: VEGF/IL-6 mediated HUVEC proliferation in the presence of inhibitors**

*IL-6 and VEGF mediated tubule formation of HUVECs:*

TAF protein of KSI-501 was also tested in an endothelial cell tubule formation assay. Treatment of HUVECs seeded on an extracellular basement membrane matrix (Matrigel) with VEGF and IL-6 together stimulate tubule formation to a higher degree than either treatment alone. The TAF protein of KSI-501 demonstrated superior inhibition of this tubule formation when compared to Eylea or control anti-IL-6 antibody.

Furthermore, quantification of the effects of each inhibitor on twenty parameters of HUVEC tubule formation show that the TAF protein significantly inhibited 17 of 20 angiogenic parameters versus control (compared to 4 of 20 for Eylea and 7 of 20 for control anti-IL-6 antibody). TAF protein was statistically better than Eylea and anti-IL-6 control in 12 of 20 parameters.

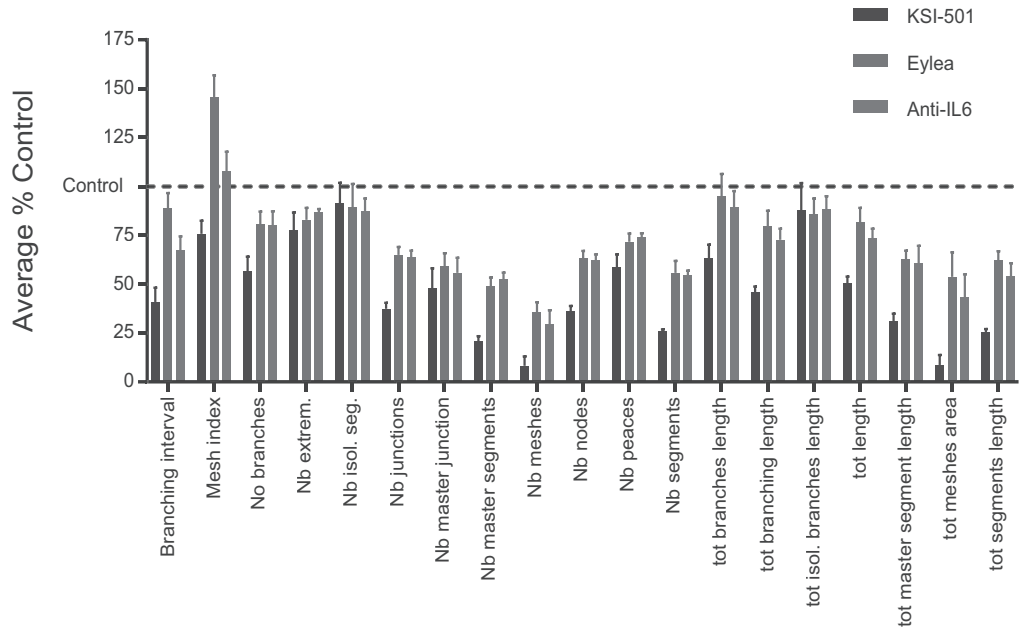



**Figure: Quantification of IL-6/VEGF mediated HUVEC tubule formation in the presence or absence of inhibitor molecules using the Angiogenesis Analyzer plugin for ImageJ**

Together, these data show that the TAF protein of KSI-501 can simultaneously bind IL-6 and VEGF to inhibit their downstream angiogenic signaling pathways. We believe that this novel dual inhibitor can provide an alternative option for the treatment of retinal vascular diseases, especially those that have a high inflammatory component and/or that do not respond adequately to anti-VEGF treatments alone.

**Research and Development**

We have committed, and expect to continue to commit, significant resources to enhancing our ABC Platform and developing new product candidates. We have assembled experienced research and development teams at our corporate headquarters with scientific, clinical and regulatory personnel. As of March 6, 2020, we had 31 employees primarily engaged in research and development. Of these employees, 12 hold a Ph.D. degree or M.D. (or equivalent) degree. From time to time we engage individuals to assist with certain research and development activities on a contractual basis for limited time periods. Our research and development expenses for the years ended December 31, 2019, 2018 and 2017 were $37.5 million, $18.8 million and $22.0 million, respectively.

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

The key competitive factors affecting the success of KSI-301, if approved, are likely to be its efficacy, safety, method and frequency of administration, on-mechanism durability of therapeutic effect, convenience, price, the level of generic competition and the availability of coverage and reimbursement from government and other third-party payors. The method of administration of KSI-301, intravitreal injection, is commonly used to administer ophthalmic drugs for the treatment of severe disease and is generally accepted by patients facing the prospect of severe visual loss or blindness. However, a therapy that offers a less invasive method of administration might have a competitive advantage over one administered by intravitreal injection, depending on the relative safety of the other method of administration.

The current standard of care for wet AMD and advanced stages of DR is monotherapy administration of anti-VEGF drugs, principally Avastin, Lucentis and Eylea, which are well-established therapies and are widely accepted by physicians, patients and third-party payors. Physicians, patients and third-party payors may not accept the addition of KSI-301 to their current treatment regimens for a variety of potential reasons, including:

- if they do not wish to incur the additional cost of KSI-301;
- if they perceive the addition of KSI-301 to be of limited benefit to patients;
- if they wish to treat with more than an anti-VEGF drug;
- if sufficient coverage and reimbursement are not available;
- if they do not perceive KSI-301 to have a favorable risk-benefit profile.

We are developing KSI-301 as an alternative to existing anti-VEGF drugs, including Avastin, Lucentis and Eylea. Accordingly, KSI-301 would directly compete with these therapies. While we believe KSI-301 will compete favorably with existing anti-VEGF drugs, future approved standalone or combination therapies for wet AMD with demonstrated improved efficacy over KSI-301 or currently marketed therapies with a favorable safety profile and any of the following characteristics might pose a significant competitive threat to us:

- a mechanism of action that does not involve VEGF;
- a duration of action that obviates the need for frequent intravitreal injection;
- a method of administration that avoids intravitreal injection; and
- significant cost savings or reimbursement advantages compared to KSI-301 and other anti-VEGF therapies.

Our commercial opportunity could be reduced or eliminated if one or more of 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 any products that we may develop. A drug with greater convenience than KSI-301 might make such a drug more attractive to physicians and patients. An anti-VEGF gene therapy product might substantially reduce the number and frequency of intravitreal injections when treating wet AMD, DME, RVO, or DR, making KSI-301 unattractive to physicians and patients. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected because in many cases insurers or other third-party payors seek to encourage the use of generic products.

In addition to currently available therapies, we are aware of a number of products in preclinical research and clinical development by third parties to treat wet AMD, DME, RVO and DR. We expect that product candidates currently in clinical development, or that could enter clinical development in the near future, that inhibit the function of VEGF or inhibit the function of both VEGF and other factors, could represent significant competition if approved. These product candidates may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. For example, Novartis has recently received FDA and EMA approval for BeoVu (brolucizumab) for the treatment of wet AMD, and is studying BeoVu as a potential treatment option for patients with DME and RVO. In addition, Allergan is developing a competing anti-VEGF therapy, abicipar, which is part of a new class of drugs called DARPin therapies that uses genetically modified antibody proteins. Positive efficacy data from Allergan's Phase 3 studies for abicipar in wet AMD were reported in 2018, demonstrating non-inferiority to ranibizumab but with a 15% incidence rate of ocular inflammation in the abicipar groups. There are also several companies and research organizations pursuing treatments targeting other molecular targets, potential gene therapy treatments, stem cell transplant treatments and medical devices for the treatment of wet AMD, DME, DR, and RVO.

Because there are a variety of means to treat wet AMD, DME, DR, and RVO, our patents and other proprietary protections for KSI-301 will not prevent development or commercialization of product candidates that are different from KSI-301.

**Funding agreement**

On December 1, 2019, we, and our subsidiary, Kodiak Sciences GmbH, entered into a funding agreement to sell a capped royalty right on global net sales of KSI-301 to BBA for $225,000,000. Under the funding agreement, BBA purchased the right to receive a capped 4.5% royalty on net sales following marketing approval of KSI-301 in exchange for $225,000,000 in committed development funding payable to us. Unless earlier terminated or re-purchased by us, the royalty "caps" or terminates upon the date that BBA has received an aggregate amount equal to 4.5 times the funding amount paid to us. Under the terms of the funding agreement, BBA was required to pay the first $100,000,000 of the funding amount at the closing of the funding transaction and the remaining $125,000,000 of the funding amount upon achieving 50% enrollment in our two planned pivotal clinical studies of KSI-301 in patients with RVO. We have the option, exercisable at any point during the term of the funding agreement, to repurchase from BBA 100% of the royalties due to BBA under the funding agreement for a purchase price equal to the funding amount paid to us as of such time times 4.5, less amounts paid by us to BBA. Under the funding agreement, BBA also received a right to a royalty interest on future net sales following marketing approval of other of our products that employ an anti-VEGF A, or VEGF-A, biology as a sole molecular or chemical biology. In the event we commercialize related products that contain both an anti-VEGF-A biology together with at least one additional molecular or chemical biology(ies), BBA would have the right to receive a fractional royalty of up to 2.25% for one additional molecular or chemical biology or 1.5% for two additional molecular or chemical biologies provided that such other products are being progressed in indications for, or patient populations with, retinal vein occlusion, wet AMD or diabetic macular edema, or indications or patient populations in which KSI-301 or a VEGF-A product has received marketing approval. Total royalty payments under the funding agreement are not to exceed the cap of 4.5 times the funding amount paid to us. The funding agreement was the result of a competitive process overseen by independent and disinterested directors of Kodiak with the assistance of outside counsel.

**Government Regulation**

Government authorities in the United States at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products. Generally, before a new drug or biologic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

***U.S. Drug Development***

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

Any future product candidates must be approved by the FDA through either a new drug application, or NDA, or a biologics license application, or BLA, process before they may be legally marketed in the United States. The process generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice, or GLP, requirements;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;

- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practice, or GCP, requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of an NDA or BLA;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to accept the filing for review;
- satisfactory completion of a FDA pre-approval inspection of the manufacturing facility or facilities where the drug or biologic will be produced to assess compliance with current good manufacturing practices, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug or biologic's identity, strength, quality and purity;
- potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of the NDA or BLA;
- FDA review and approval of the NDA or BLA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug or biologic in the United States; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

The data required to support an NDA or BLA are generated in two distinct developmental stages: preclinical and clinical. The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any future product candidates will be granted on a timely basis, or at all.

***Preclinical Studies and IND***

The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and must become effective before human clinical trials may begin.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as in vitro and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time, the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

***Clinical Trials***

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA or BLA. The FDA will accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials in the United States generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug.
- Phase 2 clinical trials involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

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

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or in vitro testing that suggest a significant risk for human subjects and any clinically important increase in the rate 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, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biologic has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the drug or biologic as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that our product candidates do not undergo unacceptable deterioration over their shelf life.

***NDA/BLA Review Process***

Following completion of the clinical trials, data are analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA or BLA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. In short, the NDA or BLA is a request for approval to market the drug or biologic for one or more specified indications and must contain proof of safety and efficacy for a drug or safety, purity and potency for a biologic. The application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of FDA. FDA approval of an NDA or BLA must be obtained before a drug or biologic may be marketed in the United States.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA or BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual product fee for human drugs and biologics and an annual establishment fee on facilities used to manufacture prescription drugs and biologics. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs or BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted NDAs and BLAs before it accepts them for filing, and may request additional information rather than accepting the NDA or BLA for filing. The FDA must make a decision on accepting an NDA or BLA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA or BLA. 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 new molecular-entity NDA or original BLA and respond to the applicant, and six months from the filing date of a new molecular-entity NDA or original BLA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs or BLAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving an NDA or BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates an NDA or BLA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA or BLA identified by the FDA. The Complete Response Letter may require additional clinical 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 Complete Response Letter is issued, the applicant may either resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

***Expedited Development and Review Programs***

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs and biologics that meet certain criteria. Specifically, new drugs and biologics are eligible for fast track designation if they are intended to treat a serious or life threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for fast track status any time before receiving NDA or BLA approval, but ideally no later than the pre-NDA or pre-BLA meeting.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies.

A product may also be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug or biologic shown to be effective can be safely used only if distribution or use is restricted, it may require such post-marketing restrictions, as it deems necessary to assure safe use of the product.

Additionally, a drug or biologic may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Fast track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process.

***Abbreviated Licensure Pathway of Biological Products as Biosimilar or Interchangeable***

The Patient Protection and Affordable Care Act, or PPACA, or Affordable Care Act, or ACA, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products shown to be highly similar to an FDA-licensed reference biological product. The BPCIA attempts to minimize duplicative testing, and thereby lower development costs and increase patient access to affordable treatments. An application for licensure of a biosimilar product must include information demonstrating biosimilarity based upon the following, unless the FDA determines otherwise:

- analytical studies demonstrating that the proposed biosimilar product is highly similar to the approved product notwithstanding minor differences in clinically inactive components;
- animal studies (including the assessment of toxicity); and
- a clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) sufficient to demonstrate safety, purity and potency in one or more conditions for which the reference product is licensed and intended to be used.

In addition, an application must include information demonstrating that:

- the proposed biosimilar product and reference product utilize the same mechanism of action for the condition(s) of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent the mechanism(s) of action are known for the reference product;
- the condition or conditions of use prescribed, recommended, or suggested in the labeling for the proposed biosimilar product have been previously approved for the reference product;
- the route of administration, the dosage form, and the strength of the proposed biosimilar product are the same as those for the reference product; and
- the facility in which the biological product is manufactured, processed, packed or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

Biosimilarity means that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and that there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. In addition, the law provides for a designation of "interchangeability" between the reference and biosimilar products, whereby the biosimilar may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product. The higher standard of interchangeability must be demonstrated by information sufficient to show that:

- the proposed product is biosimilar to the reference product;
- the proposed product is expected to produce the same clinical result as the reference product in any given patient; and
- for a product that is administered more than once to an individual, the risk to the patient in terms of safety or diminished efficacy of alternating or switching between the biosimilar and the reference product is no greater than the risk of using the reference product without such alternation or switch.

FDA approval is required before a biosimilar may be marketed in the United States. However, complexities associated with the large and intricate structures of biological products and the process by which such products are manufactured pose significant hurdles to the FDA's implementation of the law that are still being worked out by the FDA. For example, the FDA has discretion over the kind and amount of scientific evidence—laboratory, preclinical and/or clinical—required to demonstrate biosimilarity to a licensed biological product.

The FDA intends to consider the totality of the evidence, provided by a sponsor to support a demonstration of biosimilarity, and recommends that sponsors use a stepwise approach in the development of their biosimilar products. Biosimilar product applications thus may not be required to duplicate the entirety of preclinical and clinical testing used to establish the underlying safety and effectiveness of the reference product. However, the FDA may refuse to approve a biosimilar application if there is insufficient information to show that the active ingredients are the same or to demonstrate that any impurities or differences in active ingredients do not affect the safety, purity or potency of the biosimilar product. In addition, as with BLAs, biosimilar product applications will not be approved unless the product is manufactured in facilities designed to assure and preserve the biological product's safety, purity and potency.

The submission of a biosimilar application does not guarantee that the FDA will accept the application for filing and review, as the FDA may refuse to accept applications that it finds are insufficiently complete. The FDA will treat a biosimilar application or supplement as incomplete if, among other reasons, any applicable user fees assessed under the Biosimilar User Fee Act of 2012 have not been paid. In addition, the FDA may accept an application for filing but deny approval on the basis that the sponsor has not demonstrated biosimilarity, in which case the sponsor may choose to conduct further analytical, preclinical or clinical studies and submit a BLA for licensure as a new biological product.

The timing of final FDA approval of a biosimilar for commercial distribution depends on a variety of factors, including whether the manufacturer of the branded product is entitled to one or more statutory exclusivity periods, during which time the FDA is prohibited from approving any products that are biosimilar to the branded product. The FDA cannot approve a biosimilar application for twelve years from the date of first licensure of the reference product. Additionally, a biosimilar product sponsor may not submit an application for four years from the date of first licensure of the reference product. A reference product may also be entitled to exclusivity under other statutory provisions. For example, a reference product designated for a rare disease or condition (an "orphan drug") may be entitled to seven years of exclusivity, in which case no product that is biosimilar to the reference product may be approved until either the end of the twelve-year period provided under the biosimilarity statute or the end of the seven-year orphan drug exclusivity period, whichever occurs later. In certain circumstances, a regulatory exclusivity period can extend beyond the life of a patent, and thus block biosimilarity applications from being approved on or after the patent expiration date. In addition, the FDA may under certain circumstances extend the exclusivity period for the reference product by an additional six months if the FDA requests, and the manufacturer undertakes, studies on the effect of its product in children, a so-called pediatric extension.

The first biological product determined to be interchangeable with a branded product for any condition of use is also entitled to a period of exclusivity, during which time the FDA may not determine that another product is interchangeable with the reference product for any condition of use. This exclusivity period extends until the earlier of: (1) one year after the first commercial marketing of the first interchangeable product; (2) 18 months after resolution of a patent infringement against the applicant that submitted the application for the first interchangeable product, based on a final court decision regarding all of the patents in the litigation or dismissal of the litigation with or without prejudice; (3) 42 months after approval of the first interchangeable product, if a patent infringement suit against the applicant that submitted the application for the first interchangeable product is still ongoing; or (4) 18 months after approval of the first interchangeable product if the applicant that submitted the application for the first interchangeable product has not been sued.

***Post-Approval Requirements***

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping requirements, requirements to report adverse experiences, and comply with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug or biologic, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA/BLA or NDA/BLA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy, or REMS, to assure the safe use of the product. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions 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 studies;
- refusal of the FDA to approve pending applications or supplements to approved applications;
- 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 marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs and biologics may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

***Other U.S. Regulatory Matters***

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

For example, in the United States, our business operations, including any sales, marketing and scientific and educational programs, also must comply with state and federal fraud and abuse laws, including the federal Anti-Kickback Statue and false claims laws; federal data privacy and security laws; and federal transparency laws related to payments and/or other transfers of value made to physicians and other healthcare professionals and teaching hospitals. The federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act. Federal false claims laws, including the False Claims Act, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment of federal funds, and knowingly making, or causing to be made, a false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government.

Many states have similar laws and regulations that may differ from federal law in significant ways, thus complicating compliance efforts. For example, states have anti-kickback and false claims laws that may be broader in scope than analogous federal laws and may apply regardless of payer. In addition, state data privacy laws that protect the security of health information may differ from each other and may not be preempted by federal law. Moreover, several states have enacted legislation requiring pharmaceutical manufacturers to, among other things, establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales and marketing activities, report information related to drug pricing, require the registration of sales representatives, and prohibit certain other sales and marketing practices.

Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of biologic and pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in significant penalties, including administrative, civil, and criminal penalties, fines, imprisonment, disgorgement, injunctions, exclusion from participation in federal healthcare programs, integrity oversight and reporting obligations, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (1) changes to our manufacturing arrangements; (2) additions or modifications to product labeling; (3) the recall or discontinuation of our products; or (4) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. Further, the United States, there have been and continue to be a number of healthcare-related legislative initiatives that have significantly affected the healthcare industry. For example, there remain judicial challenges to certain aspects of the ACA. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case, and has allotted one hour for oral arguments, which is expected to occur in the fall. It is unclear how such litigation and other efforts to repeal and replace the ACA will impact the ACA. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

***U.S. Patent-Term Restoration and Marketing Exclusivity***

Depending upon the timing, duration and specifics of FDA approval of any future product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent-term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of a NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for a NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

A reference biological product is granted twelve years of data 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. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or

licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

***European Union Drug Development***

As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. Recently enacted Clinical Trials Regulation EU No 536/2014 ensures that the rules for conducting clinical trials in the EU will be identical. In the meantime, Clinical Trials Directive 2001/20/EC continues to govern all clinical trials performed in the EU.

***European Union Drug Review and Approval***

In the European Economic Area, or EEA, which is comprised of the 27 Member States of the European Union (including Norway and excluding Croatia), Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations.

- The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (*i.e.,* in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, 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.

***People's Republic of China Drug Regulation***

China heavily regulates the development, approval, manufacturing and distribution of drugs, including biologics. The specific regulatory requirements applicable depend on whether the drug is made and finished in China, which is referred to as a domestically manufactured drug, or made abroad and imported into China in finished form, which is referred to as an imported drug, as well as the approval or "registration" category of the drug. For both imported and domestically manufactured drugs, China typically requires regulatory approval for a clinical trial, or CTA, prior to submitting an application for marketing approval. For a domestically manufactured drug, there is also a requirement for a drug manufacturing license for a facility in China.

In 2017, the drug regulatory system entered a new and significant period of reform. The State Council and the China Communist Party jointly issued the Opinion on Deepening the Reform of the Regulatory Approval System to Encourage Innovation in Drugs and Medical Devices, or the Innovation Opinion. The expedited programs and other advantages under this and other recent reforms encourage drug manufacturers to seek market approval in China first, manufacture domestically, and develop drugs in high priority disease areas.

To implement the regulatory reform introduced by the Innovation Opinion, the China Drug Authority, or CDA, is currently revising the fundamental laws, regulations and rules regulating pharmaceutical products and the industry, which include the framework law known as the PRC Drug Administration Law, or DAL. The DAL is also generally implemented by a set of regulations issued by the State Council referred to as the DAL Implementing Regulation. The CDA has its own set of regulations implementing the DAL; the primary one governing clinical trial applications, marketing approval, and license renewal and amendment is known as the Drug Registration Regulation. However, the implementing regulations for many of the reforms in the Innovation Opinion had not been announced, and therefore, the details in the implementation of the regulatory changes remained uncertain in some respects.

*Regulatory Authorities and Recent Government Reorganization*

In the PRC, the CDA is the primary regulator for pharmaceutical products and businesses. It regulates almost all of the key stages of the life-cycle of pharmaceutical products, including nonclinical studies, clinical trials, marketing approvals, manufacturing, advertising and promotion, distribution, and pharmacovigilance (*i.e.,* post-marketing safety reporting obligations). The CDE, which is under the CDA, conducts the technical evaluation of each drug and biologic application for safety and effectiveness.

The National Health and Family Planning Commission, or NHFPC, formerly known as the Ministry of Health, or MOH, is China's chief healthcare regulator. It is primarily responsible for overseeing the operation of medical institutions, which also serve as clinical trial sites, and regulating the licensure of hospitals and other medical personnel. NHFPC plays a significant role in drug reimbursement. Furthermore, the NHFPC and its local counterparts at or below the provincial-level of local government also oversee and organize public medical institutions' centralized bidding and procurement process for pharmaceutical products. This is the chief way that public hospitals and their internal pharmacies acquire drugs.

China has recently reorganized the agencies that regulate drugs, healthcare, and the state health insurance plans, although it is still not entirely clear what effect on policy these changes will ultimately have in terms of making the drug approval process more efficient. The drug regulatory agency, CFDA, is merged into a State Administration on Market Regulation, or SAMR, along with other agencies that regulate consumer protection, product quality and anti-monopoly. The drug, device and cosmetic regulatory functions of CFDA is put under the CDA, which is subordinate to the SAMR. The National Health Commission, or the NHC, will be the healthcare regulator replacing the NHFPC, and a new, separate State Medical Insurance Bureau will focus on regulating reimbursement under the state-sponsored insurance plans.

*Pre-Clinical and Clinical Development*

The CDA requires both pre-clinical and clinical data to support registration applications for imported and domestic drugs. Pre-clinical work, including pharmacology and toxicology studies, must meet the GLP, issued in July 2017. The CDA accredits GLP labs and requires that nonclinical studies on chemical drug substances and preparations and biologics that are not yet marketed in China be conducted there. There are no approvals required from the CDA to conduct pre-clinical studies.

*Registration Categories*

Prior to engaging with the CDA on research and development and approval, an applicant will need to determine the registration category for its drug candidate (which will ultimately need to be confirmed with the CDA), which will determine the requirements for its clinical trial and marketing application. There are five categories for small molecule drugs: Category 1 ("innovative drugs") refers to drugs that have a new chemical entity that has not been marketed anywhere in the world, Category 2 ("improved new drugs") refers to drugs with a new indication, dosage form, route of administration, combination, or certain formulation changes not approved in the world, Categories 3 and 4 are for generics that reference an innovator drug (or certain well-known generic drugs) marketed either abroad or in China, respectively, and Category 5 refers to originator or generic drugs that have already been marketed abroad but are not yet approved in China (*i.e.*, many imported drugs).

Therapeutic biologics follow a similar categorization, with Category 1 being new to the world, but with fifteen product-specific categories. Like with small molecule drugs, Category 1 for biologics is also for innovative biologics that have not been approved inside or outside of China. A clear regulatory pathway for biosimilars does not yet exist, but the CDA may soon develop one in its revision of implementing rules pursuant to the Innovation Opinion. We have not yet discussed with the CDA the categorization of any of our product candidates, including KSI-301.

*Expedited Programs – Priority Evaluation and Approval Programs to Encourage Innovation*

The CDA has adopted several expedited review and approval mechanisms since 2009 and created additional expedited programs in recent years that are intended to encourage innovation. Applications for these expedited programs can be submitted after the CTA is admitted for review by the CDE. If admitted to one of these expedited programs, an applicant will be entitled to more frequent and timely communication with reviewers at the CDE, expedited review and approval, and more agency resources throughout the approval process.

*Clinical Trials and Marketing Approval*

Upon completion of pre-clinical studies, a sponsor typically needs to conduct clinical trials in China for registering a new drug in China. The materials required for this application and the data requirements are determined by the registration category. The CDA has taken a number of steps to increase efficiency for approving CTAs, and it has also significantly increased monitoring and enforcement of GCP to ensure data integrity.

*Trial Approval*

All clinical trials conducted in China must be approved and conducted at hospitals accredited by the CDA. For imported drugs, proof of foreign approval is required prior to the trial, unless the drug has never been approved anywhere in the world. In addition to a standalone China trial to support development, imported drug applicants may establish a site in China that is part of an international multicenter trial, or IMCT, at the outset of the global trial. Domestically manufactured drugs are not subject to foreign approval requirements, and in contrast to prior practice, the CDA has recently indicated its intent to permit those drugs to conduct development via an IMCT as well.

In 2015, the CDA began to issue an umbrella approval for all phases (typically three) of a new drug clinical trial, instead of issuing approval phase by phase. For certain types of new drug candidates, clinical trial applications may be prioritized over other applications, and put in a separate expedited queue for approval. Other trials that are not part of these expedited lines could still wait up to a year for approval to conduct the trial.

The Innovation Opinion also introduces a notification system for new drug clinical trial approval. In other words, trials can proceed if after certain fixed period of time (possibly 60 days), the applicant has not received any objections from the CDE, as opposed to the lengthier current clinical trial pre-approval process in which the applicant must wait for affirmative approval. The Innovation Opinion also promises to expand the number of trial sites by truncating the timeline for accreditation by converting it from a pre-approval procedure into a notification procedure. These reforms will require implementing law and regulations in order to proceed in practice. The CDA proposed implementing legislation in 2017 but it has not yet been finalized.

*Clinical Trial Process and Good Clinical Practices*

Typically drug clinical trials in China have three phases. Phase 1 refers to the initial clinical pharmacology and human safety evaluation studies. Phase 2 refers to the preliminary evaluation of a drug candidate's therapeutic efficacy and safety for target indication(s) in patients. Phase 3 (often the pivotal study) refers to clinical trials to further verify the drug candidate's therapeutic efficacy and safety on patients with target indication(s) and ultimately provide sufficient evidence for the review of drug registration application. The CDA requires that the different phases of clinical trials in China receive ethics committee approval prior to approval of the CTA and comply with GCP. The CDA conducts inspections to assess GCP compliance and will cancel the CTA if it finds substantial issues.

The CDA may reduce requirements for trials and data, depending on the drug and the existing data. The CDA has granted waivers for all or part of trials, but it is now planning to take a more official position on the acceptance of foreign data to support an application. The foreign data must meet the CDA's requirements, including, for drugs that have never been approved before in China, having sufficient Chinese ethnic data. The precise requirements are not yet clear.

*New Drug Application (NDA) and Approval*

Upon completion of clinical trials, a sponsor may submit clinical trial data to support marketing approval for the drug. For imported drugs, this means issuance of an import license. Again, the applicant must submit evidence of foreign approval, unless it is an innovative drug that has never been approved anywhere in the world.

Domestically manufactured drugs must similarly submit data in support of a drug approval number. Under the current regime, upon approval of the registration application, the CDA will first issue a new drug certificate to the applicant. Only when the applicant is equipped with relevant manufacturing capability will the CDA issue a Drug Approval Serial Number, which is effectively the marketing approval allowing the holder to market/commercialize the drug in China.

Under the authorization of the Standing Committee of the National People's Congress, the State Council issued the Pilot Plan for the Drug Marketing Authorization Holder Mechanism on May 26, 2016, which provided a detailed pilot plan for the marketing authorization holder system, or MAH pilot program. Domestically established research institutions (including domestic companies) could apply through an MAH pilot program if they were established in one of 10 designated provinces (including Beijing and Shanghai) in China. The MAH pilot program permitted research institutions and individuals to develop and hold the marketing approvals for drugs without holding a drug manufacturing license. The marketing authorization holders, or MAHs, could engage contract manufacturers and distributors.

In August 2019, the DAL was revised to contain a dedicated chapter on the MAH system. Upon the enactment of the revised DAL, the MAH system was no longer be a pilot program and was implemented nationwide. Subject to approval by the National Medical Products Administration, MAHs will be allowed to transfer their marketing authorizations. It is not sure whether the transferability of MAH will offer more flexibility in structuring cross-border transactions. In addition, the implementation of the MAH system will be accompanied by a range of new requirements for the MAHs. For example, a MAH must establish a quality assurance system and be responsible for the whole process and all aspects of preclinical research, clinical trials, manufacturing and distribution, post-marketing research, adverse drug reaction monitoring and reporting. A foreign MAH will be required to engage a local agent to fulfill the MAH's obligations and the foreign MAH shall be subject to joint and several liability in the event of any wrongdoing. It is unclear how the scope of such joint liability will be defined.

*New Drug Monitoring Period*

Currently, new varieties of domestically produced drugs approved under Categories 1 or 2 in China may be placed under a monitoring period for three to five years. Category 1 innovative drugs will be monitored for five years. During the monitoring period, the CDA will not approve another CTA from another applicant for the same type of drug, except if another sponsor has an approved CTA at the time that the monitoring period is initiated it may proceed with its trial and become part of the period. Therefore, by blocking other CTAs, the monitoring period can act as a type of market exclusivity.

*Acceptance of Foreign Clinical Trial Studies*

On July 10, 2018, the CDA issued the Technical Guidance Principles on Accepting Foreign Drug Clinical Trial Data, or the Guidance Principles, as one of the implementing rules for the Innovation Opinion. According to the Guidance Principles, sponsors may use the data of foreign clinical trials to support drug registration in China, provided that sponsors must ensure the authenticity, completeness and accuracy of foreign clinical trial data and such data must be obtained consistent with the relevant requirements under the Good Clinical Trial Practice (GCP) of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Sponsors must also comply with other relevant sections of the Drug Registration Regulation when applying for drug registrations in China using foreign clinical trial data.

*Post-Marketing Surveillance*

The manufacturer or marketing authorization holder of marketing approval is primarily responsible for pharmacovigilance, including quality assurance, adverse reaction reporting and monitoring, and product recalls. Distributors and user entities (e.g., hospitals) are also required to report, in their respective roles, adverse reactions of the products they sell or use, and assist with the manufacturer of the product recall. A drug that is currently under the new drug monitoring period has to report all adverse drug reactions (as opposed to just serious adverse reactions) for that period.

*Advertising and Promotion of Pharmaceutical Products*

China has a strict regime for the advertising of approved medicines. No unapproved medicines may be advertised. The definition of an advertisement is very broad, and does not exclude scientific exchange. It can be any media that directly or indirectly introduces the product to end users. There is no clear line between advertising and any other type of promotion.

*Other PRC national- and provincial-level laws and regulations*

We are subject to changing regulations under many other laws and regulations administered by governmental authorities at the national, provincial and municipal levels, some of which are or may become applicable to our business. For example, regulations control the confidentiality of patients' medical information and the circumstances under which patient medical information may be released for inclusion in our databases, or released by us to third parties. The privacy of human subjects in clinical trials is also protected under regulations, e.g., the case report forms must avoid disclosing names of the human subjects.

These laws and regulations governing both the disclosure and the use of confidential patient medical information may become more restrictive in the future, including restrictions on transfer of healthcare data. The Cybersecurity Law that took effect in 2017 designates healthcare as a priority area that is part of critical information infrastructure, and China's cyberspace administration is trying to finalize a draft rule on cross-border transfer of personal information.

***Coverage and Reimbursement***

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. In the United States no uniform policy of coverage and reimbursement for drug or biological products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the ACA contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs.

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP and adding a new rebate calculation for "line extensions" (*i.e.,* new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits. The Centers for Medicare & Medicaid Services, or CMS, have proposed to expand Medicaid rebate liability to the territories of the United States as well.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise

obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. In 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs. In addition, as 340B drug prices are determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. An increasing emphasis on cost containment measures in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

**Intellectual Property**

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to our business, including seeking, maintaining, and defending patent rights. We seek to protect our proprietary position by, among other methods, filing patent applications in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates and continuing innovation to develop, strengthen, and maintain our proprietary position in the field. Although we are not party to any material in-license agreements as of the date of this annual report, we may in the future pursue in-licensing opportunities to strengthen our proprietary position in the field. We additionally rely on data exclusivity, market exclusivity, and patent term extensions when available, and may seek and rely on regulatory protection afforded through orphan drug designations. Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions, and improvements; to preserve the confidentiality of our trade secrets; to defend and enforce our proprietary rights, including our patents; and to operate without infringing the valid and enforceable patents and other proprietary rights of third parties.

We have prosecuted numerous patents and patent applications and possess know-how and trade secrets relating to the development and commercialization of our ABC Platform and product candidates, including related manufacturing processes and technology. As of December 31, 2019, we were the assignee of record for approximately four U.S. issued patents, and approximately twelve U.S. pending patent applications directed to certain of our proprietary technology, inventions, and improvements and our most advanced product candidates, as well as approximately 21 patents issued in jurisdictions outside of the United States and approximately 51 patent applications pending in jurisdictions outside of the United States that, in many cases, are counterparts to the foregoing U.S. patents and patent applications. We also have one pending PCT application. For example, these patents and patent applications include claims directed to:

- therapeutic proteins and biologically active agents conjugated to a biopolymer, which comprise our ABC Platform;
- specific therapeutics, including KSI-301; and
- components of our therapeutics.

The following patents and patent applications (including anticipated 20-year expiration dates, which could be altered by, for example, a disclaimer, patent term adjustment or patent term extension) relate to KSI-301 and/or ABC Platform:

| Patent and Patent Application Numbers | Anticipated U.S. Expiration Date | Description of Representative U.S. Claims |
|---|---|---|
| US 8,846,021, US Appl. No. 16/424265, EP Patent No. 1988910, JP Patent No. 5528710, JP Patent No. 5745009, and foreign applications in certain jurisdictions claiming priority to PCT/US2007/005372 | 2/28/2027 | Representative claims include conjugates |
| US Appl. No. 15/368,376, AU Patent No. 2011239434, AU Patent No. 2017201930, CA Patent No. 2795667, EP Patent No. 2558538, JP Patent No. 6568748, MX Patent No. 365521, and foreign applications in certain jurisdictions claiming priority to PCT/US2011/032768 | 4/15/2031 | Representative claims include conjugates |
| US 8,765,432, US Appl. No. 15/099,234, AU Patent No. 2010330727, CA Patent No. 2783615, EP Patent No. 2512462, CN Patent No. ZL201080062252.7, IN Patent No. 319269, JP Patent No. 5760007, JP Patent No. 5990629, JP Patent No. 6416832, MX Patent No. 346423, KR Patent No. 10-1852044, MO Patent No. J/002943, and foreign applications in certain jurisdictions claiming priority to PCT/US2010/061358 | 5/10/2030 | Representative claims include copolymers and methods of making copolymers (ABC Platform specifically) |
| US Appl. No. 14/916,180, JP Patent No. 6463361, and foreign applications in certain jurisdictions claiming priority to PCT/US2014/054622 | 9/8/2034 | Representative claims include polymers and method of making polymers |
| US Appl. No. 15/394500 and foreign applications in certain jurisdictions claiming priority to PCT/US2016/069336 | 12/29/2036 | Representative claims include antibody and antibody conjugate claims, as well as methods of making and using the conjugates |

In the normal course of business, we intend to pursue, when possible, composition, method of use, dosing and formulation patent protection, as well as manufacturing and drug development processes and technology. The patents and patent applications we have filed outside of the United States are in Europe, Japan, and various other jurisdictions.

Individual patents extend for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance, and the legal term of patents in the countries in which they are obtained. Generally, patents issued for applications filed in the United States are effective for 20 years from the earliest effective filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The duration of patents outside of the United States varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date.

Our issued U.S. patents will expire on dates ranging from 2027 to 2035. If patents are issued on our pending patent applications, the resulting patents are projected to expire on dates ranging from 2027 to 2040. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent.

We have filed 26 trademark applications. These include three applications that have matured to registration in the United States, two of which have been cancelled. One application has been abandoned in the United States. Eleven of our applications have matured to registration, of which six are in China, and one is in each of Canada, the European Union, Japan, Singapore and Switzerland. We have eleven pending trademark applications, of which three are in the United States and eight are in China. We also may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets are difficult to protect. We seek to protect our technology and product candidates, in part, by entering into confidentiality agreements with those who have access to our confidential information, including our employees, contractors, consultants, collaborators, and advisors. We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations, and systems, agreements or security measures may be breached and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or may be independently discovered by competitors. To the extent that our employees, contractors, consultants, collaborators, and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For this and more comprehensive risks related to our proprietary technology, inventions, improvements and products, please see the section on "Risk Factors—Risks Related to Intellectual Property."

We are also a party to an assignment and license agreement with a former collaborator, whereby we were assigned and non-exclusively licensed certain intellectual property relating to KSI-201 and related technology. Under this agreement, we agreed to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize KSI-201, and will owe milestone payments to our former collaborator upon the achievement of certain milestones related to KSI-201, as well as a low single digit percentage royalty on net sales of KSI-201. The assignment and license agreement includes customary termination provisions, including the right of the company to terminate for convenience and the right of either party to terminate for cause.

**Employees**

As of March 6, 2020, we had 39 employees, all of whom were full-time. 31 employees were primarily engaged in research and development activities, of whom 12 hold a Ph.D. degree or M.D. (or equivalent) degree. Substantially all of our employees are located in Palo Alto, California. None of our employees are represented by a labor union or covered under a collective bargaining agreement.

**Legal Proceedings**

As of the date of this annual report, we are not a party to any material legal proceedings. In the normal course of business, we may be named as a party to various legal claims, actions and complaints. We cannot predict whether any resulting liability would have a material adverse effect on our financial position, results of operations or cash flows.

**Corporate Information**

We were formed as a limited liability company on June 22, 2009 under the name Oligasis LLC, and subsequently changed our name to Kodiak Sciences Inc. and converted into a corporation which was incorporated in the state of Delaware on September 8, 2015. Our mailing address and executive offices are located at 2631 Hanover Street, Palo Alto, California. We maintain an internet website at the following address: https://kodiak.com. The information on our website is not incorporated by reference in this annual report on Form 10-K or in any other filings we make with the Securities and Exchange Commission, or SEC.

We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the SEC in accordance with the Securities Exchange Act of 1934, as amended. These include our annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC.

## ITEM 1A. RISK FACTORS

You should consider carefully the following risk factors, together with all the other information in this report, including the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section and our consolidated financial statements and notes thereto. The occurrence of any events described in the following risk factors and the risks described elsewhere in this report could harm our business, operating results, financial condition, and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements that we have made in this report and those we may make from time to time. You should consider all of the risk factors described when evaluating our business.

### Risks Related to Our Business, Financial Condition and Capital Requirements

***We are in the early clinical stage of drug development and have a very limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.***

We are a clinical stage biopharmaceutical company specializing in novel therapeutics to treat chronic, high-prevalence retinal diseases. We commenced operations in June 2009, have no products approved for commercial sale and have not generated any revenue. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have enrolled 121 patients with wet AMD, DME, or RVO in our Phase 1b multiple-dose clinical trial of KSI-301 and we are currently enrolling wet AMD patients in our pivotal 'DAZZLE' clinical trial of KSI-301. We have not initiated clinical trials for any of our other product candidates. To date, we have not completed a pivotal clinical trial, obtained marketing approval for any product candidates, manufactured a commercial scale product, or conducted sales and marketing activities necessary for successful product commercialization. Our limited operating history as a company and early stage of drug development make any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer.

***We have incurred significant net losses in each period since our inception and anticipate that we will continue to incur significant and increasing net losses for the foreseeable future.***

We have incurred net losses in each reporting period since our inception, including net losses of $47.4 million, $41.4 million and $27.9 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had an accumulated deficit of $158.1 million.

We have invested significant financial resources in research and development activities, including for our product candidates and our ABC Platform. We do not expect to generate revenue from product sales for several years, if at all. The amount of our future net losses will depend, in part, on the level of our future expenditures and our ability to generate revenue. Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We expect to continue to incur significant and increasingly higher expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- progress our current and any future product candidates through preclinical and clinical development;
- work with our contract manufacturers to scale up the manufacturing processes for our product candidates or, in the future, establish and operate a manufacturing facility;
- continue our research and discovery activities;
- continue the development of our ABC Platform;
- initiate and conduct additional preclinical, clinical or other studies for our product candidates;
- change or add additional contract manufacturers or suppliers;
- seek regulatory approvals and marketing authorizations for our product candidates;
- establish sales, marketing and distribution infrastructure to commercialize any products for which we obtain approval;
- acquire or in-license product candidates, intellectual property and technologies;

- make milestone, royalty or other payments due under any current or future collaboration or license agreements;
- obtain, maintain, expand, protect and enforce our intellectual property portfolio;
- attract, hire and retain qualified personnel;
- experience any delays or encounter other issues related to our operations;
- meet the requirements and demands of being a public company; and
- defend against any product liability claims or other lawsuits related to our products.

Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

As of December 31, 2019, we had cash, cash equivalents and marketable securities of $348.2 million. We believe that our cash, cash equivalents and marketable securities will be sufficient to fund our projected operations for at least the next 12 months.

***Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have never generated any revenue from product sales, and we may never generate revenue or be profitable.***

We have no products approved for commercial sale and have not generated any revenue from product sales. We do not anticipate generating any revenue from product sales until after we have successfully completed clinical development and received regulatory approval for the commercial sale of a product candidate, if ever.

Our ability to generate revenue and achieve profitability depends significantly on many factors, including:

- successfully completing research and preclinical and clinical development of our product candidates;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials;
- developing a sustainable and scalable manufacturing process for our product candidates, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and any commercial demand for our product candidates;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- launching and successfully commercializing product candidates for which we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;
- obtaining and maintaining an adequate price for our product candidates, both in the United States and in foreign countries where our products are commercialized;
- obtaining adequate reimbursement for our product candidates from payors;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- maintaining, protecting, expanding and enforcing our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA or foreign regulatory agencies, to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our future collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and ongoing compliance efforts.

Even if we are able to generate revenue from the sale of any approved products, we may not become profitable, and we will need to obtain additional funding through one or more debt or equity financings in order to continue operations. Revenue from the sale of any product candidate for which regulatory approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price and whether we own the commercial rights for that territory. If the number of addressable patients is not as significant as we anticipate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. 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 could 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 pipeline of product candidates or continue our operations and cause a decline in the value of our common stock, all or any of which may adversely affect our viability.

***If we fail to obtain additional financing, we may be unable to complete the development and, if approved, commercialization of our product candidates.***

Our operations have required substantial amounts of cash since inception. To date, we have financed our operations primarily through the sale of equity securities. Developing our product candidates is expensive, and we expect to substantially increase our spending as we advance KSI-301 into Phase 3 clinical trials. Even if we are successful in developing our product candidates, obtaining regulatory approvals and launching and commercializing any product candidate will require substantial additional funding.

As of December 31, 2019, we had cash, cash equivalents and marketable securities of $348.2 million. We believe that our cash, cash equivalents and marketable securities will be sufficient to fund our projected operations for at least the next 12 months. Our estimate as to how long we expect our existing cash, cash equivalents and marketable securities to be available to fund our operations is based on assumptions that may prove inaccurate, and we could deplete our available capital resources sooner than we currently expect. In addition, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

We will require additional capital for the further development and, if approved, commercialization of our product candidates. Additional capital may not be available when we need it, on terms acceptable to us or at all. We have no committed source of additional capital. If adequate capital is not available to us on a timely basis, we may be required to significantly delay, scale back or discontinue our research and development programs or the commercialization of any product candidates, if approved, or be unable to continue or expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations and cause the price of our common stock to decline.

***Due to the significant resources required for the development of our product candidates, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on product candidates that do not yield a successful product and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Due to the significant resources required for the development of our product candidates, we must decide which product candidates and indications to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties in respect of certain product candidates may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our product candidates or misread trends in the biopharmaceutical industry, in particular for retinal diseases, our business, financial condition and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

**Risks Related to the Discovery, Development and Commercialization of Our Product Candidates**

***Our prospects are heavily dependent on KSI-301, which is in the early stages of clinical development and is the only product candidate that we expect to be in clinical development in the near term.***

KSI-301 is our only product candidate that we expect to be in clinical studies in the near term. We initiated an ongoing Phase 1a clinical trial of KSI-301 in July 2018, reached the primary endpoint in September 2018, and we completed the last patient last visit of that Phase 1a portion in November 2018. The Phase 1b extension study dosed first patient in January 2019, is fully enrolled now at 121 patients, and patients continue to be followed towards an 18 month or longer duration of treatment. Patients are also now being enrolled in our DAZZLE wet AMD clinical study which we plan to submit as one of our required registrational studies. It may be years before DAZZLE and/or any other registrational type trial is completed, if at all. Further, we cannot be certain that either KSI-301 or any of our product candidates will be successful in clinical trials.

Our early encouraging preclinical and Phase 1 clinical trial results for KSI-301 are not necessarily predictive of the results of our ongoing or future discovery programs or clinical studies. Our Phase 1 clinical trial was designed to evaluate safety and tolerability of KSI-301. Although it has yielded early evidence of bioactivity, it consisted of only nine subjects. The Phase 1b study is in a larger set of 121 subjects that has generated encouraging safety, efficacy and durability data, yet we expect that our Phase 2 and Phase 3 trials will have different design parameters and be compared against an active comparator agent such as Eylea. Notably, our Phase 1 trial did not evaluate durability of KSI-301 across the planned 12-, 16- or 20- week dosing intervals that we are evaluating in our ongoing DAZZLE trial in wet AMD patients, nor did it evaluate the dosing intervals we are planning for our pivotal trials in the other retinal disease indications. Promising results in preclinical studies and Phase 1 clinical trials of a drug candidate may not be predictive of similar results in later-stage preclinical studies or in humans during clinical studies. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical studies after achieving positive results in early-stage development, including early-stage clinical studies, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical studies were underway or safety or efficacy observations made in preclinical studies and clinical studies, including previously unreported adverse events.

There can be significant variability in safety or efficacy results between different clinical studies of the same product candidate due to numerous factors, including changes in study procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical study protocols and the rate of dropout among clinical study participants. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical studies nonetheless failed to obtain FDA approval.

We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion. While we have certain preclinical programs in development and intend to develop other product candidates, it will take additional investment and time for such programs to reach the same stage of development as KSI-301.

***A failure of KSI-301 in clinical development may require us to discontinue development of other product candidates based on our ABC Platform.***

If KSI-301 fails in development as a result of any underlying problem with our platform, then we may discontinue development of some or all of our product candidates that are based on our ABC Platform. If we discontinue development of KSI-301, or if KSI-301 were to fail to receive regulatory approval or were to fail to achieve sufficient market acceptance, we could be prevented from or significantly delayed in achieving profitability.

***Research and development of biopharmaceutical products is inherently risky. We cannot give any assurance that any of our product candidates will receive regulatory, including marketing, approval, which is necessary before they can be commercialized.***

We are at an early stage of development of our product candidates. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following:

- our product candidates may not successfully complete preclinical studies or clinical trials;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- our competitors may develop therapeutics that render our product candidates obsolete or less attractive;
- our competitors may develop platform technologies that render our ABC Platform obsolete or less attractive;

- the product candidates and ABC Platform that we develop may not be sufficiently covered by intellectual property for which we hold exclusive rights or may be covered by third party patents or other intellectual property or exclusive rights;
- the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate, to gain market acceptance; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

If any of these events occur, we may be forced to abandon our development efforts for a product candidate or candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations. Failure of a product candidate may occur at any stage of preclinical or clinical development, and, because our product candidates and our ABC Platform are in an early stage of development, there is a relatively higher risk of failure and we may never succeed in developing marketable products or generating product revenue.

We may not be successful in our efforts to further develop our ABC Platform and current product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Each of our product candidates is in the early stages of development and will require significant additional clinical development, management of preclinical, clinical, and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization, and significant marketing efforts before we generate any revenue from product sales, if at all. Any clinical studies that we may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates. If the results of our ongoing or future clinical studies are inconclusive with respect to the efficacy of our product candidates or if we do not meet the clinical endpoints with statistical significance or if there are safety concerns or adverse events associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for our product candidates.

If any of our product candidates successfully completes clinical trials, we generally plan to seek regulatory approval to market our product candidates in the United States, the EU, and in additional foreign countries where we believe there is a viable commercial opportunity. We have never commenced, compiled or submitted an application seeking regulatory approval to market any product candidate. We may never receive regulatory approval to market any product candidates even if such product candidates successfully complete clinical trials, which would adversely affect our viability. To obtain regulatory approval in countries outside the United States, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing, and distribution of our product candidates. We may also rely on our collaborators or partners to conduct the required activities to support an application for regulatory approval, and to seek approval, for one or more of our product candidates. We cannot be sure that our collaborators or partners will conduct these activities successfully or do so within the timeframe we desire. Even if we (or our collaborators or partners) are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected.

Even if we receive regulatory approval to market any of our product candidates, we cannot assure you that any such product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. That approval may be for indications or patient populations that are not as broad as intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We may also be required to perform additional or unanticipated clinical studies to obtain approval or be subject to additional post-marketing testing requirements to maintain regulatory approval. In addition, 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, or REMS. The failure to obtain timely regulatory approval of product candidates, any product marketing limitations or a product withdrawal would negatively impact our business, results of operations and financial condition.

Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We cannot provide any assurance that we will be able to successfully advance any of our product candidates through the development process or, if approved, successfully commercialize any of our product candidates.

***We may encounter substantial delays in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.***

Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. We cannot be sure that submission of an IND application or a clinical trial application, or CTA, will result in the FDA, European Medicines Agency, or EMA, the China Drug Authority, or CDA, or any other regulatory authority as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials;
- delays in reaching a consensus with regulatory agencies on study design or, in the case of China, the registration category for the drug candidate to be studied in the clinical trial;
- the determination by the reviewing regulatory authority to require more costly or lengthy clinical trials than we currently anticipate;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND or amendment, CTA or amendment, or equivalent application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; a negative finding from an inspection of our clinical trial operations or study sites; developments on trials conducted by competitors for related technology that raises FDA, EMA, CDA or any other regulatory authority concerns about risk to patients of the technology broadly; or if the FDA, EMA, CDA or any other regulatory authority finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays in identifying, recruiting and enrolling suitable patients to participate in our clinical trials, and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's or any other regulatory authority's current good clinical practices, or cGCPs, requirements, or applicable EMA, CDA or other regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;
- transfer of manufacturing processes to larger-scale facilities operated by CMOs or by us, and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing.

Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to or we may elect to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board for such trial or by the FDA, EMA, CDA or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA, CDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Delays in the commencement or completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

***Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.***

Adverse events or other undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA, CDA or other comparable foreign regulatory authorities.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were not observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our product candidates has side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would severely harm our business, prospects, operating results and financial condition.

Our most advanced product candidate, KSI-301, is an anti-VEGF biologic that we intend to study in wet AMD, DME/DR and RVO. There are some potential side effects associated with intravitreal anti-VEGF therapies such as intraocular hemorrhage, intraocular pressure elevation, retinal detachment, inflammation, vasculitis, artery occlusion or infection inside the eye and over-inhibition of VEGF, as well as the potential for potential systemic side effects such as heart attack, stroke, wound healing problems, and high blood pressure. Recent trends in the development of anti-VEGF therapies have favored increased molar dosages, as compared to currently marketed treatments. To date these heightened dosages have not exhibited a safety profile significantly worse than that of current treatments. However, anti-VEGF product candidates featuring higher molar dosages, including KSI-301, may heighten the risk of adverse effects associated with anti-VEGF treatments generally, both in the eye and in the rest of the body. There are risks inherent in the intravitreal injection procedure of drugs like KSI-301 which can cause injury to the eye and other complications including conjunctival hemorrhage, punctate keratitis, eye pain, conjunctival hyperemia, intra-ocular inflammation, and endophthalmitis.

Drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the study and/or result in potential product liability claims. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical trial participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates and decreased demand for our product candidates, if approved for commercial sale.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to create a Risk Evaluation and Mitigation Strategy plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers and/or other elements to assure safe use;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations, and prospects.

***We may encounter difficulties enrolling patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected.***

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

- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol, including certain highly-specific criteria related to stage of disease progression, which may limit the patient populations eligible for our clinical trials to a greater extent than competing clinical trials for the same indication that do not have such patient eligibility criteria;
- the size of the study population required for analysis of the trial's primary endpoints;
- the proximity of patients to a trial site;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials for similar therapies or targeting patient populations meeting our patient eligibility criteria;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies and product candidates;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will not complete such trials, for any reason.

For example, because patients with early stages of DR often lack symptoms, it may be challenging to identify and enroll patients at early stages of disease that may be required for a clinical trial. Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, delay or halt the development of and approval processes for our product candidates and jeopardize our ability to commence sales of and generate revenues from our product candidates, which may harm our business and results of operation.

***Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy or durability of our product candidates, which would prevent, delay or limit the scope of regulatory approval and commercialization.***

Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. For those product candidates that are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure, and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use. This is especially true for anti-VEGF biologic agents where Lucentis and Eylea are established products with accepted safety profiles.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies of our product candidates may not be predictive of the results of early-stage or later-stage clinical trials, and results of early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. The results of clinical trials in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety, efficacy or durability results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. Product candidates in later stages of clinical trials may fail to show the desired safety, efficacy and durability profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

We may be unable to design and execute clinical trials that support marketing approval. We cannot be certain that our planned clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition and results of operations.

In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidate, which may also limit its commercial potential.

***We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates, our commercial opportunity may be limited.***

One of our strategies is to identify and pursue clinical development of additional product candidates through our ABC Platform. Our ABC Platform may not produce a pipeline of viable product candidates, or our competitors may develop platform technologies that render our ABC Platform obsolete or less attractive. Our research methodology may be unsuccessful in identifying potential product candidates, or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make them unmarketable or unlikely to receive marketing approval. Identifying, developing, obtaining regulatory approval and commercializing additional product candidates for the treatment of retinal diseases will require substantial additional funding and is prone to the risks of failure inherent in drug development. If we are unable to successfully identify, acquire, develop and commercialize additional product candidates, our commercial opportunity may be limited.

***We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may retain their market share with existing drugs, or achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.***

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

There are a number of large pharmaceutical and biotechnology companies that are currently pursuing the development of products for the treatment of the retinal disease indications for which we have product candidates, including wet AMD and DME/DR. Certain of our competitors have commercially approved products for the treatment of retinal diseases that we are pursuing or may pursue in the future, including Roche, Regeneron and Novartis for the treatment of wet AMD and DME/DR. These drugs are well established therapies and are widely accepted by physicians, patients and third-party payors, which may make it difficult to convince these parties to switch to KSI-301. Companies that we are aware are developing therapeutics in the retinal disease area include large companies with significant financial resources, such as Roche, Novartis, Bayer and Regeneron, Allergan, Mylan, Momenta, and Samsung Bioepis. In addition to competition from other companies targeting retinal indications, any products we may develop may also face competition from other types of therapies, such as gene-editing therapies and drug delivery devices.

Many of our current or potential competitors, either alone or with their strategic partners, 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 or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific 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 product candidates. 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 any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of retinal disease indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA, EMA, CDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate or otherwise violate their intellectual property. For more information regarding potential disputes concerning intellectual property, see the subsection of this report titled "Risks Related to Our Intellectual Property."

***The manufacture of our product candidates is highly complex and requires substantial lead time to produce.***

Manufacturing our product candidates involves complex processes, including developing cells or cell systems to produce the biologic, growing large quantities of such cells, and harvesting and purifying the biologic produced by them. These processes require specialized facilities, highly specific raw materials and other production constraints. As a result, the cost to manufacture a biologic is generally far higher than traditional small molecule chemical compounds, and the biologics manufacturing process is less reliable and is difficult to reproduce. Because of the complex nature of our products, we need to oversee the manufacture of multiple components that require a diverse knowledge base and specialized personnel.

Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as our product candidates generally cannot be adequately characterized prior to manufacturing the final product. As a result, an assay of the finished product is not sufficient to ensure that the product will perform in the intended manner. Accordingly, we expect to employ multiple steps to attempt to control our manufacturing process to assure that the process works and the product or product candidate is made strictly and consistently in compliance with the process

Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, improper storage or transfer, inconsistency in yields and variability in product characteristics. Even minor deviations from normal manufacturing, distribution or storage processes could result in reduced production yields, product defects and other supply disruptions. Some of the raw materials required in our manufacturing process are derived from biological sources. Such raw materials are difficult to procure and may also be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt commercialization. Production of additional drug substance and drug product for any of our product candidates may require substantial lead time. For example, currently any new large-scale batches of KSI-301 would require at least 12 months to manufacture. In the event of significant product loss and materials shortages, we may be unable to produce adequate amounts of our product candidates or products for our operational needs.

Further, as product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials.

These challenges are magnified by the international nature of our supply chain, which, for KSI-301, requires drug substance and drug product sourced from single source suppliers from China, Japan, the United Kingdom, and Switzerland.

***We have no experience manufacturing any of our product candidates at a commercial scale. If we or any of our third-party manufacturers encounter difficulties in production, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to establish a commercially viable cost structure.***

In order to conduct clinical trials of our product candidates, or supply commercial products, if approved, we will need to manufacture them in small and large quantities. Our third-party manufacturer has made only a limited number of lots of KSI-301 to date and has not made any commercial lots. The manufacturing processes for KSI-301 have never been tested at commercial scale and the process validation requirement (the requirement to consistently produce the active pharmaceutical ingredient used in KSI-301 in commercial quantities and of specified quality on a repeated basis and document its ability to do so) has not yet been satisfied. Our manufacturing partners may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If our manufacturing partners are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of our product candidates may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. The same risks would apply to any internal manufacturing facilities, should we in the future decide to build internal manufacturing capacity.

In addition, the manufacturing process for any products that we may develop is subject to FDA, EMA, CDA and foreign regulatory authority approval processes and continuous oversight. We will need to contract with manufacturers who can meet all applicable FDA, EMA, CDA and foreign regulatory authority requirements, including complying with current good manufacturing practices, or cGMPs, on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to the FDA, EMA, CDA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CMOs will be able to manufacture the approved product to specifications acceptable to the FDA, EMA, CDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects.

***If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.***

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

Factors that may inhibit our efforts to commercialize any approved product on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs and other support personnel;
- the inability of sales personnel to obtain access to physicians or educate adequate numbers of physicians on the benefits of prescribing any future approved products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- 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 creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved.

***Even if any product candidates we develop receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.***

The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors and others in the medical community. Even if any product candidates we may develop receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors, and others in the medical community. The degree of market acceptance of any product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in pivotal clinical trials and published in peer-reviewed journals;
- the potential and perceived advantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;
- the ability to offer appropriate patient access programs, such as co-pay assistance;
- the extent to which physicians recommend our products to their patients;
- convenience and ease of dosing and administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA, EMA, CDA or other regulatory agencies;
- product labeling or product insert requirements of the FDA, EMA, CDA or other comparable foreign regulatory authorities, including any limitations, contraindications or warnings contained in a product's approved labeling;
- restrictions on how the product is distributed;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

If any product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenue, and we may not become profitable.

***Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.***

The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to successfully commercialize any products that we may develop also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, 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. Government authorities currently impose mandatory discounts for certain patient groups, such as Medicare, Medicaid and Veterans Affairs, or VA, hospitals, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our products, if approved. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, that the level of reimbursement will be sufficient.

Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to get reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the medicine is approved by the FDA, EMA, CDA or other comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates, and our overall financial condition.

***Our product candidates for which we intend to seek approval as biologic products may face competition from biological products that are biosimilar to or interchangeable with our product candidates sooner than anticipated.***

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological 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 full 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 their 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.

We believe that any of our product candidates approved as a biological 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 product candidates 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 approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

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

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

- decreased or interrupted demand for our products;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate; and
- a decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. Our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

**Risks Related to Regulatory Approval and Other Legal Compliance Matters**

***The regulatory approval processes of the FDA, EMA, CDA and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.***

The time required to obtain approval by the FDA, EMA, CDA and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve 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. We have not submitted for or obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA, EMA, CDA or comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA, CDA or comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use of our products;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- we may be unable to demonstrate to the FDA, EMA, CDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication, when compared to the standard of care, is acceptable;
- the FDA, EMA, CDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA, BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA, EMA, CDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA, CDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects.

***We plan to conduct clinical trials for our product candidates outside the United States, and the FDA, EMA, CDA and applicable foreign regulatory authorities may not accept data from such trials.***

We plan to conduct one or more of our clinical trials outside the United States, including Europe, China and other foreign countries. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA, EMA, CDA or applicable foreign regulatory authority may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (1) the data are applicable to the U.S. population and U.S. medical practice and (2) the trials were performed by clinical investigators of recognized competence and pursuant to cGCP regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA, CDA or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction, including any trials that we may conduct in China. If the FDA, EMA, CDA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming, would delay aspects of our business plan and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

***Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.***

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA, EMA or CDA grants marketing approval of a product candidate, we would not be permitted to manufacture, market or promote the product candidate in other countries unless and until comparable regulatory authorities in foreign jurisdictions had approved the candidate for use in their countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials. There can be no assurance that any clinical trials conducted in one jurisdiction will be accepted by regulatory authorities in other jurisdictions.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any collaborator we work with fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

***Even if we obtain regulatory approval for a product candidate, our products will remain subject to extensive regulatory scrutiny.***

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

Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA, EMA, CDA and comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, BLA or marketing authorization application, or MAA. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates will be subject to limitations on the approved indicated uses for which the product may be marketed and promoted or to the conditions of approval (including the requirement to implement a Risk Evaluation and Mitigation Strategy), or contain requirements for potentially costly post-marketing testing. We will be required to report certain adverse reactions and production problems, if any, to the FDA, EMA, CDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA, BLA or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters that would result in adverse publicity;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approvals;

- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities;
- seize or detain products; or
- require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

***Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.***

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the United States and certain international jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, in 2010, the Affordable Care Act, or ACA, was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government's comparative effectiveness research.

Since the ACA's enactment, there have been, and continue to be, numerous challenges to the ACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance and delaying the implementation of certain ACA-mandated fees. Further, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. In addition, on December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case and has allotted one hour for oral arguments, which are expected to occur in the fall. It is unclear how such litigation and other efforts to repeal and replace the ACA will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, 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. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in 2013, and due to subsequent legislative amendments to the statute, will remain in effect through 2029 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to receive or set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Moreover, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies. At the federal level, the Trump administration's budget proposal for fiscal 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. In addition, the Trump administration previously released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contained proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services, or HHS, has started implementing some of these measures under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. While some of these and other measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement and new payment methodologies. This could lower the price that we receive for any approved product. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize our product candidates, if approved.

***Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements or insider trading violations, which could significantly harm our business.***

We are exposed to the risk of fraud, misconduct or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the laws of the FDA, EMA, CDA and other comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA, EMA, CDA and other comparable foreign regulatory authorities; comply with manufacturing standards we have established; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. Employee misconduct could also involve the improper use of, including improper trading based upon, information obtained in the course of clinical studies, which could result in regulatory sanctions and serious harm to our reputation.

In connection with our IPO, we adopted a code of business conduct and ethics that applies to all our employees, including management, and our directors. However, it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. 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.

***If we fail to comply with healthcare laws, we could face substantial penalties and our business, operations and financial conditions could be adversely affected.***

Our current and future arrangements with healthcare providers, third-party payors, customers, and others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, which may constrain the business or financial arrangements and relationships through which we research, as well as, sell, market and distribute any products for which we obtain marketing approval. The laws that may impact our operations include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- federal civil and criminal false claims laws, including the False Claims Act, which can be enforced by private citizens on behalf of the government through civil whistleblower or qui tam actions, and civil monetary penalty laws, which impose criminal and civil penalties against individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other third-party payors that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;
- the federal Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Centers for Medicare & Medicaid Services under the Open Payments Program, information related to payments or other transfers of value made to physicians, as defined by such law, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws that require the registration of pharmaceutical sales representatives; 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 may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could, despite our efforts to comply, be subject to challenge under one or more of such laws. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and 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 civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

***Our business is subject to complex and evolving U.S. and foreign laws and regulations relating to privacy and data protection. These laws and regulations are subject to change and uncertain interpretation, and could result in claims, changes to our business practices, or monetary penalties, and otherwise may harm our business.***

A wide variety of provincial, state, national, and international laws and regulations apply to the collection, use, retention, protection, disclosure, transfer and other processing of personal data. These data protection and privacy-related laws and regulations are evolving and may result in ever-increasing regulatory and public scrutiny and escalating levels of enforcement and sanctions. For example, the European Union General Data Protection Regulation, or GDPR, which became fully effective on May 25, 2018, imposes stringent data protection requirements and provides for penalties for noncompliance of up to the greater of 20 million euros or four percent of worldwide annual revenues. Additionally, California recently enacted legislation, the California Consumer Privacy Act, or CCPA, that, effective January 1, 2020, among other things, requires covered companies to provide new disclosures to California consumers, and afford such consumers new abilities to opt-out of certain sales of personal information. The GDPR, CCPA and many other laws and regulations relating to privacy and data protection are still being tested in courts, and they are subject to new and differing interpretations by courts and regulatory officials. We are working to comply with the GDPR, CCPA and other privacy and data protection laws and regulations that apply to us, and we anticipate needing to devote significant additional resources to complying with these laws and regulations. It is possible that the GDPR, CCPA or other laws and regulations relating to privacy and data protection may be interpreted and applied in a manner that is inconsistent from jurisdiction to jurisdiction or inconsistent with our current policies and practices.

Our actual or perceived failure to adequately comply with applicable laws and regulations relating to privacy and data protection, or to protect personal data and other data we process or maintain, could result in regulatory fines, investigations and enforcement actions, penalties and other liabilities, claims for damages by affected individuals, and damage to our reputation, any of which could materially affect our business, financial condition, results of operations and growth prospects.

***If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. 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. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***Our business activities may be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery and anti-corruption laws.***

Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate or may operate in the future, including the U.K. Bribery Act. The FCPA generally prohibits offering, promising, giving or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There can be no assurance that all of our employees, agents, contractors or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

**Risks Related to Our Reliance on Third Parties**

***We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.***

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct some aspects of our research, preclinical testing and clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for research and 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 cGCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible, reproducible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We are also required to register ongoing clinical trials and to post the results of completed clinical trials on a government-sponsored database within certain 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 any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

We also expect 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 any product candidates we may develop or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

***We contract with third parties for the manufacture of materials for our product candidates and preclinical studies and clinical trials and for commercialization of any product candidates that we may develop. This reliance on third parties carries and may increase the risk that we will not have sufficient quantities of such materials, product candidates or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.***

We do not have any manufacturing facilities. We currently rely exclusively on a third-party manufacturer, Lonza AG, for the manufacture of our materials for preclinical studies and clinical trials and expect to continue to do so for preclinical studies, clinical trials and for commercial supply of any product candidates that we may develop.

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

- the possible breach of the manufacturing agreement by the third party or us;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- the possible early termination of the agreement by us at a time that requires us to pay a cancellation fee;
- reliance on the third party for regulatory compliance, quality assurance, safety and pharmacovigilance and related reporting; and
- the inability to produce required volume in a timely manner and to quality standards.

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

Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for any of our product candidates. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer and may incur added costs and delays in identifying and qualifying any such replacement. Furthermore, securing and reserving production capacity with contract manufacturers may result in significant costs.

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

***Reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

Reliance on third parties to conduct clinical trials, assist in research and development and to manufacture our product candidates, will at times require us to share trade secrets with them. We seek to protect our proprietary technology by in part entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's independent discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

***We rely on third-party suppliers for key raw materials used in our manufacturing processes, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials could harm our business.***

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

***We may depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.***

We may seek third-party collaborators for the research, development and commercialization of certain of the product candidates we may develop. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies and academic institutions. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our product candidates we may develop, pose the following risks to us:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not properly obtain, maintain, enforce or defend intellectual property or proprietary rights relating to our product candidates or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property covering our product candidates that result from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to collaborations;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborators may decide not to pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, 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;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may undergo a change of control and the new owners may decide to take the collaboration in a direction which is not in our best interest;
- collaborators may become party to a business combination transaction and the continued pursuit and emphasis on our development or commercialization program by the resulting entity under our existing collaboration could be delayed, diminished or terminated;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know-how or intellectual property of the collaborator relating to our products, product candidates;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or our ABC Platform; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate or delay its potential commercialization 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 increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elect not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Any collaborator may also be subject to many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section, and any negative impact on our collaborators may adversely affect us.

**Risks Related to Our Intellectual Property**

***If we are unable to obtain and maintain patent protection for any product candidates we develop or for our ABC Platform, our competitors could develop and commercialize products or technology similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop, and our technology may be adversely affected.***

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 ABC Platform and any proprietary product candidates and other technologies we may develop. We seek to protect our proprietary position by in-licensing intellectual property and filing patent applications in the United States and abroad relating to our ABC Platform, product candidates and other technologies that are important to our business. Given that the development of our technology and product candidates is at an early stage, our intellectual property portfolio directed to certain aspects of our technology and product candidates is also at an early stage. We have filed or intend to file patent applications on core aspects of our technology and product candidates; however, there can be no assurance that any such patent applications will issue as granted patents. Furthermore, in some cases, we only have filed provisional patent applications on certain aspects of our technology and product candidates, and none of these provisional patent applications is eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing date of the applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications. Furthermore, in some cases, we may not be able to obtain issued claims covering compositions relating to our ABC Platform and product candidates, as well as other technologies that are important to our business, and instead may need to rely on filing patent applications with claims covering a method of use and/or method of manufacture for protection of such ABC Platform, product candidates and other technologies. There can be no assurance that any such patent applications will issue as granted patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our ABC Platform and product candidates could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***If any of our patent applications does not issue as a patent in any jurisdiction, we may not be able to compete effectively.***

Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, and obtain, maintain and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. In addition, our own fixed applications may become prior art against our current or future patent applications. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, and in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in any of our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

***If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical technology and product candidates would be adversely affected.***

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. 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 not result in patents being issued that protect our ABC Platform, product candidates or other technologies or that effectively prevent others from commercializing competitive technologies and product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents may be challenged, narrowed, circumvented, rendered unenforceable or invalidated by third parties. Consequently, we do not know whether our ABC Platform, product candidates or other technologies will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant and inter partes review, or interference proceedings or other similar proceedings challenging our patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our ABC Platform, product candidates or other technologies 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. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions and other challenges in a foreign patent office or administrative tribunal, that challenge our or our licensor's priority of invention or other features of patentability with respect to our owned or in-licensed patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our ABC Platform, product candidates and other technologies. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us.

In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Filing, prosecuting and defending patents relating to our ABC Platform, product candidates and other technologies 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 U.S. laws. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our 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, costly or impossible 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 are 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.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. Payment within these late fee windows may be employed in order to simplify the payment of these fees generally. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, while not relevant for KSI-301, if we rely on a different product, its development could involve the use of government funds, which can require additional compliance aspects to make certain all rights are transferred to or remain with us.

***Issued patents may be challenged or invalidated, and recent changes in U.S. patent law have diminished and may further diminish the value of patents in general. We rely on patents to protect our products, and any diminishment in the scope or value of our patents would adversely affect our business.***

If we initiated legal proceedings against a third party to enforce a patent directed to our ABC Platform, product candidates or other technologies, the defendant could allege that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including obviousness, lack of novelty, lack of written description, or non-enablement. Grounds for an unenforceability challenge include an allegation that someone connected with prosecution of the patent withheld material information from the USPTO with an intent to deceive the USPTO, or made a misleading statement, during prosecution. The filing of a legal proceeding could also result in the third party challenging the patent at the USPTO, such as in post-grant and inter partes review.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. For patent filings beginning in March 2013, the United States employs a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. Under the current patent laws, a third party that files a patent application in the USPTO before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either (1) file any patent application related to our ABC Platform, product candidates or other technologies or (2) invent any of the inventions claimed in our or our licensor's patents or patent applications.

Changes to U.S. patent laws since 2011 also include allowing third party submissions of prior art to the USPTO during patent prosecution and additional procedures for attacking the validity of a patent through USPTO administered post-grant proceedings, including re-examination, post-grant review, inter partes review, interference proceedings and derivation proceedings. Some of these changes apply to patents issued prior to 2011. These and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings) could result in the revocation of, cancellation of or amendment to our patents in such a way that they no longer cover our ABC Platform, product candidates or other technologies. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standards applied in United States federal courts that apply to actions seeking to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if challenged in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not otherwise have been invalidated if first challenged by the third party as a defendant in a district court action.

As compared to intellectual property-reliant companies generally, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. These rulings have created uncertainty with respect to the validity and enforceability of patents, even once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Any future changes to patent laws could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our ABC Platform, product candidates or other technologies. Increased uncertainty with respect to, or loss of, patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

***If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.***

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our owned or in-licensed U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent term extension of up to five years as compensation for 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, only one patent 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. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate. Patent term extension in the United States and/or foreign countries and territories may not be available if, among other things, we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to the expiration of relevant patents, or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension received is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

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

We may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor or co-inventor or owner or co-owner. For example, we may have inventorship disputes arise from conflicting obligations of employees, collaborators, consultants or others who are involved in developing our ABC Platform, product candidates or other technologies. Litigation may be necessary to defend against these and other claims challenging inventorship or our ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our ABC Platform, product candidates and other technologies. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

***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 ABC Platform, product candidates and other technologies, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information and to maintain our competitive position. Trade secrets and know-how can be difficult to protect. Over time, we expect our trade secrets and know-how to be disseminated within the industry through independent development, the publication of journal articles describing the methodology and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, 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, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants, train our employees not to bring or use proprietary information or technology from former employers to us or in their work and remind former employees when they leave their employment of their confidentiality obligations to us. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite our 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 contain such breaches or disclosures or obtain adequate remedies for such breaches. 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 or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed without the protection of a confidentiality agreement found unenforceable by relevant courts or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

***We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.***

Many of our employees, consultants and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors and potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have improperly used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or 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, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects. Where post-filing date patent assignments are not executed by an inventor, it is our practice to employ and record the assignment provision that can be found in the employee's employment agreement. This is done when possible, and when the intellectual property is of interest to us.

***Third-party claims of intellectual property infringement, misappropriation or other violation against us or our collaborators may prevent or delay the development and commercialization of our ABC Platform, product candidates and other technologies.***

The field of discovering treatments for retinal diseases is highly competitive and dynamic. Due to the focused research and development that is taking place in this field by several companies, including us and our competitors, the intellectual property landscape is in flux, and it may remain uncertain in the future. As such, there may be significant intellectual property related litigation and proceedings relating to our owned, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends in part on our and our collaborators' ability to avoid infringing, misappropriating and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings challenging patents, including interference, derivation and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. As discussed above, due to changes in U.S. law referred to as patent reform, new procedures including *inter partes* review and post-grant review have been implemented. As stated above, this reform adds uncertainty to the possibility of challenge to our patents in the future.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist relating to ABC technology and in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our ABC Platform, product candidates and other technologies may give rise to claims of infringement of the patent rights of others. We cannot assure you that our ABC Platform, product candidates and other technologies that we have developed, are developing or may develop in the future will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued or that a third party, including a competitor in the fields in which we are developing our ABC Platform, product candidates and other technologies, might assert are infringed by our current or future ABC Platform, product candidates or other technologies. Such a dispute may concern claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our ABC Platform, product candidates or other technologies. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our ABC Platform, product candidates or other technologies, could be found to be infringed by our ABC Platform, product candidates or other technologies. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that later result in issued patents that our ABC Platform, product candidates or other technologies may infringe.

Third parties may have patents or obtain patents in the future and claim that the manufacture, use or sale of our ABC Platform, product candidates or other technologies infringes these patents. If a third party alleges that we infringe their patents or that we are otherwise employing their proprietary technology without authorization and initiates litigation against us, a court of competent jurisdiction could hold that such patents are valid, enforceable and infringed by our ABC Platform, product candidates or other technologies, even if we believe such claims are without merit. In that event, the successful plaintiff may be able to block our ability to commercialize the applicable product candidate or technology unless we obtain a license under the applicable patents, or such patents expire or are finally determined to be invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees, royalties or both. Any license granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our ABC Platform, product candidates or other technologies, or our commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

We are aware of a number of patents and applications that are directed to one or more aspects of KSI-301. Our intent is to maintain our development efforts under 35 U.S.C. Section 271(e)(1) (which provides a safe harbor from patent infringement claims related to certain drug development activities) through to at least the launch of any KSI-301 product. As such, we do not intend to launch KSI-301 when any valid patent is still in force. We are aware of at least one pending application with claims that are directed to some aspect of KSI-301, and that could, if issued, result in a patent term beyond our intended launch date of KSI-301. If this were to occur, we may challenge the validity of the claims, obtain a license, modify KSI-301, or delay launch.

If we choose to further the pipeline and develop a different product, such a product would be delayed until the expiration of any valid patent that is still in force on such product. Alternatively, our options for addressing any such patents relating to these non-KSI-301 products would include the following: challenge the validity of the claims, obtain a license, or modify the non-KSI-301 product.

Defending against infringement claims, regardless of their merit, would involve substantial litigation expense, would be a substantial diversion of management and other employee resources from our business and may adversely impact our reputation. We may be subject to an injunction that prevents or delays us from commercializing our ABC Platform technology, product candidates or other technologies during ongoing litigation even if we ultimately prevail in the litigation proceedings or the litigation is settled in our favor. We may be subject to an injunction that prevents or delays us from commercializing our ABC Platform, product candidates or other technologies during ongoing litigation even if we ultimately prevail in the litigation proceedings or the litigation is settled in our favor. In the event of a successful claim of infringement against us, we may be enjoined from further developing or commercializing our infringing ABC Platform, product candidates or other technologies. In addition, we may have to pay substantial damages (including treble damages and attorneys' fees for willful infringement) obtain one or more licenses from third parties, pay royalties and/or redesign our infringing product candidates or technologies, which may be impossible or require substantial time and monetary expenditure. If we were unable to further develop and commercialize our ABC Platform, product candidates or other technologies, it would harm our business significantly.

Engaging in litigation to defend against third parties alleging that we have infringed, misappropriated or otherwise violated their patents or other intellectual property rights is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings against us could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition or results of operations.

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

Competitors may infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. If we assert our intellectual property against others, it could increase the likelihood that our patents or the patents of our licensing partners become involved in inventorship, priority or validity disputes. As discussed above, countering or defending against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent owned or in-licensed by us is invalid or unenforceable, the other party's use of our patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1), or may refuse to stop the other party from using the technology at issue on the grounds that our owned and in-licensed patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated, rendered unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Even if we prevail in asserting our intellectual property, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our 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 or to assert all claims we believe to be viable. 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 more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

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

We rely on trademarks, service marks, tradenames and brand names. We cannot assure you that our trademark applications will be approved. During trademark registration proceedings, we may receive rejections. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, any registered or unregistered trademarks or trade names that we currently have or may in the future acquire may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. We own a registered trademark for the mark "KODIAK" in the United States. The application for registration of the mark "KODIAK SCIENCES" in the United States has been allowed. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We engage a third party watching service to monitor use by third parties of names that are identical or similar to our name. We have identified at least two companies that are using names that we continue to monitor. We have sent a cease and desist letter to one of the companies. If we deem it appropriate, we may decide to take further action with respect to those companies. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects.

***Intellectual property rights do not necessarily address all potential threats.***

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

- others may be able to make products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of the patents that we may license or own;
- we, or our current or future licensors or collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or own now or in the future;

- we, or our current or future licensors or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our current or future pending owned or licensed patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

**Risks Related to Our Operations**

***We are highly dependent on our key personnel, and if we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.***

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract, motivate and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, particularly our Chief Executive Officer, Dr. Victor Perlroth, and our scientific and medical personnel. The loss of the services provided by any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements, could result in delays in the development of our product candidates and harm our business.

We conduct our operations at our facility in Palo Alto, California, in a region that is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel is intense and the turnover rate can be high, which may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We expect that we may need to recruit talent from outside of our region and doing so may be costly and difficult.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided restricted stock and stock option grants, including early exercise stock options exercisable for restricted stock that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain "key man" insurance policies on the lives of all of these individuals or the lives of any of our other employees. If we are unable to attract, incentivize and retain quality personnel on acceptable terms, or at all, it may cause our business and operating results to suffer.

***We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth.***

As of March 6, 2020, we had 39 employees, all of whom were full-time. As our development plans and strategies develop, and as we transition into operating as a public company, we must add a significant number of additional managerial, operational, financial and other personnel. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, retaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our current and future product candidates, while complying with our contractual obligations to contractors and other third parties;

- expanding our operational, financial and management controls, reporting systems and procedures; and
- managing increasing operational and managerial complexity.

Our future financial performance and our ability to continue to develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to manage these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services. There can be no assurance that the services of these independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop our product candidates and, accordingly, may not achieve our research, development, and commercialization goals.

***A failure to maintain an effective system of internal control over financial reporting could result in material misstatements of our financial statements in future periods and may impair our ability to comply with the accounting and reporting requirements applicable to public companies.***

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements in accordance with U.S. generally accepted accounting principles. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of annual or interim consolidated financial statements will not be prevented or detected on a timely basis.

***If we engage in acquisitions, in-licensing or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.***

We may engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any acquisition or strategic partnership may entail numerous risks, including:

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

In addition, if we undertake such a transaction, we may incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

***Our internal computer systems, or those used by our third-party research institution collaborators, CROs or other contractors or consultants, may fail or suffer security breaches.***

Despite the implementation of security measures, our internal computer systems may be vulnerable to damage from computer viruses and unauthorized access. Although to our knowledge, we have not experienced any such material system failure or security breach to date, if such an event were to occur, it could result in a material disruption of our development programs and our business operations, whether due to a loss of trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third-party research institution collaborators, CROs, other contractors and consultants for many aspects of our business, including research and development activities and manufacturing of our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business.

The secure maintenance of information is critical to our business and reputation. We believe that companies have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access. These threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state-sponsored attack. Cyber threats may be generic, or they may be custom-crafted against our information systems. Over the past few years, cyber-attacks have become more prevalent and much harder to detect and defend against.

Our network and storage applications and those of our collaborators, CROs and vendors may be subject to unauthorized access by hackers or breached due to operator error, malfeasance or other system disruptions. It is often difficult to anticipate or immediately detect such incidents and the damage caused by them. These data breaches and any unauthorized access or disclosure of our information or intellectual property could compromise our intellectual property and expose sensitive business information. A data security breach could also lead to public exposure of personal information of our employees. Cyber-attacks could cause us to incur significant remediation costs, disrupt key business operations and divert attention of management and key information technology resources. Our network security and data recovery measures and those of our collaborators, CROs and vendors may not be adequate to protect against such security breaches and disruptions. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of our product candidates could be delayed.

***Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.***

Our operations, and those of our CROs, CMOs, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are partly uninsured. In addition, we rely on our third-party research institution collaborators for conducting research and development of our product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. For example, in December 2019, an outbreak of a novel strain of coronavirus, COVID-19, originated in Wuhan, China. Since the manufacturing facilities of some of our third-party CMOs are in China, an outbreak of communicable diseases in China or elsewhere, or the perception that such an outbreak could occur, and the measures taken by the governments of countries affected, could adversely affect our business, financial condition or results of operations by limiting our ability to manufacture product within or outside China, forcing temporary closure of facilities that we rely upon or increasing the costs associated with obtaining clinical supplies of our product candidates. The extent to which the coronavirus impacts our results will depend on future developments, which are highly uncertain and cannot be accurately predicted, including new information which may emerge concerning the severity of the coronavirus and the actions to contain the coronavirus or treat its impact, among others.

All of our operations including our corporate headquarters are located in a single facility in Palo Alto, California. Damage or extended periods of interruption to our corporate, development or research facilities due to fire, natural disaster, power loss, communications failure, unauthorized entry or other events could cause us to cease or delay development of some or all of our product candidates. Although we maintain property damage and business interruption insurance coverage on these facilities, our insurance might not cover all losses under such circumstances and our business may be seriously harmed by such delays and interruption.

We recently implemented a new enterprise resource planning, or ERP, system as well as other systems as part of our ongoing technology and process improvements. Our ERP system is critical to our ability to accurately maintain books and records and prepare our financial statements. If we encounter unforeseen problems with our ERP system or other systems and infrastructure, our business, operations, and financial results could be adversely affected.

***Our business is subject to economic, political, regulatory and other risks associated with international operations.***

Our business is subject to risks associated with conducting business internationally. Some of our suppliers and collaborative relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements, pricing and reimbursement regimes in non-U.S. countries;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- potential liability under the FCPA or comparable foreign laws; and
- business interruptions resulting from geo-political actions, including war and terrorism or natural disasters.

In June 2016, the United Kingdom, or UK, held a referendum in which voters approved an exit from the EU, commonly referred to as "Brexit." This referendum has created political and economic uncertainty, particularly in the UK and the EU, and this uncertainty may persist for years. The UK officially withdrew from the EU on January 31, 2020, however the effects of the departure on both the EU and the UK are still highly uncertain, as many details of the divorce have yet to be addressed. The withdrawal may cause increased economic volatility, affecting our operations and business. Brexit may adversely impact our ability to obtain regulatory approvals of our product candidates in the EU, result in restrictions or imposition of taxes and duties for importing our product candidates into the EU, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the EU.

These and other risks associated with our planned international operations may materially adversely affect our ability to attain profitable operations.

***Our business could be adversely affected by the effects of health epidemics, including the recent COVID-19 outbreak, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. If COVID-19 becomes a worldwide pandemic, it could materially affect our operations, including at our headquarters in the San Francisco Bay Area and at our clinical trial sites, as well as the business or operations of our manufacturers, CROs or other third parties with whom we conduct business.***

Our business could be adversely affected by health epidemics in regions where we have concentrations of clinical trial sites or other business operations and could cause significant disruption in the operations of third party manufacturers and CROs upon whom we rely. For example, in December 2019, a novel strain of coronavirus was reported to have surfaced in Wuhan, China. Since then, the COVID-19 coronavirus has spread to multiple countries, including the United States and several European countries. Our headquarters is located in the San Francisco Bay Area. In March 2020, the State of California declared a state of emergency related to the spread of COVID-19, and the San Francisco Department of Public Health announced aggressive recommendations to reduce the spread of the disease, including recommendations to suspend nonessential travel, encourage telecommuting and cancel or postpone large gatherings. On March 10, 2020, the World Health Organization declared the COVID-19 outbreak a pandemic, and the U.S. government suspended all travel from Europe for a 30-day period. We continue to monitor our operations and government recommendations and may elect to temporarily close our office and/or laboratory space to protect our employees. There is a risk that other countries or regions may be less effective at containing COVID-19, or it may be more difficult to contain if the outbreak reaches a larger population or broader geography, in which case the risks described herein could be elevated significantly.

Quarantines for COVID-19 or other viruses could impact personnel at third party manufacturing facilities in China, Switzerland and other countries, or the availability or cost of materials, which would disrupt our supply chain. In particular, some of our suppliers of certain materials used in the production of our drug products are located in China. While many of these materials may be obtained by more than one supplier, including suppliers outside of China, port closures and other restrictions resulting from the coronavirus outbreak in the region may disrupt our supply chain or limit our ability to obtain sufficient materials for our drug products.

In addition, our current and future clinical trials may be affected by the COVID-19 outbreak. Site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 outbreak. Some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 and adversely impact our clinical trial operations. Kodiak staff and/or our CRO partners may not be able to travel to study sites, impacting further site initiations. Other Kodiak vendors on whom we depend, such as supply chain and logistics partners and our image reading centers may be disrupted, and our operations could be affected. Our clinical studies enroll patients who have underlying risk factors such as advanced age, hypertension and/or diabetes which could lead to higher than expected study discontinuation rates if these patients are adversely affected by the COVID-19 outbreak.

The global outbreak of COVID-19 continues to rapidly evolve. The ultimate impact of the COVID-19 outbreak or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely.

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

As of December 31, 2019, we had federal net operating loss carryforwards, or NOLs, of $31.8 million. A portion of the federal net operating loss carryforwards begin to expire in 2035. Under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50-percentage-point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change taxable income or taxes may be limited. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. As a result, our ability to use our pre-change net operating loss carryforwards and other pre-change tax attributes to offset post-change taxable income or taxes may be subject to limitation. We will be unable to use our NOLs if we do not attain profitability sufficient to offset our available NOLs prior to their expiration.

***Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations.***

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could affect the tax treatment of our domestic and foreign earnings. Any new taxes could adversely affect our domestic and international business operations, and our business and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us.

**Risks Related to Ownership of Our Common Stock**

***The market price of our common stock may be volatile, which could result in substantial losses for investors purchasing shares.***

The market price of our common stock may be volatile. As a result, you may not be able to sell your common stock at or above the price that you paid for such shares. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive products or technologies;
- the timing and results of clinical trials for our current product candidates and any future product candidates that we may develop;
- commencement or termination of collaborations for our product candidates;
- failure or discontinuation of any of our product candidates;
- failure to develop our ABC Platform;

- results of preclinical studies, clinical trials or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- 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 personnel;
- the commencement of litigation;
- the level of expenses related to any of our research programs, product candidates that we may develop;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders;
- expiration of market standoff or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this "Risk Factors" section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

***If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.***

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

***Future sales of our common stock in the public market could cause our share price to decline, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales, particularly sales by our directors, executive officers and significant stockholders, may have on the prevailing market price of our common stock. All of our outstanding shares of common stock are available for sale in the public market, subject only to the restrictions of Rule 144 under the Securities Act in the case of our affiliates. In addition, the shares of common stock subject to outstanding options under our equity incentive plans and the shares reserved for future issuance under our equity incentive plans, as well as shares issuable upon vesting of restricted stock unit awards, will become eligible for sale in the public market in the future, subject to certain legal and contractual limitations. In addition, certain holders of our common stock have the right, subject to various conditions and limitations, to request we include their shares of our common stock in registration statements we may file relating to our

securities. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

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

We will seek additional capital through one or a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. We, and indirectly, our stockholders, will bear the cost of issuing and servicing such securities. Because our decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing or nature of any future offerings. To the extent that we raise additional capital through the sale of equity securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

***Our principal stockholders own a significant percentage of our common stock, which could limit your ability to affect the outcome of key transactions, including a change of control.***

Our directors, executive officers, significant holders of outstanding common stock and their respective affiliates beneficially own a significant amount of our common stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

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

We are an "emerging growth company," as defined in the JOBS Act. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or SOX, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. In addition, to the extent that we continue to qualify as a "smaller reporting company," as defined in the Exchange Act, we may choose to provide the scaled disclosure available to smaller reporting companies. As a result, the information we provide stockholders may be different than the information that is available with respect to other public companies. We cannot predict whether investors will find our common stock less attractive if we rely 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 will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.***

As a public company, and particularly after we are no longer an emerging growth company, we will continue to incur significant legal, accounting, and other expenses that we did not incur as a private company. SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq, 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. We expect that we will need to hire additional accounting, finance, and other personnel in connection with our efforts to comply with the requirements of being a public company, and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are continually evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure

and governance practices.

While we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be 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, 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 SOX Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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

As a public company, we are subject to reporting and other obligations under the Exchange Act, including the requirements of SOX Section 404, which require annual management assessments of the effectiveness of our internal control over financial reporting.

The rules governing the standards that must be met for management to determine that our internal control over financial reporting is effective are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by SOX. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources.

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

***We have broad discretion in the use of proceeds from any offering and may not use them effectively.***

Our management has broad discretion in the application of the net proceeds received from any offering. Our management may spend a portion or all of the net proceeds from any offering in ways that our stockholders may not desire or that may not yield a favorable return. The failure by our management to apply these funds effectively could harm our business, financial condition, results of operations and prospects. Pending their use, we may invest the net proceeds from any offering in a manner that does not produce income or that loses value.

***Delaware law and provisions in our certificate of incorporation and bylaws might discourage, delay, or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.***

Provisions in our certificate of incorporation and bylaws may discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our charter documents:

- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- eliminate cumulative voting in the election of directors;
- authorize our board of directors to issue shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- provide our board of directors with the exclusive right to elect a director to fill a vacancy or newly created directorship;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- prohibit stockholders from calling a special meeting of stockholders;

- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- authorize our board of directors, by a majority vote, to amend the bylaws; and
- require the affirmative vote of at least 66 2/3% or more of the outstanding shares of common stock to amend many of the provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware, or DGCL, prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our certificate of incorporation, bylaws, or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

***Our bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.***

Our bylaws provide that the Court of Chancery of the State of Delaware will be the exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of fiduciary duty;
- any action asserting a claim against us arising under the DGCL, our certificate of incorporation, or our bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

Our bylaws further provide that the U.S. federal district courts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act of 1933, as amended.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees. If a court were to find either exclusive-forum provision in our bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business. Our bylaws further provide that unless we otherwise consent in writing, the U.S. federal district courts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, which we refer to as the Federal Forum Provision. However, on December 19, 2018, the Delaware Chancery Court issued an opinion in *Sciabacucchi v. Salzberg*, C.A. No. 2017-0931-JTL, finding that provisions similar to the Federal Forum Provision are not valid under Delaware Law. As previously disclosed in a Current Report on Form 8-K we filed on January 28, 2019, in light of the *Sciabacucchi* decision, we do not currently intend to enforce the foregoing federal forum selection provision unless the *Sciabacucchi* decision is reversed. If the Delaware Supreme Court affirms the Chancery Court's decision, then we intend to amend the Bylaws to remove the invalid provision. Such amendment could cause us to incur additional costs, which could have an adverse effect on our business, financial condition or results of operations.

## ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

## ITEM 2. PROPERTIES

Our corporate headquarters are located in Palo Alto, California, where we lease approximately 11,000 square feet of office, research and development, engineering and laboratory space pursuant to a lease agreement which commenced in October 2013 and would expire in October 2018. In March 2016, we executed a third lease amendment agreement that became effective March 31, 2016 and extended the lease term until October 31, 2023. This facility houses substantially all of our personnel. We anticipate the need for additional space to accommodate our operational plans.

## ITEM 3. LEGAL PROCEEDINGS

We are not a party to any material legal proceedings at this time. From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

## ITEM 4. MINE SAFETY DISCLOSURES

None.

## PART II

## ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock has been listed on the Nasdaq Global Market under the symbol "KOD" since October 4, 2018. Prior to this date, there was no public market for our common stock.

### Holders of Common Stock

As of March 2, 2020, there were approximately 34 holders of record of our common stock. The approximate number of holders is based upon the actual number of holders registered in our records at such date and excludes holders in "street name" or persons, partnerships, associations, corporations, or other entities identified in security positions listings maintained by depository trust companies.

### Dividend Policy

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

### Recent Sales of Unregistered Securities

None.

### Use of Proceeds from Public Offering of Common Stock

On October 9, 2018, we closed our IPO, in which we sold and issued 9,000,000 shares of common stock at a price to the public of $10.00 per share. On November 6, 2018, we sold and issued an additional 400,000 shares of common stock at $10.00 per share to the underwriters of our IPO following the partial exercise of their over-allotment option.

The offer and sale of all of the shares of our common stock in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-227237), which was declared effective by the SEC on October 3, 2018. Following the sale of the above shares, the offering terminated. We received aggregate gross proceeds from our IPO of $94.0 million, or aggregate net proceeds of $83.5 million, inclusive of the partial over-allotment option exercise, after deducting underwriting discounts and commissions and other offering costs. Morgan Stanley, BofA Merrill Lynch and Barclays acted as joint book-running managers and Chardan acted as lead manager. None of the underwriting discounts and commissions or offering expenses were incurred or paid, directly or indirectly, to (i) our directors or officers or their associates, (ii) persons owning 10% or more of our common stock or (iii) any of our affiliates.

There has been no material change in our planned use of the net proceeds from our IPO as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on October 5, 2018.

### Purchases of Equity Securities by the Issuer and Affiliated Purchases

None.

## ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

You should read the selected historical financial data below in conjunction with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. The selected financial data set forth below is derived from our audited consolidated financial statements and may not be indicative of future operating results.

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2019 | 2018 | 2017 |
| | (in thousands, except share and per share data) | | |
| **Consolidated Statements of Operations Data:** | | | |
| Operating expenses | | | |
| Research and development | $ 37,506 | $ 18,793 | $ 22,022 |
| General and administrative | 11,684 | 7,581 | 3,499 |
| Total operating expenses | 49,190 | 26,374 | 25,521 |
| Loss from operations | (49,190) | (26,374) | (25,521) |
| Interest income | 1,568 | 617 | 29 |
| Interest expense | (8) | (5,519) | (1,185) |
| Other income (expense), net | 265 | (4,688) | (1,259) |
| Loss on extinguishment of debt | — | (5,479) | — |
| Net loss | $ (47,365) | $ (41,443) | $ (27,936) |
| Net loss per share attributable to common stockholders, basic and diluted | $ (1.25) | $ (2.77) | $ (3.72) |
| Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted | 37,853,616 | 14,976,515 | 7,515,336 |

| | As of December 31, | | |
|---|---|---|---|
| | 2019 | 2018 | 2017 |
| | | (in thousands) | |
| **Consolidated Balance Sheet Data:** | | | |
| Cash, cash equivalents and marketable securities | $ 348,177 | $ 88,254 | $ 1,395 |
| Working capital | 327,519 | 85,623 | (7,563) |
| Total assets | 358,866 | 92,189 | 3,244 |
| Total liabilities | 13,507 | 5,356 | 21,965 |
| Accumulated deficit | (158,131) | (110,766) | (69,323) |
| Total stockholders' equity (deficit) | 345,359 | 86,833 | (68,738) |

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

### Overview

Our goal is to prevent and treat the major causes of blindness by developing next-generation therapeutics for chronic, high-prevalence retinal diseases.

Throughout 2019 and into 2020, we have generated clinical data with our most advanced product candidate, KSI-301, a biologic therapy built with our antibody biopolymer conjugate platform, or ABC Platform, which is designed to maintain potent and effective drug levels in ocular tissues for longer periods than the currently-marketed biologic medicines used to treat retinal diseases. To date, KSI-301 has been administered more than 500 times to over 200 patients. We believe that KSI-301, if approved, has the potential to be an important therapy to treat patients with wet age-related macular degeneration, or wet AMD, diabetic retinopathy, or DR, including diabetic macular edema, or DME, and macular edema due to retinal vein occlusion, or RVO.

In our ongoing Phase 1b clinical study, we have completed enrollment and administered multiple doses of KSI-301 to treatment-naïve patients with wet AMD, DME or RVO, and we are observing promising safety, efficacy, and clinical durability in the emerging data in each of the retinal diseases under study. We believe the data support an acceleration of efforts to bring KSI-301 to the market in these retinal diseases and that the data lend confidence to the design of our current and planned pivotal studies of KSI-301, which studies we believe, if successful, may demonstrate a meaningfully differentiated clinical profile of KSI-301 as compared to current therapies. Based on this encouraging data, we are entering into the manufacturing-related commitments necessary for pre-commercial scale-up and BLA submission.

We have completed an end of phase 2 meeting with the U.S. Food and Drug Administration, or FDA, where we agreed on the order and number of clinical studies required to support the licensure of KSI-301 in wet AMD, DME, RVO and DR (without DME). Two pivotal studies will be required in RVO and one study each in wet AMD, DME, and DR in order to support the potential U.S. approval of KSI-301 across these four indications. The pivotal study for wet AMD began recruiting patients in the third quarter of 2019, and we plan to initiate the pivotal studies in DME, RVO and DR in 2020.

The ABC Platform and KSI-301 were developed at Kodiak, and we own worldwide rights to these assets. We have applied our ABC Platform to develop additional product candidates beyond KSI-301, including KSI-501, our bispecific anti-IL-6/VEGF bioconjugate, and we are expanding our early research pipeline to include ABC Platform-based triplet inhibitors for multifactorial retinal diseases such as dry AMD and the neurodegenerative aspects of glaucoma. We intend to progress these and other product candidates to address high-prevalence ophthalmic diseases.

Our overall objective is to develop our product candidates, seek FDA and worldwide health authority marketing authorization approvals, and ultimately commercialize our product candidates.

**Recent developments**

On December 1, 2019, we and our subsidiary, Kodiak Sciences GmbH, entered into a funding agreement with Baker Bros. Advisors, or BBA, pursuant to which BBA purchased the right to receive a capped 4.5% royalty on future net sales of KSI-301 in exchange for $225,000,000 in committed development funding payable to us. Unless earlier terminated or re-purchased by us, the royalty terminates upon the date that BBA has received an aggregate amount equal to 4.5 times the funding amount paid to us. On February 4, 2020, BBA paid us the first $100,000,000 of the funding amount, and the remaining $125,000,000 of the funding amount will be paid following the achievement of 50% enrollment in each of (i) the planned Phase 3 clinical trial of KSI-301 for branch RVO and (ii) the planned Phase 3 clinical trial of KSI-301 for central RVO. We have the option, exercisable at any point during the term of the funding agreement, to repurchase from BBA 100% of the royalties due to BBA under the funding agreement for a purchase price equal to the funding amount paid to us as of such time times 4.5, less amounts paid by us to BBA. The funding agreement was the result of a competitive process overseen by independent and disinterested directors with the assistance of outside counsel. For further details, see the "Business" section above.

On December 6, 2019, we completed a follow-on equity offering and issued and sold 6,900,000 shares of the Company's common stock at a price to the public of $46.00 per share. The gross proceeds from this offering were $317.4 million, resulting in aggregate net proceeds of $297.6 million after deducting underwriting discounts and commissions and other offering costs payable by us.

Proceeds from the royalty funding agreement together with our current cash, cash equivalents and marketable securities, which includes proceeds from the equity offering, are expected to advance the clinical programs for KSI-301 towards achieving our "2022 Vision" of a Biologics License Application, or BLA, of KSI-301 in 2022 for wet AMD, DME, RVO and potentially DR without DME, including the manufacturing activities necessary for BLA submission, as well as to advance our pipeline of drug candidates including KSI-501 and our triplet inhibitor drug candidates and for working capital and general corporate purposes.

In 2019 and into the first quarter of 2020, highlights of our activities included:

- Initiation of enrollment and on-going recruitment in our pivotal DAZZLE clinical trial of KSI-301 in patients with treatment naïve wet AMD. As of March 6, 2020, more than 175 patients have been enrolled in the study randomized 1:1 between KSI-301 and Eylea as active comparator;
- Completion of recruitment into our ongoing Phase 1b study of KSI-301 in 121 treatment-naïve patients with wet AMD, DME and RVO;
- Presentation of promising on-going clinical safety, efficacy and durability data at the American Society of Retina Specialists 2019 Annual Meeting, the Macula Society 2019 Annual Meeting, the American Academy of Ophthalmology 2019 Annual Meeting Retina Subspecialty Day, and the Angiogenesis, Exudation, and Degeneration 2020 Annual Meeting;
- Completion of a Type B (End of Phase 2 or EOP) meeting with the FDA where we discussed and agreed on:
    - Certain recommended clinical, non-clinical, and manufacturing activities to support the licensure of KSI-301, and
    - The order and number of clinical studies required to support a BLA in wet AMD, DME, RVO and DR;
- Announcement of an accelerated registration strategy for KSI-301 which includes: (i) running our pivotal clinical studies in the major retinal vascular disease indications in parallel (rather than in series), and (ii) engaging in BLA and pre-commercial manufacturing validation and scale-up activities;
- Expansion of our Board of Directors with the appointment of Taiyin Yang, Ph.D., Executive Vice President, Pharmaceutical Development and Manufacturing of Gilead Sciences, who brings expertise and experience in the relevant pre-commercial areas of clinical and commercial manufacturing, quality and supply chain operations;
- Entry into a royalty funding agreement with BBA in which we sold a capped, pre-payable 4.5% royalty on future net sales of KSI-301 in exchange for $225,000,000 in committed development funding payable to us.; and
- Closing of a $317.4 million follow-on offering of our common stock.

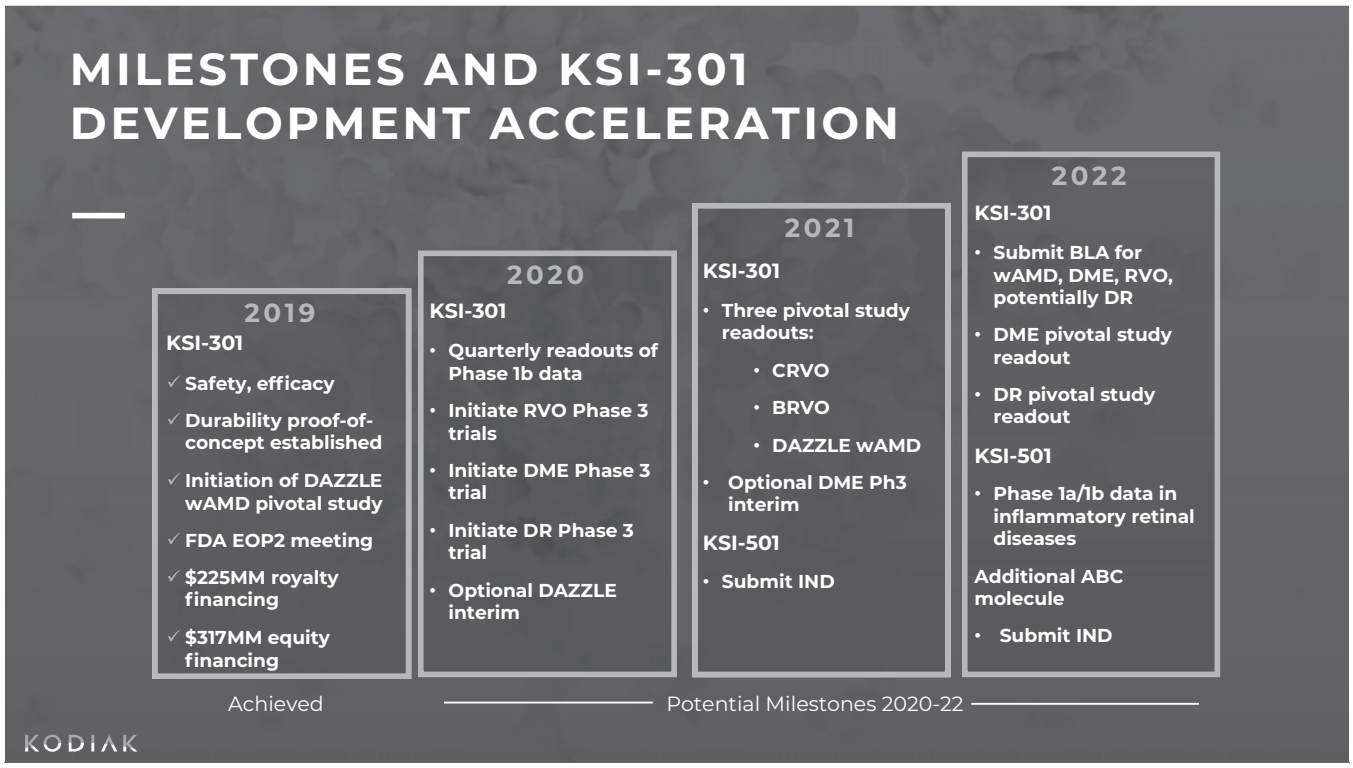
Based on the emerging clinical data, our productive EOP meeting with the FDA, and our substantive financing events, we are accelerating our BLA- and pre-commercial manufacturing activities to match the clinical timelines for KSI-301, with the goal of demonstrating a meaningfully-differentiated (*i.e.,* first line) clinical profile in each of wet AMD, DME, RVO, and DR as compared to currently-marketed medicines.

Our current cash, cash equivalents and marketable securities which includes the net proceeds from the December 2019 public offering, and together with the royalty funding agreement, provide the resources for us to advance the KSI-301 program towards achieving our "2022 Vision," and also to advance our pipeline of drug candidates including KSI-501 and our triplet inhibitor drug candidates, and for working capital and general corporate purposes.

**Kodiak's 2022 Vision and KSI-301 accelerated development strategy**

We believe that we can achieve our "2022 Vision" of a BLA submission and initial FDA approval for KSI-301 in wet AMD, DME, RVO and DR with a total of five pivotal trials— two in RVO, one in wet AMD, one in DME and one in DR without DME. Consequently, we now intend to initiate at least four US/EU-based pivotal trials in 2020 – one in DME, one in central RVO (CRVO), one in branch RVO (BRVO), and one in DR without DME. These studies, together with our ongoing pivotal study in wet AMD, will be the basis of our intended BLA and sBLA submissions. We currently expect to submit the wet AMD, DME, and RVO indications in a single initial BLA for KSI-301 and the DR indication in a supplemental BLA in the United States. We continue to invest in our science and our pipeline, including our bispecific ABC product candidate KSI-501 for retinal vascular diseases with a strong inflammatory component and our new triplet inhibitors for the high prevalence multifactorial retinal diseases dry AMD and the neurodegenerative aspects of glaucoma.

Our 2022 Vision includes the following potential catalysts and milestones in 2020, 2021 and 2022, along with the important milestones achieved in 2019 that support the accelerated development program:




Further details of our ongoing KSI-301 Phase 1b trial and our accelerating development strategy are described in the "Business" section above.

Since inception in June 2009, we have devoted substantially all of our resources to discovering and developing product candidates and manufacturing processes, building our ABC Platform and assembling our core capabilities in drug development for ophthalmic disease. We plan to continue to use third-party contract research organizations, or CROs, to carry out our preclinical and clinical development. We rely on third-party contract manufacturing organizations, or CMOs, to manufacture and supply our preclinical and clinical materials to be used during the development of our product candidates. We are evaluating investments in commercial manufacturing capacity. We do not have any products approved for sale and have not generated any product revenue since inception.

We have funded our operations primarily through the sale and issuance of equity securities. In October 2018, we completed our initial public offering, or IPO. In December 2019, we completed a follow-on offering.

We have incurred significant operating losses to date and expect that our operating losses will increase significantly as we advance our product candidates, particularly KSI-301, through preclinical and clinical development, seek regulatory approval, prepare for and, if approved, proceed to commercialization; broaden and improve our platform; acquire, discover, validate and develop additional product candidates; obtain, maintain, protect and enforce our intellectual property portfolio; and hire additional personnel. In addition, we expect to incur additional costs associated with operating as a public company. Our net loss was $47.4 million, $41.4 million and $27.9 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had an accumulated deficit of $158.1 million.

Our ability to generate product revenue will depend on the successful development and eventual commercialization of one or more of our product candidates. Until such time as we can generate significant revenue from sales of our product candidates, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. Adequate funding may not be available to us on acceptable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back, or discontinue the development and commercialization of KSI-301 for wet AMD, RVO, DME or NPDR or delay our efforts to advance and expand our product pipeline.

On November 1, 2019, we filed a shelf registration statement on Form S-3 (File No. 333-234443) with the SEC covering the offer and sale of up to $400.0 million of the Company's securities for a period of up to three years from the date of effectiveness of the shelf registration statement. In December 2019, we completed a follow-on offering pursuant to the shelf registration on Form S-3 and issued and sold 6,900,000 shares of the Company's common stock, including the underwriters' full exercise of their over-allotment option, at a price to the public of $46.00 per share. The gross proceeds from this offering were $317.4 million, resulting in aggregate net proceeds of $297.6 million after deducting underwriting discounts and commissions and other offering costs payable by us.

As of December 31, 2019, we had cash, cash equivalents and marketable securities of $348.2 million.

**Components of Operating Results**

***Operating Expenses***

*Research and Development Expenses*

Substantially all of our research and development expenses consist of expenses incurred in connection with the development of our ABC Platform and product candidates. These expenses include certain payroll and personnel expenses, including stock-based compensation, for our research and product development employees; laboratory supplies and facility costs; consulting costs; contract manufacturing and fees paid to CROs to conduct certain research and development activities on our behalf; and allocated overhead, including rent, equipment, depreciation and utilities. We expense both internal and external research and development expenses as they are incurred. Costs of certain activities, such as manufacturing and preclinical and clinical studies, are generally recognized based on an evaluation of the progress to completion of specific tasks. Nonrefundable payments made prior to the receipt of goods or services that will be used or rendered for future research and development activities are deferred and capitalized. The capitalized amounts are recognized as expense as the goods are delivered or the related services are performed.

We are focusing substantially all of our resources and development efforts on the development of our product candidates, in particular KSI-301. We expect our research and development expenses to increase substantially during the next few years as we initiate our Phase 3 studies, complete our clinical program, pursue regulatory approval of our drug candidates and prepare for a possible commercial launch. Predicting the timing or the final cost to complete our clinical program or validation of our commercial manufacturing and supply processes is difficult and delays may occur because of many factors, including factors outside of our control. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those that we currently anticipate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development. Furthermore, we are unable to predict when or if our drug candidates will receive regulatory approval with any certainty.

*General and Administrative Expenses*

General and administrative expenses consist principally of payroll and personnel expenses, including stock-based compensation; professional fees for legal, consulting, accounting and tax services; allocated overhead, including rent, equipment, depreciation and utilities; and other general operating expenses not otherwise classified as research and development expenses.

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

*Interest Income*

Interest income consists primarily of interest income earned on our cash, cash equivalents and marketable securities.

*Interest Expense*

Interest expense consists primarily of interest expense related to our convertible notes, including accretion of debt discount and debt issuance costs, which converted into shares of common stock upon the closing of our IPO.

*Other Income (Expense), Net*

Other income (expense), net consists primarily of accretion income on marketable debt securities in 2019 and primarily consists of changes in the fair value of warrants for Series B redeemable convertible preferred stock, changes in fair value of the derivative instruments in 2018.

*Loss on Extinguishment of Debt*

Loss on extinguishment of debt was recognized for the year ended December 31, 2018 related to the convertible notes issued in February 2018 which converted into shares of common stock upon closing of our IPO.

**Results of Operations**

The following table summarizes our results of operations for the periods indicated:

| | Year Ended December 31, | | | 2019 vs 2018 Change | |
|---|---|---|---|---|---|
| | 2019 | 2018 | 2017 | Dollar | Percent |
| | (in thousands, except percentages) | | | | |
| Operating expenses: | | | | | |
| Research and development | $ 37,506 | $ 18,793 | $ 22,022 | $ 18,713 | 100% |
| General and administrative | 11,684 | 7,581 | 3,499 | 4,103 | 54% |
| Loss from operations | (49,190) | (26,374) | (25,521) | (22,816) | 87% |
| Interest income | 1,568 | 617 | 29 | 951 | 154% |
| Interest expense (includes $0, $3,030 and $914 attributable to related parties for the years ended December 31, 2019, 2018 and 2017, respectively) | (8) | (5,519) | (1,185) | 5,511 | * |
| Other income (expense), net (includes $0, $2,736 and $1,008 attributable to related parties for the years ended December 31, 2019, 2018 and 2017, respectively) | 265 | (4,688) | (1,259) | 4,953 | * |
| Loss on extinguishment of debt (includes $1,587 attributable to related parties for the year ended December 31, 2018) | — | (5,479) | — | 5,479 | * |
| Net loss | $ (47,365) | $ (41,443) | $ (27,936) | $ (5,922) | 14% |

* Percentage is not meaningful

*Research and Development Expenses*

Research and development expenses increased $18.7 million, or 100%, from the year ended December 31, 2018 to the year ended December 31, 2019.

The following table summarizes our research and development expenses:

| | Year Ended December 31, | | | 2019 vs 2018 |
|---|---|---|---|---|
| | 2019 | 2018 | 2017 | Change |
| | (in thousands) | | | |
| ABC Platform external expenses [1] | $ 2,218 | $ 1,397 | $ 931 | $ 821 |
| KSI-301 program external expenses [2] | 19,285 | 8,252 | 14,021 | 11,033 |
| KSI-501 program external expenses [3] | 1,188 | — | — | 1,188 |
| Payroll and personnel expenses [4] | 11,978 | 6,825 | 3,288 | 5,153 |
| Other research and development expenses [5] | 2,837 | 2,319 | 3,782 | 518 |
| Total research and development expenses | $ 37,506 | $ 18,793 | $ 22,022 | $ 18,713 |

(1) ABC Platform external expenses primarily relates to manufacturing of biopolymer intermediate drug substance which can be used with multiple product candidates. These expenses are primarily for services provided by CMOs and CROs.

(2) KSI-301 program external expenses relates to development of KSI-301, including manufacturing and clinical trial costs. These expenses are primarily for services provided by CMOs and CROs.

(3) KSI-501 program external expenses relates to research and development of KSI-501.
(4) Payroll and personnel expenses includes salaries, benefits and stock-based compensation for our personnel involved in research and development activities. These expenses are separately classified and not allocated to specific programs because these expenses relate to multiple programs.
(5) Other research and development expenses includes direct costs related to research and development activities other than those listed above.

ABC Platform external expenses increased $0.8 million during the year ended December 31, 2019 as compared to 2018. The increase was primarily driven by manufacturing runs to support our product candidate pipeline.

KSI-301 program external expenses increased $11.0 million during the year ended December 31, 2019 as compared to 2018. The increase was primarily due to clinical trial costs as well as manufacturing runs for KSI-301.

KSI-501 program external expenses increased $1.2 million during the year ended December 31, 2019, due to ongoing research and development of KSI-501.

Payroll and personnel expenses increased $5.2 million during the year ended December 31, 2019 as compared to 2018. The increase was a result of increased headcount and stock-based compensation expense.

Other research and development expenses increased $0.5 million during the year ended December 31, 2019 as compared to 2018. Our other research and development expenses may fluctuate in future periods as we elect to develop other product candidates.

*General and Administrative Expenses*

General and administrative expenses increased $4.1 million, or 54%, from the year ended December 31, 2018 to the year ended December 31, 2019. The increase in general and administrative expenses was primarily attributable to an increase of $2.1 million in professional services related to accounting, audit, legal and consulting services and additional costs associated with operating as a public company, and an increase of $2.0 million in salaries, including stock-based compensation.

*Interest Income*

Interest income increased $1.0 million from the year ended December 31, 2018 to the year ended December 31, 2019 which was mainly attributable to interest income earned on increased cash balances from our IPO in October 2018 and follow-on offering in December 2019.

*Interest Expense*

Interest expense decreased $5.5 million from the year ended December 31, 2018 to the year ended December 31, 2019, which was mainly attributable to interest expense in 2018 on convertible notes issued in August 2017 and February 2018, including accretion of debt discount and issuance costs. The convertible notes converted into shares of common stock upon the closing of our IPO.

*Other Income (Expense), Net*

Other income (expense), net decreased $5.0 million from the year ended December 31, 2018 to the year ended December 31, 2019, which was mainly attributable to the movement in fair value of the redeemable convertible preferred stock warrant liability and derivative instrument related to the convertible notes issued in February 2018 prior to our IPO in 2018, offset by accretion income on marketable debt securities of $0.3 million in 2019. The preferred stock warrants converted into common stock warrants and the derivative liability was extinguished upon our IPO.

*Loss on Extinguishment of Debt*

Loss on extinguishment of the convertible notes issued in February 2018 was $5.5 million for the year ended December 31, 2018.

**Liquidity and Capital Resources; Plan of Operations**

***Sources of Liquidity***

We have funded our operations primarily through the sale and issuance of common stock, redeemable convertible preferred stock, convertible notes and warrants. As of December 31, 2019, we had cash, cash equivalents and marketable securities of $348.2 million.

***2017 Convertible Notes***

In August 2017, we received $10.0 million in gross proceeds from the issuance of the 2017 convertible notes and warrants to purchase Series B redeemable convertible preferred stock. Upon the closing of our IPO, 500,000 redeemable convertible preferred stock warrants automatically converted into common stock warrants and 100,000 of such warrants were exercised immediately following the closing of our IPO. The 2017 convertible notes converted into 2,637,292 shares of common stock at the closing of our IPO.

***2018 Convertible Notes***

In February 2018, we received $33.0 million in gross proceeds from the issuance of the 2018 convertible notes. The 2018 convertible notes converted into 4,295,677 shares of common stock at the closing of our IPO.

***IPO***

In October 2018, we completed our IPO. We sold and issued 9,400,000 shares of common stock at a price to the public of $10.00 per share. The aggregate net proceeds from our IPO, inclusive of the partial over-allotment option exercise, were $83.5 million after deducting underwriting discounts and commissions and other offering costs.

***Follow-On Offering***

In December 2019, we completed a follow-on offering pursuant to the shelf registration on Form S-3 and issued and sold 6,900,000 shares of common stock at a price to the public of $46.00 per share. The gross proceeds from this offering were $317.4 million, resulting in aggregate net proceeds of $297.6 million after deducting underwriting discounts and commissions and other offering costs payable by us.

***Future Funding Requirements***

We have incurred net losses since our inception. For the years ended December 31, 2019, 2018 and 2017, we had net losses of $47.4 million, $41.4 million, and $27.9 million, respectively, and we expect to continue to incur additional losses in future periods. As of December 31, 2019, we had an accumulated deficit of $158.1 million. We currently plan to raise additional funding as required based on the status of its clinical trials and projected cash flows, however based on our current business plan, we believe that our existing cash, cash equivalents and marketable securities are sufficient to fund our projected operations for at least the next 12 months.

To date, we have not generated any product revenue. We do not expect to generate any product revenue unless and until we obtain regulatory approval of and commercialize any of our product candidates or enter into collaborative agreements with third parties, and we do not know when, or if, either will occur. We expect to continue to incur significant losses for the foreseeable future, and we expect our losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. We are subject to all of the risks typically related to the development of new product candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Moreover, we expect to continue incurring additional costs associated with operating as a public company.

We have based these estimates on assumptions that may prove to be wrong, and we could deplete our capital resources sooner than we expect. The timing and amount of our operating expenditures and capital requirements will depend on many factors, including:

- the scope, timing, rate of progress and costs of our drug discovery, preclinical development activities, laboratory testing and clinical trials for our product candidates;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing development and commercial manufacturing activities;
- the extent to which we acquire or in-license other product candidates and technologies;
- the cost, timing and outcome of regulatory review of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all;

- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our product candidates;
- the costs associated with being a public company; and
- the cost and timing associated with commercializing our product candidates, if they receive marketing approval.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we will continue to require additional capital to meet operational needs and capital requirements associated with such operating plans. If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any future debt financing into which we enter may impose upon us additional covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, repurchase our common stock, make certain investments and engage in certain merger, consolidation or asset sale transactions. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders. If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license rights to our product candidates in certain territories or indications to others that we would prefer to develop and commercialize ourselves.

Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. See the section titled "Risk Factors" for additional risks associated with our substantial capital requirements.

***Summary Statement of Cash Flows***

The following table sets forth the primary sources and uses of cash for each of the periods presented below:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2019 | 2018 | 2017 |
| | | (in thousands) | |
| Net cash (used in) provided by: | | | |
| Operating activities | $ (39,146) | $ (29,031) | $ (17,655) |
| Investing activities | $ (136,998) | $ (581) | $ (209) |
| Financing activities | $ 299,687 | $ 116,471 | $ 9,637 |
| Net increase (decrease) in cash, cash equivalents and restricted cash | $ 123,543 | $ 86,859 | $ (8,227) |

**Cash Flows from Operating Activities**

Net cash used in operating activities was $39.1 million for year ended December 31, 2019. Cash used in operating activities was primarily due to the use of funds in our operations to continue to develop KSI-301 and in connection with our operations as a public company, resulting in a net loss of $47.4 million, adjusted by non-cash charges of $6.8 million offset by a change in operating assets and liabilities of $1.4 million. The non-cash charges consisted of $0.5 million of depreciation expense, $6.1 million of stock-based compensation, $0.2 million net accretion of discount on marketable securities, and $0.4 million amortization of the operating lease right-of-use asset. The change in net operating assets and liabilities was primarily due to an increase in accounts payable of $1.6 million due to timing of vendor payments, an increase in accrued liabilities of $4.9 million mainly related to an increase in accrued research and development expenses and an increase in accrued compensation expenses, and an increase in other assets of $4.5 million mainly due to an increase in advance payments.

**Cash Flows from Investing Activities**

Net cash used in investing activities was $137.0 million for year ended December 31, 2019 and primarily related to purchases of marketable securities, net of maturities.

**Cash Flows from Financing Activities**

Net cash provided in financing activities was $299.7 million for year ended December 31, 2019, which consisted primarily of $297.6 million of net proceeds from our follow-on offering, and $2.3 million of proceeds from the exercise of stock options.

**Contractual Obligations and Commitments**

The following table summarizes our contractual obligations as of December 31, 2019:

| | Payments Due by Period | | | | |
|---|---|---|---|---|---|
| | Less than 1 year | 1 to 3 years | 3 to 5 years | More than 5 years | Total |
| | (in thousands) | | | | |
| Operating lease obligations[1] | $ 533 | $ 1,214 | $ 526 | $ — | $ 2,273 |
| Manufacturing agreements[2] | 4,577 | 752 | — | — | 5,329 |
| Tenant improvement obligations[3] | 39 | 86 | 102 | 109 | 336 |
| Total | $ 5,149 | $ 2,052 | $ 628 | $ 109 | $ 7,938 |

(1) We lease our facility under a non-cancelable operating lease. In January 2013, we entered into a lease for our current laboratory and office space that commenced in October 2013 and expired in October 2018. In March 2016, we entered into a lease amendment that extended the lease term to October 2023. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) We have entered into service agreements with a third-party CMO, pursuant to which the CMO agreed to perform activities in connection with the manufacturing process of certain compounds. Such agreements, and related amendments, state that planned activities that are included in some signed work orders are, in some cases, binding and, hence, obligate us to pay the full price of the work order upon satisfactory delivery of products and services. Per the terms of the agreements, we have the option to cancel signed orders at any time upon written notice, which may or may not be subject to payment of a cancellation fee depending on the timing of the written notice in relation to the commencement date of the work, with the maximum cancellation fee equal to the full price of the work order. Although the payment of the cancellation fee will generally be due at the scheduled commencement date, we may record the manufacturing expense and related obligation as an accrued liability at the time of cancellation. In the normal course of business, we have entered into purchase commitments to support research and development activities that cannot be terminated without incurring cancellation fees. The level of cancellation fees may vary and are generally based on the passage of time within a 12-month period.

(3) We have tenant improvement obligations under our facilities lease agreements, which are required to be paid over the contractually agreed period.

We enter into contracts in the normal course of business with third party contract organizations for preclinical and clinical studies and testing, manufacturing, and providing other services and products for operating purposes. These contracts generally provide for termination following a certain period after notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

**Critical Accounting Policies, Significant Judgments and Use of Estimates**

Our consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

***Accrued Research and Development***

Our preclinical and clinical accruals are a component of research and development expenses and are based on patient enrollment and related costs as well as estimates for the services received and efforts expended pursuant to contracts with multiple research institutions and CROs. We estimate research and development accruals, including preclinical and clinical expenses, based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development provided, but not yet invoiced, are included in accrued liabilities and other current liabilities on the consolidated balance sheets. If the actual timing of the performance of services or the level of effort varies from the original estimates, we will adjust the accrual accordingly. Payments made to CROs or CMOs under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets until the services are rendered.

***Stock-Based Compensation Expense***

We measure and recognize compensation expense for all stock-based awards made to employees, directors and non-employees, based on estimated fair values of the awards on the grant date and recognized using the straight-line method over the requisite service period.

The fair value of options is estimated on the grant date using the Black-Scholes option valuation model. The calculation of stock-based compensation expense requires that we make certain assumptions and judgments about a number of complex and subjective variables used in the Black-Scholes model, including the expected term, expected volatility of the underlying common stock and risk-free interest rate. Our stock-based awards are subject to either service or performance-based vesting conditions. We evaluate whether achievement of the performance conditions is probable and record expense over the appropriate service period based on this assessment.

Changes in these assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop.

***Income Taxes***

We provide for income taxes under the asset and liability method. Current income tax expense or benefit represents the amount of income taxes expected to be payable or refundable for the current year. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax bases of assets and liabilities and net operating loss and credit carryforwards, and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all of the tax benefits will not be realized.

We assess all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement.

As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and we will determine whether (1) the factors underlying the sustainability assertion have changed and (2) the amount of the recognized tax benefit is still appropriate. The recognition and measurement of tax benefits requires significant judgment. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available. Our policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Net operating loss carryforwards, or NOLs, and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service, or IRS, and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50% as defined under Sections 382 and 383 in the Internal Revenue Code, which could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on our value immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. We have completed a Section 382 study through December 31, 2019 which concluded no such ownership change had occurred through December 31, 2019.

As of December 31, 2019 and 2018, we had unrecognized tax benefits, all of which would affect income tax expense if recognized, before consideration of our valuation allowance. We do not expect that our uncertain tax positions will materially change in the next twelve months.

**Off-Balance Sheet Arrangements**

Since our inception, we have not engaged in any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

**JOBS Act Accounting Election**

The Jumpstart Our Business Startups Act of 2012, or JOBS Act, permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until such pronouncements are made applicable to private companies, unless we otherwise irrevocably elect not to avail ourselves of this exemption. However, we have chosen to irrevocably "opt out" of such extended transition period, and as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision to not take advantage of the extended transition period for complying with new or revised accounting standards is irrevocable.

**Recent Accounting Pronouncements**

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is discussed under Note 2 to our consolidated financial statements included in this report.

## ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK

We are exposed to market risk related to changes in interest rates. As of December 31, 2019, we had cash, cash equivalents and marketable securities of $348.2 million, primarily invested in money market funds, overnight repurchase agreements, U.S. treasury securities, commercial paper and corporate notes. As of December 31, 2018, we had cash and cash equivalents of $88.3 million, invested in money market funds. Changes in the general level of interest rates can affect the fair value of our investment portfolio. If market interest rates were to increase immediately and uniformly by 100 basis points, or one percentage point, from levels at December 31, 2019, the net fair value of our interest-sensitive marketable securities would have resulted in a hypothetical decline of $0.9 million.

We do not believe that other market risks, like foreign currency exchange rate risk, had a significant impact on our results of operations for any periods presented herein.

## ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

### INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

## Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Kodiak Sciences Inc.

***Opinion on the Financial Statements***

We have audited the accompanying consolidated balance sheets of Kodiak Sciences Inc. and its subsidiaries (the "Company") as of December 31, 2019 and 2018, and the related consolidated statements of operations and comprehensive loss, of redeemable convertible preferred stock and stockholders' equity (deficit) and of cash flows for each of the three years in the period ended December 31, 2019, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019 in conformity with accounting principles generally accepted in the United States of America.

*Change in Accounting Principle*

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for leases in 2019.

***Basis for Opinion***

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated 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 of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated 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 consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP
San Jose, California
March 16, 2020

We have served as the Company's auditor since 2016.

**Kodiak Sciences Inc.**
**Consolidated Balance Sheets**
**(in thousands, except share and per share amounts)**

| | December 31, 2019 | December 31, 2018 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 211,797 | $ 88,254 |
| Marketable securities | 124,684 | — |
| Prepaid expenses and other current assets | 2,749 | 2,195 |
| Total current assets | 339,230 | 90,449 |
| Marketable securities | 11,696 | — |
| Restricted cash | 140 | 140 |
| Property and equipment, net | 996 | 1,097 |
| Operating lease right-of-use asset | 1,790 | — |
| Other assets | 5,014 | 503 |
| Total assets | $ 358,866 | $ 92,189 |
| **Liabilities and stockholders' equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 2,619 | $ 1,050 |
| Accrued and other current liabilities | 8,658 | 3,776 |
| Operating lease liability | 434 | — |
| Total current liabilities | 11,711 | 4,826 |
| Operating lease liability, net of current portion | 1,501 | — |
| Other liabilities | 295 | 530 |
| Total liabilities | 13,507 | 5,356 |
| Commitments and contingencies (Note 7) | | |
| Stockholders' equity: | | |
| Preferred stock, $0.0001 par value, 10,000,000 shares authorized; 0 shares issued and outstanding at December 31, 2019 and 2018 | — | — |
| Common stock, $0.0001 par value, 490,000,000 shares authorized at December 31, 2019 and 2018; 44,413,404 and 36,829,857 shares issued and outstanding at December 31, 2019 and 2018, respectively | 5 | 4 |
| Additional paid-in capital | 503,475 | 197,595 |
| Accumulated other comprehensive income | 10 | — |
| Accumulated deficit | (158,131) | (110,766) |
| Total stockholders' equity | 345,359 | 86,833 |
| Total liabilities and stockholders' equity | $ 358,866 | $ 92,189 |

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

**Kodiak Sciences Inc.**
**Consolidated Statements of Operations and Comprehensive Loss**
**(in thousands, except share and per share amounts)**

| | Year Ended December 31, 2019 | Year Ended December 31, 2018 | Year Ended December 31, 2017 |
|---|---|---|---|
| Operating expenses | | | |
| Research and development | $ 37,506 | $ 18,793 | $ 22,022 |
| General and administrative | 11,684 | 7,581 | 3,499 |
| Total operating expenses | 49,190 | 26,374 | 25,521 |
| Loss from operations | (49,190) | (26,374) | (25,521) |
| Interest income | 1,568 | 617 | 29 |
| Interest expense (includes $0, $3,030 and $914 attributable to related parties for the years ended December 31, 2019, 2018 and 2017, respectively) | (8) | (5,519) | (1,185) |
| Other income (expense), net (includes $0, $2,736 and $1,008 attributable to related parties for the years ended December 31, 2019, 2018 and 2017, respectively) | 265 | (4,688) | (1,259) |
| Loss on extinguishment of debt (includes $1,587 attributable to related parties for the year ended December 31, 2018) | — | (5,479) | — |
| Net loss | $ (47,365) | $ (41,443) | $ (27,936) |
| Net loss per common share, basic and diluted | $ (1.25) | $ (2.77) | $ (3.72) |
| Weighted-average common shares outstanding used in computing net loss per common share, basic and diluted | 37,853,616 | 14,976,515 | 7,515,336 |
| Other comprehensive income | | | |
| Change in unrealized gains related to available-for-sale debt securities, net of tax | 10 | — | — |
| Total other comprehensive income | 10 | — | — |
| Comprehensive loss | $ (47,355) | $ (41,443) | $ (27,936) |

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

**Kodiak Sciences Inc.**
**Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)**
**(in thousands, except share and per share amounts)**

| | Redeemable Convertible Preferred Stock | | Common Stock | | Additional Paid-In | Accumulated Other Comprehensive | Accumulated | Total Stockholders' Equity |
|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | Capital | Income (Loss) | Deficit | (Deficit) |
| Balance at December 31, 2016 | 12,385,154 | $ 50,017 | 7,930,831 | $ 1 | $ 303 | $ — | $ (41,387) | $ (41,083) |
| Issuance of common stock upon exercise of stock options | — | — | 5,603 | — | 3 | — | — | 3 |
| Vesting of early exercised stock options | — | — | — | — | 3 | — | — | 3 |
| Stock-based compensation expense | — | — | — | — | 275 | — | — | 275 |
| Net loss | — | — | — | — | — | — | (27,936) | (27,936) |
| Balance at December 31, 2017 | 12,385,154 | 50,017 | 7,936,434 | 1 | 584 | — | (69,323) | (68,738) |
| Issuance of common stock upon exercise of stock options | — | — | 47,800 | — | 49 | — | — | 49 |
| Issuance of restricted stock awards | — | — | 27,500 | — | — | — | — | — |
| Conversion of redeemable convertible preferred stock into common stock | (12,385,154) | (50,017) | 12,385,154 | 1 | 50,016 | — | — | 50,017 |
| Conversion of redeemable convertible preferred stock warrants into common stock warrants | — | — | — | — | 5,000 | — | — | 5,000 |
| Issuance of common stock upon exercise of common stock warrants | — | — | 100,000 | — | — | — | — | — |
| Conversion of 2017 and 2018 convertible notes into common stock | — | — | 6,932,969 | 1 | 55,732 | — | — | 55,733 |
| Issuance of common stock upon initial public offering, net of issuance cost of $10,542 | — | — | 9,400,000 | 1 | 83,458 | — | — | 83,459 |
| Stock-based compensation expense | — | — | — | — | 2,756 | — | — | 2,756 |
| Net loss | — | — | — | — | — | — | (41,443) | (41,443) |
| Balance at December 31, 2018 | — | — | 36,829,857 | 4 | 197,595 | — | (110,766) | 86,833 |
| Issuance of common stock upon exercise of stock options | — | — | 662,079 | — | 2,287 | — | — | 2,287 |
| Vesting of restricted stock units, net of taxes withheld | — | — | 21,467 | — | (132) | — | — | (132) |
| Issuance of common stock upon exercise of common stock warrants | — | — | 1 | — | — | — | — | — |
| Issuance of common stock upon follow-on offering, net of issuance cost of $19,784 | — | — | 6,900,000 | 1 | 297,615 | — | — | 297,616 |
| Stock-based compensation expense | — | — | — | — | 6,110 | — | — | 6,110 |
| Other comprehensive income | — | — | — | — | — | 10 | — | 10 |
| Net loss | — | — | — | — | — | — | (47,365) | (47,365) |
| Balance at December 31, 2019 | — | $ — | 44,413,404 | $ 5 | $ 503,475 | $ 10 | $ (158,131) | $ 345,359 |

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

**Kodiak Sciences Inc.**
**Consolidated Statements of Cash Flows**
**(in thousands)**

| | Year Ended December 31, 2019 | Year Ended December 31, 2018 | Year Ended December 31, 2017 |
|---|---|---|---|
| **Cash flows from operating activities** | | | |
| Net loss | $ (47,365) | $ (41,443) | $ (27,936) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Depreciation | 538 | 490 | 549 |
| Non-cash interest expense and amortization of debt discount and issuance cost | — | 5,482 | 1,161 |
| Change in fair value of redeemable convertible preferred stock warrant liability | — | 2,700 | 1,260 |
| Change in fair value of derivative instrument | — | 1,988 | — |
| Extinguishment of debt | — | 5,479 | — |
| Stock-based compensation | 6,110 | 2,665 | 275 |
| Amortization (accretion) of premium (discount) on marketable securities | (241) | — | — |
| Amortization of operating lease right-of-use asset | 373 | — | — |
| Changes in assets and liabilities: | | | |
| Prepaid expense and other current assets | (168) | (1,995) | 368 |
| Other assets | (4,511) | — | 8 |
| Accounts payable | 1,569 | (2,323) | 2,282 |
| Accrued and other current liabilities | 4,932 | (2,105) | 4,330 |
| Operating lease liability | (383) | — | — |
| Other liabilities | — | 31 | 48 |
| Net cash used in operating activities | (39,146) | (29,031) | (17,655) |
| **Cash flows from investing activities** | | | |
| Purchase of property and equipment | (437) | (78) | (209) |
| Deposits on property and equipment | — | (503) | — |
| Purchases of marketable securities | (150,961) | — | — |
| Maturities of marketable securities | 14,400 | — | — |
| Net cash used in investing activities | (136,998) | (581) | (209) |
| **Cash flows from financing activities** | | | |
| Proceeds from issuance of common stock, net of offering costs | 297,616 | 83,755 | — |
| Proceeds from issuance of common stock upon option exercise | 2,287 | 49 | 3 |
| Payments for restricted stock units, net of taxes withheld | (132) | — | — |
| Proceeds from issuance of convertible notes (includes $9,560 and $8,000 from related parties for the years ended December 31, 2018 and 2017, respectively) | — | 33,000 | 10,000 |
| Debt issuance cost | — | (140) | (181) |
| Principal payments of capital lease | (48) | (108) | (97) |
| Principal payments of tenant improvement allowance payable | (36) | (85) | (88) |
| Net cash provided by financing activities | 299,687 | 116,471 | 9,637 |
| Net increase (decrease) in cash, cash equivalents and restricted cash | 123,543 | 86,859 | (8,227) |
| Cash, cash equivalents and restricted cash, at beginning of year | 88,394 | 1,535 | 9,762 |
| Cash, cash equivalents and restricted cash, at end of year | $ 211,937 | $ 88,394 | $ 1,535 |
| Reconciliation of cash, cash equivalents and restricted cash to consolidated balance sheets | | | |
| Cash and cash equivalents | $ 211,797 | $ 88,254 | $ 1,395 |
| Restricted cash | 140 | 140 | 140 |
| Cash, cash equivalents and restricted cash in consolidated balance sheets | $ 211,937 | $ 88,394 | $ 1,535 |
| **Supplemental cash flow information:** | | | |
| Cash paid for interest | $ 8 | $ 19 | $ 24 |
| **Supplemental disclosures of non-cash investing and financing information:** | | | |
| Operating lease right-of-use asset obtained in exchange for operating lease liability | $ 2,163 | $ — | $ — |
| Unpaid offering costs | $ 459 | $ 205 | $ — |
| Offering costs paid in restricted stock awards | $ — | $ 91 | $ — |
| Derivative instrument related to convertible notes | $ — | $ 6,603 | $ — |
| Redeemable convertible preferred stock warrant issued in connection with convertible notes | $ — | $ — | $ 1,040 |
| Acquisition of equipment through capital lease | $ — | $ — | $ 73 |

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

## 1. The Company

Kodiak Sciences Inc. (the "Company") is a clinical stage biopharmaceutical company specializing in novel therapeutics to treat high-prevalence ophthalmic diseases. The Company devotes substantially all of its time and efforts to performing research and development, raising capital and recruiting personnel.

### *Initial Public Offering*

In October 2018, the Company sold and issued 9,000,000 shares of common stock at a price to the public of $10.00 per share for gross proceeds of $90.0 million. In November 2018, the Company sold and issued an additional 400,000 shares of common stock at $10.00 per share to the underwriters of the initial public offering ("IPO") following the partial exercise of their over-allotment option for gross proceeds of $4.0 million. The aggregate net proceeds to the Company from the IPO, inclusive of the partial over-allotment option exercise, were $83.5 million after deducting underwriting discounts and commissions and other offering costs.

Upon the closing of the IPO, all convertible preferred shares then outstanding automatically converted into 12,385,154 shares of common stock, 500,000 redeemable convertible preferred stock warrants automatically converted into common stock warrants and 100,000 of such warrants were exercised immediately following the closing of the IPO. The 2017 convertible notes converted into 2,637,292 shares of common stock and the 2018 convertible notes converted into 4,295,677 shares of common stock upon closing of the IPO. In connection with the IPO, the Company amended and restated its certificate of incorporation and bylaws.

### *Follow-On Offering*

In December 2019, the Company sold and issued 6,900,000 shares of common stock, including the underwriters' full exercise of their over-allotment option, at a price to the public of $46.00 per share for gross proceeds of $317.4 million. The aggregate net proceeds to the Company from the follow-on offering were $297.6 million after deducting underwriting discounts and commissions and other offering costs.

## 2. Summary of Significant Accounting Policies

### *Basis of Presentation*

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("US GAAP").

### *Reclassification*

Certain prior period amounts in the consolidated financial statements have been reclassified to conform to the current period presentation.

### *Principles of Consolidation*

The consolidated financial statements include the Company's accounts and the accounts of Kodiak Sciences Financing Corporation and Kodiak Sciences China, the Company's direct wholly owned subsidiaries, incorporated in the United States and Cayman Islands, respectively, and Kodiak Sciences GmbH, the Company's indirect wholly owned subsidiary, incorporated in Switzerland. All intercompany accounts and transactions have been eliminated. The functional and reporting currency of the Company and its subsidiaries is the U.S. dollar. The aggregate foreign currency transaction loss included in determining net loss was less than $0.1 million, $0.3 million and less than $0.1 million for the years ended December 31, 2019, 2018 and 2017, respectively.

### *Segments*

The Company operates and manages its business as one reportable and operating segment, which is the business of research and development of drugs for ophthalmic diseases. The chief operating decision maker reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance.

***Use of Estimates***

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities as of the date of the consolidated financial statements and expenses during the reporting period. Such estimates include, but are not limited to, the accrual for research and development expenses, the valuation of deferred tax assets, useful lives of property and equipment, the measurement of right-of-use assets and lease liabilities, stock-based compensation, and the valuation of common shares, convertible debt, derivatives and redeemable convertible preferred stock warrants prior to the Company's IPO. Actual results could differ from those estimates.

***Risk and Uncertainties***

The Company's future results of operations involve a number of risks and uncertainties common to clinical-stage companies in the biotechnology industry. The Company's product candidates are in development and the Company operates in an environment of rapid change in technology and substantial competition from other pharmaceutical and biotechnology companies. Factors that could affect the Company's future operating results and cause actual results to vary materially from expectations include, but are not limited to, uncertainty of results of clinical trials and reaching milestones, uncertainty of regulatory approval of the Company's potential drug candidates, uncertainty of market acceptance of any of the Company's product candidates that receive regulatory approval, competition from new technological innovations, substitute products and larger companies, securing and protecting proprietary technology, strategic relationships and dependence on key individuals, contract manufacturer and research organizations, and other suppliers.

Products developed by the Company require approvals from the U.S. Food and Drug Administration ("FDA") or other international regulatory agencies prior to commercial sales. There can be no assurance that any of the Company's product candidates will receive the necessary approvals. If the Company is denied approval, approval is delayed or the Company is unable to maintain approvals, it could have a materially adverse impact on the Company. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales.

The Company expects to incur substantial operating losses for the next several years and will need to obtain additional financing in order to complete clinical trials and launch and commercialize any product candidates for which it receives regulatory approval. There can be no assurance that such financing will be available or will be on terms acceptable by the Company.

***Concentration of Credit Risk***

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents and marketable securities. As of December 31, 2019 and 2018, cash, cash equivalents and marketable securities were invested primarily in money market funds, overnight repurchase agreements, U.S. treasury securities, commercial paper and corporate notes through highly rated financial institutions. Investments are restricted, in accordance with the Company's investment policy, to a concentration limit per issuer or sector.

***Cash and Cash Equivalents***

The Company considers all highly liquid investments with stated maturities of three months or less at the date of purchase to be cash equivalents.

***Marketable Securities***

The Company invests excess cash balances in marketable securities. The investments in marketable securities are classified as either held-to-maturity or available-for-sale based on facts and circumstances present at the time of purchase. Marketable securities with a remaining maturity date greater than one year are classified as non-current. The Company's marketable securities consist of U.S. treasury securities, commercial paper, and corporate bonds. Marketable securities are carried at fair value with the unrealized gains and losses included in other comprehensive income (loss) as a component of stockholders' equity until realized. Any premium or discount arising at purchase of marketable debt securities is amortized and/or accreted to other income (expense), net over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included in other income (expense), net.

If any adjustment to fair value reflects a decline in value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is "other-than-temporary" and, if so, marks the investment to market through a charge to the Company's statement of operations and comprehensive loss.

***Restricted Cash***

As of December 31, 2019, and 2018, the Company had $0.1 million of long-term restricted cash deposited with a financial institution. The entire amount is held in a separate bank account to support a letter of credit agreement related to the Company's headquarter facility lease which expires in 2023.

***Fair Value of Financial Instruments***

Accounting Standards Codification ("ASC") 820, *Fair Value Measurement*, establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

*Level 1*—Observable inputs, such as quoted prices in active markets for identical assets or liabilities at the measurement date.

*Level 2*—Observable inputs other than Level 1 prices such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

*Level 3*—Unobservable inputs which reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and inputs to the model.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts of the Company's financial instruments consisting of cash and cash equivalents, prepaid expenses and other current assets, accounts payable and accrued liabilities and other current liabilities, approximate fair value due to their relatively short maturities.

***Leases***

The Company determines if an arrangement is, or contains, a lease at inception and then classifies the lease as operating or financing based on the underlying terms and conditions of the contract. Leases with terms greater than one year are initially recognized on the balance sheet as right-of-use assets and lease liabilities 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 incremental borrowing rate, which is the rate incurred to borrow, on a collateralized basis, an amount equal to the lease payments over a similar term and in a similar economic environment of the applicable country or region. Variable lease payments are excluded from the right of use assets and operating lease liabilities and are recognized in the period in which the obligation for those payments is incurred.

***Property and Equipment, Net***

Property and equipment are stated at cost less accumulated depreciation for acquired assets. Depreciation is computed using the straight-line method over the estimated useful lives of assets, which is generally four years for laboratory equipment, three years for computer equipment and office equipment, five years for computer software and five to seven years for furniture and fixtures. Leasehold improvements are stated at cost and amortized over the shorter of the useful life of the assets or the length of the lease. Upon sale or retirement of assets, the costs and related accumulated depreciation are removed from the consolidated balance sheet and the resulting gain or loss is reflected in operations. Maintenance and repairs are charged to operations as incurred.

***Impairment of Long-Lived Assets***

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amount to the future undiscounted net cash flows which the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows arising from the assets. There have been no such impairments of long-lived assets in the years ended December 31, 2019 and 2018.

***Research and Development Expenses***

Costs related to research, design and development of products are charged to research and development expense as incurred. Research and development costs include, but are not limited to, payroll and personnel expenses, including stock-based compensation, laboratory supplies, outside services and allocated overhead, including rent, equipment, depreciation and utilities.

***Accrued Research and Development***

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

***Stock-Based Compensation***

The Company accounts for stock-based compensation in accordance with the provisions of ASC 718, *Compensation-Stock* Compensation. The Company measures stock-based compensation expense for stock options and restricted stock units granted to its employees, directors and non-employees based on the estimated fair value of the awards on the grant date. The fair value of options is calculated using the Black-Scholes valuation model, which requires the input of subjective assumptions, including (i) the expected stock price volatility, (ii) the calculation of expected term of the award, (iii) the risk-free interest rate, and (iv) expected dividends. The expense is recorded on a straight-line basis over the requisite service period, which is generally the vesting period, for the entire award. The Company accounts for forfeitures as they occur.

Prior to the adoption of Accounting Standards Update ("ASU") No. 2018-07, *Compensation - Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"), the measurement date for non-employee awards was generally the date the services are completed, resulting in financial reporting period adjustments to stock-based compensation during the vesting terms for changes in the fair value of the awards. After adoption of ASU 2018-07 as of January 1, 2019, the measurement date for non-employee awards is the date of grant without changes in the fair value of the award.

The Company has certain stock options and restricted stock units that vest in conjunction with certain performance conditions. At each reporting date, the Company is required to evaluate whether achievement of the performance conditions is probable. Compensation expense is recorded over the appropriate service period based upon the Company's assessment of accomplishing each performance provision.

***Income Taxes***

The Company accounts for income taxes under the asset and liability method, which requires, among other things, that deferred income taxes be provided for temporary differences between the tax basis of the Company's assets and liabilities and their financial statement reported amounts. In addition, deferred tax assets are recorded for the future benefit of utilizing net operating losses ("NOLs") and research and development credit carryforwards and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. A valuation allowance is provided against deferred tax assets unless it is more likely than not that they will be realized.

The Company accounts for uncertain tax positions by assessing all material positions taken in any assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. The Company's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

***Comprehensive Loss***

Comprehensive loss is composed of net loss and other comprehensive income (loss). Other comprehensive income (loss) consists primarily of unrealized gains and losses on debt securities.

***Net Loss per Share Attributable to Common Stockholders***

Basic net loss per common share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common stock outstanding during the period, without consideration of potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common stock and potentially dilutive securities outstanding for the period. For purposes of this calculation, the redeemable convertible preferred stock, preferred stock warrants, convertible notes, common stock subject to repurchase, and stock options are considered to be potentially dilutive securities. Basic and diluted net loss attributable to common stockholders per share is presented in conformity with the two-class method required for participating securities as the redeemable convertible preferred stock is considered a participating security. The Company's participating securities do not have a contractual obligation to share in the Company's losses. As such, the net loss is attributed entirely to common stockholders. Since the Company has reported net loss for all periods presented, diluted net loss per share is the same as basic net loss per common share for those periods.

***Recent Accounting Pronouncements***

From time to time, new accounting pronouncements are issued by the FASB, under its ASC or other standard setting bodies, and adopted by the Company as of the specified effective date, unless otherwise discussed below.

*Recently Adopted Accounting Pronouncements*

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842)*, which set out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (*i.e.,* lessees and lessors). In July 2018, the FASB issued ASU 2018-10, *Leases (Topic 842), Codification Improvements*, and ASU 2018-11, *Leases (Topic 842), Targeted Improvements*. ASU 2018-10 clarified certain provisions and corrected unintended applications of the guidance such as the application of implicit rate, lessee reassessment of lease classification, and certain transition adjustments that should be recognized to earnings rather than to stockholders' equity. ASU 2018-11 provided an alternative transition method and practical expedient for separating contract components for the adoption of Topic 842. ASU 2016-02, ASU 2018-10, and ASU 2018-11 (collectively, "the new lease standards") superseded the previous leases standard, ASC 840 *Leases*.

The Company adopted ASC 842 effective January 1, 2019 using the modified retrospective approach to recognize a cumulative-effect adjustment on the effective date and to not adjust financial information and disclosures required under the new lease standards for comparative prior periods. The Company did not elect for the package of practical expedients and assessed all contracts at the transition date. The Company did not utilize the practical expedient which allows the use of hindsight in determining lease term and assessing impairment in right-of-use assets. The Company elected to apply the practical expedient and accounted for each lease component and related non-lease component as one single component. The Company elected the practical expedient not to recognize leases with terms of one year or less on the balance sheet.

The adoption of the new lease standards on January 1, 2019 resulted in the initial recognition of right-of-use asset of $2.2 million and operating lease liability of $2.3 million and derecognition of noncurrent deferred liabilities of $0.2 million related to the operating lease for the Company's office and laboratory space in Palo Alto, California on the consolidated balance sheets with no material impact to the consolidated statements of operations, stockholders' equity or cash flows. Refer to Note 7.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share (Topic 260) Distinguishing Liabilities from Equity (Topic 480) Derivatives and Hedging (Topic 815) (Part I) Accounting for Certain Financial Instruments with Down Round Features, (Part II) Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception*. This update simplifies the accounting for certain financial instruments with down round features, a provision in an equity-linked financial instrument (or embedded feature) that provides a downward adjustment of the current exercise price based on the price of future equity offerings. Down round features are common in warrants, preferred shares, and convertible debt instruments issued by private companies and early-stage public companies. This update requires companies to disregard the down round feature when assessing whether the instrument is indexed to its own stock, for purposes of determining liability or equity classification. ASU 2017-11 is effective for interim and annual periods beginning after December 15, 2018. The Company adopted this new guidance as of January 1, 2019, which did not impact its consolidated financial statements and related disclosures.

In June 2018, the FASB issued ASU 2018-07, *Compensation — Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, which expands the scope of Topic 718 to include all share-based payment transactions for acquiring goods and services from nonemployees. ASU 2018-07 specifies that Topic 718 applies to all share-based payment transactions in which the grantor acquires goods and services to be used or consumed in its own operations by issuing share-based payment awards. ASU 2018-07 also clarifies that Topic 718 does not apply to share-based payments used to effectively provide (1) financing to the issuer or (2) awards granted in conjunction with selling goods or services to customers as part of a contract accounted for under ASC 606. ASU 2018-07 is effective for interim and annual periods beginning after December 15, 2018. The Company adopted this new guidance as of January 1, 2019, which did not result in a material impact on its consolidated financial statements and related disclosures.

*New Accounting Pronouncements Not Yet Adopted*

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments - Credit Losses (Topic 362): Measurement of Credit Losses on Financial Statements* and ASU 2018-19, *Codification Improvements to Topic 326, Financial Instruments—Credit Losses*, which intends to improve financial reporting by requiring earlier recognition of credit losses on certain financial assets, such as available-for-sale debt securities. The standard is effective for interim and annual periods after December 15, 2019. Early adoption is permitted. The Company is currently evaluating the impact of adopting this guidance on its consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU 2018-13, *Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurements*, which eliminates, adds and modifies certain disclosure requirements for fair value measurements as part of the FASB's disclosure framework project. The standard is effective for interim and annual periods beginning after December 15, 2019. The standard specifies certain amendments which should be applied prospectively while all other amendments should be applied retrospectively. Early adoption is permitted. The Company is currently evaluating the impact of adopting this guidance on its consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU 2018-15, *Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract,* which clarifies the accounting for implementation, set-up, and other upfront costs incurred in cloud computing arrangements. The standard is effective for interim and annual periods beginning after December 15, 2019. Early adoption is permitted. The Company is currently evaluating the impact of adopting this guidance on its consolidated financial statements and related disclosures.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The new standard will be effective beginning January 1, 2021. The Company is currently evaluating the impact of adopting this guidance on its consolidated financial statements and related disclosures.

### 3. Property and Equipment, net

Property and equipment, net consists of the following (in thousands):

| | December 31, 2019 | December 31, 2018 |
|---|---|---|
| Leasehold improvement | $ 1,265 | $ 1,260 |
| Laboratory equipment | 1,125 | 1,133 |
| Furniture and fixtures | 204 | 225 |
| Computer software | 79 | 85 |
| Office equipment | 94 | 79 |
| Total property and equipment | 2,767 | 2,782 |
| Less: Accumulated depreciation | (1,771) | (1,685) |
| Property and equipment, net | $ 996 | $ 1,097 |

All property and equipment are maintained in the United States. Depreciation expense, including depreciation of assets under capital leases, was $0.5 million, $0.5 million and $0.5 million for the years ended December 31, 2019, 2018 and 2017, respectively.

### 4. Accrued Liabilities and Other Current Liabilities

Accrued liabilities and other current liabilities consist of the following (in thousands):

| | December 31, 2019 | December 31, 2018 |
|---|---|---|
| Accrued research and development | $ 4,894 | $ 1,387 |
| Accrued salaries and benefits | 3,108 | 2,061 |
| Accrued legal fees | 302 | 82 |
| Accrued professional fees | 195 | 117 |
| Accrued other liabilities | 159 | 129 |
| Total accrued and other current liabilities | $ 8,658 | $ 3,776 |

### 5. Fair Value Measurements

The following tables present the Company's fair value hierarchy for assets and liabilities measured at fair value on a recurring basis (in thousands):

| | Fair Value Measurements at December 31, 2019 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| Cash equivalents: | | | | |
| Money market funds | $ 155,276 | $ — | $ — | $ 155,276 |
| Repurchase agreement | 50,000 | — | — | 50,000 |
| Commercial paper | — | 5,987 | — | 5,987 |
| Marketable securities: | | | | |
| U.S. treasury securities | — | 50,185 | — | 50,185 |
| Commercial paper | — | 34,533 | — | 34,533 |
| Corporate notes | — | 51,662 | — | 51,662 |
| Total | $ 205,276 | $ 142,367 | $ — | $ 347,643 |

| | Fair Value Measurements at December 31, 2018 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| Cash equivalents: | | | | |
| Money market funds | $ 87,957 | $ — | $ — | $ 87,957 |
| Total | $ 87,957 | $ — | $ — | $ 87,957 |

There were no liabilities measured at fair value on a recurring and non-recurring basis as of December 31, 2019 and 2018. There were no transfers of assets or liabilities between the fair value measurement levels during the years ended December 31, 2019 and 2018.

## 6. Marketable Securities

The marketable securities are classified as available-for-sale and consist of U.S. treasury securities, corporate notes and commercial paper. The fair value measurement data for marketable securities is obtained from independent pricing services. The Company validates the prices provided by the third-party pricing services by understanding the valuation methods and data sources used and analyzing the pricing data in certain instances.

The following table summarizes the marketable securities held at December 31, 2019 (in thousands):

| | Amortized Cost | Unrealized Gains | Unrealized Losses | Fair Value |
|---|---|---|---|---|
| U.S. treasury securities | $ 50,190 | $ — | $ (5) | $ 50,185 |
| Commercial paper | 34,532 | 1 | — | 34,533 |
| Corporate notes | 39,956 | 13 | (3) | 39,966 |
| Total marketable securities, current | $ 124,678 | $ 14 | $ (8) | $ 124,684 |
| | | | | |
| Corporate notes | $ 11,692 | $ 4 | $ — | $ 11,696 |
| Total marketable securities, noncurrent | $ 11,692 | $ 4 | $ — | $ 11,696 |

All marketable securities held at December 31, 2019 had effective maturities of less than two years. There were no realized gains or losses recognized on the sale or maturity of available-for-sale debt securities during the year ended December 31, 2019 and as a result, the Company did not reclassify any amounts out of accumulated comprehensive loss. All marketable securities with unrealized losses as of December 31, 2019 have been in a loss position for less than twelve months and the loss is not material. These marketable securities were not considered to be other-than-temporarily impaired as of December 31, 2019.

## 7. Commitments and Contingencies

***Leases***

In January 2013, the Company executed a non-cancellable lease agreement for office and laboratory space in Palo Alto, California. The lease began in October 2013 and would expire in October 2018. In March 2016, the Company executed a lease amendment agreement which was effective March 2016 and extended the lease term until October 2023.

The Company recognizes rent expense on a straight-line basis over the lease period. Rent expense recognized under all leases was $0.6 million and $0.6 million and $0.6 million for the years ended December 31, 2019, 2018 and 2017, respectively. Note that the Company adopted ASC 842 using the required modified retrospective approach effective January 1, 2019. Therefore, the amounts disclosed for the years ended December 31, 2018 and 2017 are presented under previous accounting guidance and are therefore not comparable to the amounts recorded in the current period under ASC 842.

The Company recognized an operating lease right-of-use asset and corresponding liability on January 1, 2019 based on the present value of remaining lease payments discounted at the Company's estimated incremental borrowing rate of 8.5% over the remaining lease term of 4.83 years for the facility in Palo Alto, California. For the year ended December 31, 2019, the operating lease cost was $0.6 million and the variable lease costs were $0.2 million. The cash paid for amounts included in the measurement of the operating lease liability was $0.6 million for the year ended December 31, 2019. The short-term lease costs were immaterial for the year ended December 31, 2019.

The maturities of the operating lease liabilities as of December 31, 2019 were as follows (in thousands):

| Year ending December 31, | As of December 31, 2019 |
|---|---|
| 2020 | $ 533 |
| 2021 | 598 |
| 2022 | 616 |
| 2023 | 526 |
| Total undiscounted lease payments | 2,273 |
| Less: imputed interest | (338) |
| Total operating lease liabilities | $ 1,935 |

The future minimum lease payments under all non-cancelable operating lease obligations as of December 31, 2018 were as follows (in thousands):

| Year ending December 31, | As of December 31, 2018 |
|---|---|
| 2019 | $ 564 |
| 2020 | 581 |
| 2021 | 598 |
| 2022 | 616 |
| 2023 | 526 |
| Total payments | $ 2,885 |

***Other Commitments and Contingencies***

The Company has entered into service agreements with Lonza AG and its affiliates ("Lonza"), pursuant to which Lonza agreed to perform activities in connection with the manufacturing process of certain compounds. Such agreements, and related amendments, state that planned activities that are included in the signed work orders are, in some cases, binding and, hence, obligate the Company to pay the full price of the work order upon satisfactory delivery of products and services. Per the terms of the agreements, the Company has the option to cancel signed orders at any time upon written notice, which may or may not be subject to payment of a cancellation fee. The level of cancellation fees may be dependent on the timing of the written notice in relation to the commencement date of the work, with the maximum cancellation fee equal to the full price of the work order. As of December 31, 2019 and 2018, the total amount of unconditional purchase obligations, including accrued amounts, under these agreements were $4.7 million and $3.2 million, respectively. Purchases under this agreement for the years ended December 31, 2019, 2018 and 2017 were $7.9 million, $2.8 million and $13.9 million, respectively. As of December 31, 2019, the Company had not incurred any cancellation fees for the work performed by Lonza.

In the normal course of business, the Company enters into purchase commitments to support research and development activities that cannot be terminated without incurring cancellation fees. The level of cancellation fees may vary and are generally based on the passage of time within a 12-month period. As of December 31, 2019, the total amount of cancellation fees related to manufacturing equipment was $0.7 million and none as of December 31, 2019 and 2018, respectively.

The Company is also party to a cancellable assignment and license agreement that would require the Company to make milestone payments of up to $33.2 million and royalty payments on net sales of products utilizing KSI-201 and related technology. Such milestones and royalties are dependent on future activity or product sales and are not estimable.

***Tenant Improvement Allowance Payable***

In May 2013, the Company entered into a tenant improvement allowance agreement with its landlord. The agreement allowed the Company to draw down $0.3 million for tenant improvements related to the office lease over the period from the execution of the agreement to October 2018. The interest rate is 8% per year over the lease period. This tenant improvement allowance was repaid in October 2018.

In March 2016, the Company entered into a lease amendment, under which the Company is allowed to draw down an additional allowance of $0.4 million for tenant improvements related to the office lease over the period from the execution of the agreement to October 2023. The interest rate is 8% per year over 10 years. Principal and interest are payable on the first day of every month.

As of December 31, 2019 and 2018, the current portion of the tenant improvement allowance payable in accrued and other current liabilities was less than $0.1 million and less than $0.1 million, respectively. As of December 31, 2019 and 2018, the non-current portion of the tenant improvement allowance payable in other liabilities was $0.3 million and $0.3 million, respectively.

***Legal Proceedings***

From time to time, the Company may become involved in legal proceedings arising from the ordinary course of its business. Management is currently not aware of any matters that could have a material adverse effect on the Company's financial position, results of operations or cash flows. The Company records a legal liability when it believes that it is both probable that a liability may be imputed, and the amount of the liability can be reasonably estimated. Significant judgment by the Company is required to determine both probability and the estimated amount.

***Indemnification***

To the extent permitted under Delaware law, the Company has agreed to indemnify its directors and officers for certain events or occurrences while the director or officer is, or was serving, at the Company's request in such capacity. The indemnification period covers all pertinent events and occurrences during the director's or officer's service. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is not specified in the agreements; however, the Company has director and officer insurance coverage that reduces its exposure and enables the Company to recover a portion of any future amounts paid. The Company believes the estimated fair value of these indemnification agreements in excess of applicable insurance coverage is minimal.

**8. Income Taxes**

The Company has not recorded any income tax expense. The Company has a net operating loss and has provided a valuation allowance against net deferred tax assets due to uncertainties regarding the Company's ability to realize these assets.

The components of loss before income taxes were as follows (in thousands):

| | Year Ended December 31, 2019 | Year Ended December 31, 2018 | Year Ended December 31, 2017 |
|---|---|---|---|
| United States | $ 2,633 | $ (17,273) | $ (3,240) |
| Foreign | (49,998) | (24,170) | (24,696) |
| Total loss before income taxes | $ (47,365) | $ (41,443) | $ (27,936) |

The tax effects of temporary differences that give rise to significant components of the net deferred tax assets are as follows (in thousands):

| | December 31, 2019 | December 31, 2018 | December 31, 2017 |
|---|---|---|---|
| Deferred tax assets: | | | |
| Net operating loss carryforwards | $ 18,523 | $ 11,044 | $ 11,270 |
| Intangible assets | 12,112 | 7,588 | 618 |
| Research and development tax credits | 4,037 | 1,559 | 788 |
| Stock-based compensation | 1,539 | 394 | - |
| Accruals | 885 | 700 | 393 |
| Operating lease liability | 577 | - | - |
| Property and equipment | 143 | 109 | 97 |
| Other | — | — | 26 |
| Total deferred tax assets | 37,816 | 21,394 | 13,192 |
| Valuation allowance | (37,249) | (21,394) | (13,192) |
| Net deferred tax assets | 567 | — | — |
| Deferred tax liabilities: | | | |
| Operating lease right-of-use asset | (534) | — | — |
| Capitalized legal fees | (33) | — | — |
| Total deferred tax liabilities | (567) | — | — |
| Total net deferred tax assets | $ — | $ — | $ — |

The Company has recorded a full valuation allowance against its net deferred tax assets due to the uncertainty as to whether such assets will be realized. The net change in the total valuation allowance for the years ended December 31, 2019, 2018 and 2017 was an increase of approximately $15.9 million, $8.2 million and $4.8 million, respectively.

On December 22, 2017, H.R. 1 (the "Tax Act") was enacted and included broad tax reforms. The Tax Act reduced the U.S. corporate tax rate from 35% to 21% effective January 1, 2018. The rate change resulted in a $2.5 million reduction in the Company's deferred tax assets from 2016 to 2017. The Tax Act also imposed a deemed repatriation of foreign earnings of subsidiaries; Kodiak Sciences GmbH is considered an E&P deficit corporation for the purposes of this provision and thus no income inclusion was required. The Company has elected to treat taxes on Global Intangible Low Tax Income ("GILTI") as period costs starting in 2018.

NOLs and tax credit carry-forwards are subject to review and possible adjustment by the Internal Revenue Service ("IRS") and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50% as defined under Sections 382 and 383 in the Internal Revenue Code, which could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the Company's value immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed a Section 382 study through December 31, 2019 which concluded no such ownership change had occurred through December 31, 2019.

As of December 31, 2019, the Company had $31.8 million of federal and $131.2 million of state net operating loss available to offset future taxable income. A portion of the federal net operating loss carryforwards begin to expire in 2035 and the state net operating loss carryforwards begin to expire in 2035, if not utilized. $13.7 million of the federal net operating loss are not subject to expiration.

As of December 31, 2019, the Company also had federal and state research and development credit carryforwards of $3.6 million and $2.3 million, respectively. The federal research and development credit carryforwards expire beginning 2035. The California tax credit can be carried forward indefinitely.

A reconciliation of the Company's effective tax rate to the statutory U.S. federal rate is as follows:

| | December 31, 2019 | December 31, 2018 | December 31, 2017 |
|---|---|---|---|
| Federal statutory income tax rate | 21.0% | 21.0% | 34.0% |
| State taxes | 11.0 | 5.6 | 7.1 |
| Foreign tax rate differential | (12.4) | (3.8) | (17.1) |
| Change in valuation allowance | (30.5) | (18.3) | (15.4) |
| Stock-based compensation | 7.7 | (0.6) | (0.3) |
| Research tax credit | 3.3 | 1.3 | 0.8 |
| Other | (0.1) | (0.1) | (0.3) |
| Remeasurement of deferred tax due to tax law change | — | — | (8.8) |
| Fair value adjustments | — | (2.4) | — |
| Extinguishment of convertible note | — | (2.7) | — |
| Provision for income taxes | 0.0% | 0.0% | 0.0% |

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on their technical merits, as the largest amount of benefit that is more likely than not to be realized upon the ultimate settlement. As of December 31, 2019, 2018 and 2017, none of the unrecognized tax benefits would affect income tax expense with consideration of the valuation allowance. The Company does not anticipate the uncertain tax positions will materially change in the next 12 months. It is the Company's policy to include interest and penalties as a component of income tax expense or benefit as necessary.

The beginning and ending unrecognized tax benefits amounts are as follows (in thousands):

| | December 31, 2019 | December 31, 2018 | December 31, 2017 |
|---|---|---|---|
| Unrecognized tax benefits at beginning of period | $ 398 | $ 357 | $ 235 |
| Increases related to prior year tax positions | — | — | 102 |
| Increases related to current year tax positions | 1,440 | 41 | 20 |
| Unrecognized tax benefits at end of period | $ 1,838 | $ 398 | $ 357 |

The Company files income tax returns in the United States and Switzerland. The Company is not currently under examination by income tax authorities in federal, state or other jurisdictions. All tax returns remain open for examination by the federal and state authorities for three and four years, respectively, from the date of utilization of any net operating loss or credits.

**9. Preferred Stock**

As of December 31, 2019 and 2018, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue up to 10,000,000 shares of preferred stock at the par value of $0.0001 per share. As of December 31, 2019, there are no holders of the Company's preferred stock.

**10. Common Stock**

As of December 31, 2019 and 2018, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue 490,000,000 shares of common stock at the par value of $0.0001 per share. Each share of common stock is entitled to one vote. The board of directors may declare and pay dividends to holders of common stock. The Company has never declared or paid any dividends on common stock.

The Company had reserved common stock for future issuances as follows:

| | December 31, 2019 | December 31, 2018 |
|---|---|---|
| Exercise of options outstanding | 6,830,442 | 5,135,267 |
| Exercise of common stock warrants outstanding | 399,999 | 400,000 |
| Issuance of common stock under the 2018 Equity Incentive Plan | 2,118,877 | 3,024,404 |
| Issuance of common stock under the 2018 Employee Share Purchase Plan | 460,000 | 460,000 |
| Total | 9,809,318 | 9,019,671 |

## 11. Stock-Based Compensation

### *2018 Equity Incentive Plan*

In August 2018, the Company adopted the 2018 Equity Incentive Plan ("2018 Plan"), which became effective on the business day prior to the effectiveness of the registration statement relating to the IPO. The 2018 Plan initially reserved 4,300,000 shares of common stock for the issuance of incentive stock options ("ISOs"), nonstatutory stock options, restricted stock, restricted stock units ("RSUs"), stock appreciation rights, performance units and performance shares to employees, directors and consultants of the Company. The number of shares available for issuance will increase annually on the first day of each fiscal year beginning in 2019 equal to the least of (1) 4,300,000 shares, and (2) 4% of outstanding shares of common stock as of the last day of the immediately preceding year, and (3) such other amount as determined by the board of directors. The exercise price of options must be equal to at least the fair market value of the common stock on the grant date. For ISOs, the term may not exceed ten years, except in respect to any participant with more than 10% of voting power of all classes or stock, then the term may not exceed five years and the exercise price must be equal to at least 110% of the fair market value of the common stock on the grant date. Options granted generally vest over four years.

The 2015 Equity Incentive Plan was terminated in connection with the adoption of the 2018 Plan and the 63,359 shares that were then unissued and available for future award under the 2015 Equity Incentive Plan became available under the 2018 Plan. The awards outstanding under the 2015 Equity Incentive Plan continue to be governed by their existing terms.

The number of shares available for issuance increased by 1,473,194 shares in 2019 and there were 2,118,877 shares available for grant under the 2018 Plan as of December 31, 2019.

### *2015 Equity Incentive Plan*

In September 2015, the Company adopted the 2015 Equity Incentive Plan ("2015 Plan") under which 2,810,513 shares of common stock were reserved for issuance through grants of incentive stock options, nonqualified stock options and restricted stock awards ("RSAs") to employees, directors and consultants of the Company. During 2018, the board of directors approved an increase of 2,125,000 shares to the common stock reserved under the 2015 Plan. The awards outstanding under the previously terminated 2009 Share Incentive Plan continue to be governed by their existing terms.

***Stock Options***

Stock option activity under the 2018 Plan and 2015 Plan is summarized as follows (in thousands, except share and per share data):

| | | Outstanding Awards | | | |
|---|---|---|---|---|---|
| | Number of Shares Available for Grant | Number of Shares Underlying Outstanding Options | Weighted Average Exercise Price | Weighted Average Contractual Term (in years) | Aggregate Intrinsic Value |
| **Balance, January 1, 2017** | 551,817 | 1,263,757 | $ 0.98 | 9.42 | $ 100 |
| Options granted | (137,500) | 137,500 | $ 1.06 | | |
| Options exercised | — | (5,603) | $ 0.50 | | 3 |
| Options forfeited or canceled | 191,240 | (191,240) | $ 1.04 | | |
| **Balance, December 31, 2017** | 605,557 | 1,204,414 | $ 0.98 | 8.49 | $ 41 |
| Shares authorized | 6,425,000 | — | | | |
| Options granted | (4,103,653) | 4,103,653 | $ 7.45 | | |
| Options exercised | — | (47,800) | $ 1.03 | | 290 |
| RSAs granted | (27,500) | — | | | |
| RSUs granted | (60,000) | 60,000 | $ 10.00 | | |
| Options forfeited or canceled | 185,000 | (185,000) | $ 5.19 | | |
| **Balance, December 31, 2018** | 3,024,404 | 5,135,267 | $ 5.99 | 9.07 | $ 10,681 |
| Shares authorized | 1,473,194 | — | | | |
| Options granted | (2,539,493) | 2,539,493 | $ 36.70 | | |
| Options exercised | — | (662,079) | $ 3.45 | | 45,355 |
| RSUs granted | (128,900) | 128,900 | $ 73.51 | | |
| RSUs vested | — | (21,467) | $ 9.90 | | |
| Shares withheld related to net share settlement of RSUs | 8,533 | (8,533) | | | |
| Options forfeited or canceled | 281,139 | (281,139) | $ 7.86 | | |
| **Balance, December 31, 2019** | 2,118,877 | 6,830,442 | $ 17.49 | 8.32 | $ 373,514 |
| Shares exercisable, December 31, 2018 | | 1,766,385 | $ 3.11 | 8.28 | $ 7,182 |
| Vested and expected to vest, December 31, 2018 | | 5,135,267 | $ 5.99 | 9.07 | $ 10,681 |
| Shares exercisable, December 31, 2019 | | 2,773,881 | $ 11.82 | 8.17 | $ 126,346 |
| Vested and expected to vest, December 31, 2019 | | 6,830,442 | $ 17.49 | 8.32 | $ 373,514 |

***Shares Subject to Repurchase***

The Company has a right of repurchase with respect to unvested shares issued upon early exercise of options at an amount equal to the lower of (1) the exercise price of each restricted share being repurchased and (2) the fair market value of such restricted share at the time the Company's right of repurchase is exercised. The Company's right to repurchase these shares lapses as those shares vest over the requisite service period.

Shares purchased by employees pursuant to the early exercise of stock options are not deemed, for accounting purposes, to be issued until those shares vest according to their respective vesting schedules. Cash received for early exercised stock options is recorded as accrued liabilities and other current liabilities on the consolidated balance sheet and is reclassified to common stock and additional paid-in capital as such shares vest. At December 31, 2019 and 2018, there are no early exercised stock options that remained subject to the Company's right of repurchase.

***Employee Stock Options***

Prior to the Company's IPO, the fair value of the shares of common stock underlying the stock options was determined by the board of directors with assistance from management and external appraisers as there has been no historical public market for the Company's common stock. Subsequent to the Company's IPO, the fair value of the Company's common stock is determined based on its closing market price.

During the years ended December 31, 2019, 2018 and 2017, the Company granted 2,354,343, 3,888,653 and 107,500 stock options, respectively, to employees with a weighted-average grant date fair value of $34.11, $4.36 and $0.61 per share, respectively.

The Company estimated the fair value of employee stock options using the Black-Scholes valuation model. The fair value of employee stock options was estimated using the following weighted-average assumptions:

| | Year Ended December 31, 2019 | Year Ended December 31, 2018 | Year Ended December 31, 2017 |
|---|---|---|---|
| Expected volatility | 68% | 59% | 63% |
| Risk-free interest rate | 1.65% | 2.82% | 1.89% |
| Dividend yield | 0% | 0% | 0% |
| Expected term | 5.78 | 6.06 | 6.00 |

*Expected Term*. The expected term is calculated using the simplified method, which is available where there is insufficient historical data about exercise patterns and post-vesting employment termination behavior. The simplified method is based on the vesting period and the contractual term for each grant, or for each vesting-tranche for awards with graded vesting. The mid-point between the vesting date and the maximum contractual expiration date is used as the expected term under this method. For awards with multiple vesting-tranches, the times from grant until the mid-points for each of the tranches may be averaged to provide an overall expected term.

*Expected Volatility*. The Company used an average historical stock price volatility of a peer group of publicly traded companies to be representative of its expected future stock price volatility, as the Company does not have sufficient trading history for its common stock. For purposes of identifying these peer companies, the Company considered the industry, stage of development, size and financial leverage of potential comparable companies. For each grant, the Company measured historical volatility over a period equivalent to the expected term. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

*Risk-Free Interest Rate*. The risk-free interest rate is based on the implied yield currently available on U.S. Treasury zero-coupon issues with a remaining term equivalent to the expected term of a stock award.

*Expected Dividend Rate*. The Company has not paid and does not anticipate paying any dividends in the near future. Accordingly, the Company has estimated the dividend yield to be zero.

The total fair value of employee options vested during the years ended December 31, 2019, 2018 and 2017 was $4.6 million, $1.2 million and $0.2 million, respectively. Stock-based compensation expense recognized during the years ended December 31, 2018, 2017 and 2016 for options granted to employees was $5.7 million, $2.0 million and $0.2 million, respectively.

***Non-Employee Stock Options***

The Company granted 15,000, 215,000 and 30,000 stock options to non-employees during the years ended December 31, 2019, 2018 and 2017, respectively.

Subsequent to the adoption of ASU 2018-07 effective January 1, 2019, existing stock options granted to non-employees will no longer be revalued, and the estimated fair value of new stock options granted to non-employees will be calculated on the date of grant and not remeasured, similar to stock options granted to employees. The fair value of non-employee stock options was estimated using the following weighted-average assumptions:

| | Year Ended December 31, 2019 | Year Ended December 31, 2018 | Year Ended December 31, 2017 |
|---|---|---|---|
| Expected volatility | 73% | 68% | 63% |
| Risk-free interest rate | 1.61% | 2.71% | 2.31% |
| Dividend yield | 0% | 0% | 0% |
| Expected term | 6.08 | 9.30 | 9.35 |

Stock-based compensation expense recognized during the years ended December 31, 2019, 2018 and 2017 for options granted to non-employees was $0.1 million, $0.4 million and less than $0.1 million, respectively.

***Performance-Based Stock Options and Restricted Stock Units***

The Company granted 170,150 performance-based stock options and 128,900 performance-based restricted stock units ("RSUs") to employees in 2019. These performance-based equity awards will vest one-quarter upon the achievement of specific clinical development milestones. The remaining shares will then vest in three equal annual installments after that date. Performance-based stock options and performance-based restricted stock units are recorded as expense beginning when vesting events are determined to be probable.

The fair value of performance-based stock options was estimated using the following weighted-average assumptions:

| | Year Ended December 31, 2019 |
|---|---|
| Expected volatility | 72% |
| Risk-free interest rate | 1.67% |
| Dividend yield | 0% |
| Expected term | 6.31 |

The weighted-average grant date fair value was $47.89 per share for performance-based stock options and $73.51 per share for performance-based restricted stock units. None of these performance-based equity awards vested during 2019. The Company believes that the achievement of the requisite performance condition is probable and stock-based compensation expense recognized during the year ended December 31, 2019 was less than $0.1 million related to these awards.

***Restricted Stock Awards***

Restricted stock award ("RSAs") activity is summarized as follows:

| | Number of Shares Underlying Outstanding RSAs | Weighted Average Grant Date Fair Value |
|---|---|---|
| Unvested, December 31, 2016 | 549,351 | $ 0.41 |
| Vested | (257,718) | $ 1.00 |
| Unvested, December 31, 2017 | 291,633 | $ 0.45 |
| Granted | 27,500 | $ 5.38 |
| Vested | (268,683) | $ 0.89 |
| Unvested, December 31, 2018 | 50,450 | $ 0.79 |
| Vested | (48,603) | $ 0.78 |
| Unvested, December 31, 2019 | 1,847 | $ 1.04 |

Under the terms of the restricted stock agreements, 1/48th of the award vests monthly over four years, which is the requisite service period. Recipients of restricted stock awards generally have voting and dividend rights with respect to such shares upon grant without regard to vesting. Shares of restricted stock that do not vest are subject to forfeiture. The Company recognizes stock-based compensation expense for RSAs on a straight-line basis over the requisite service period for the entire award. The total fair value of RSAs vested during the years ended December 31, 2019, 2018 and 2017 was less than $0.1 million, $0.2 million and $0.1 million, respectively. Stock-based compensation expense recognized during the years ended December 31, 2019, 2018 and 2017 for RSAs was less than $0.1 million, $0.2 million and $0.1 million, respectively.

***Restricted Stock Units***

RSUs activity is summarized as follows:

| | Number of Shares Underlying Outstanding RSUs | Weighted Average Grant Date Fair Value |
|---|---|---|
| Unvested, December 31, 2017 | — | $ — |
| Granted | 60,000 | $ 9.90 |
| Unvested, December 31, 2018 | 60,000 | $ 9.90 |
| Vested | (21,467) | $ 9.90 |
| Shares withheld related to net share settlement of RSUs | (8,533) | $ 9.90 |
| Unvested, December 31, 2019 | 30,000 | $ 9.90 |

The total fair value of RSUs vested during the year ended December 31, 2019 was $0.3 million. Stock-based compensation expense recognized during the years ended December 31, 2019 and 2018 for RSUs was $0.3 million and less than $0.1 million, respectively.

***2018 Employee Share Purchase Plan***

In August 2018, the Company adopted the 2018 Employee Share Purchase Plan ("ESPP"), which became effective on the business day prior to the effectiveness of the registration statement relating to the IPO. A total of 460,000 shares of common stock were initially reserved for issuance under the ESPP. The offering period and purchase period will be determined by the board of directors. As of December 31, 2019, no offerings have been authorized to date.

***Stock-Based Compensation Expense***

Stock-based compensation is classified in the consolidated statements of operations and comprehensive loss as follows (in thousands):

| | Year Ended December 31, 2019 | Year Ended December 31, 2018 | Year Ended December 31, 2017 |
|---|---|---|---|
| Research and development | $ 3,496 | $ 1,535 | $ 171 |
| General and administrative | 2,614 | 1,073 | 104 |
| Total stock-based compensation | $ 6,110 | $ 2,608 | $ 275 |

As of December 31, 2019, the Company had $59.4 million and $0.2 million of unrecognized compensation expense related to unvested stock options and unvested restricted stock awards and units, respectively, that is expected to be recognized over a weighted-average period of 3.07 years and 0.77 years, respectively.

## 12. Net Loss per Share Attributable to Common Stockholders

The following table sets forth the computation of basic and diluted net loss per share attributable to common stockholders which excludes shares which are legally outstanding, but subject to repurchase by the Company (in thousands, except share and per share data):

| | Year Ended December 31, 2019 | Year Ended December 31, 2018 | Year Ended December 31, 2017 |
|---|---|---|---|
| Numerator: | | | |
| Net loss attributable to common stockholders | $ (47,365) | $ (41,443) | $ (27,936) |
| Denominator: | | | |
| Weighted-average shares outstanding | 37,869,291 | 15,136,197 | 7,932,717 |
| Less: weighted-average unvested restricted shares and shares subject to repurchase | (15,675) | (159,682) | (417,381) |
| Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted | 37,853,616 | 14,976,515 | 7,515,336 |
| Net loss per share attributable to common stockholders, basic and diluted | $ (1.25) | $ (2.77) | $ (3.72) |

The following potentially dilutive securities, presented on an as-converted to common stock basis, were excluded from the computation of diluted net loss per share attributable to common stockholders for the period presented because including them would have been antidilutive:

| | Year Ended December 31, 2019 | Year Ended December 31, 2018 | Year Ended December 31, 2017 |
|---|---|---|---|
| Exercise of options outstanding | 6,671,542 | 5,135,267 | 1,204,414 |
| Unvested restricted shares | 160,747 | 50,450 | 291,633 |
| Unvested early exercised common stock options | — | — | 2,887 |
| Conversion of redeemable convertible preferred stock | — | — | 12,385,154 |
| Conversion of convertible notes outstanding | — | — | 2,153,781 |
| Exercise of preferred stock warrants outstanding | — | — | 500,000 |
| Total | 6,832,289 | 5,185,717 | 16,537,869 |

## 13. 401(k) Plan

In 2011, the Company adopted a 401(k) retirement and savings plan covering all employees. The 401(k) plan allows employees to make pre- and post-tax contributions up to the maximum allowable amount set by the Internal Revenue Service. The 401(k) plan was amended to include an employer matching provision in 2019. The Company will make matching contributions of 100% of employee contributions up to a maximum of 50% of the individual maximum contribution limit allowed under the IRS rules. For the year ended December 31, 2019, the expense related to the matching contributions was $0.3 million.

## 14. Subsequent Events

***Funding Agreement with Baker Bros. Advisors, LP***

On December 1, 2019, the Company and its subsidiary Kodiak Sciences GmbH entered into a funding agreement with Baker Bros. Advisors, LP (“BBA”), pursuant to which BBA purchased the right to receive a capped 4.5% royalty on future net sales of KSI-301, the Company’s anti-VEGF antibody biopolymer conjugate therapy, in exchange for $225.0 million. The funding agreement with BBA, which holds more than 5% of the Company’s stock, was the result of a competitive process overseen by independent and disinterested members of the board of directors of the Company with the assistance of outside counsel.

The closing of the funding agreement was subject to certain conditions and occurred in February 2020. The Company received $100.0 million of the funding on February 4, 2020. The remaining $125.0 million shall be payable to the Company upon enrollment of 50% patients in the planned Phase 3 clinical trials of KSI-301 for branch retinal vein occlusion and central retinal vein occlusion.

**15. Selected Quarterly Financial Data (unaudited)**

The following table provides the selected quarterly financial information for the years 2019 and 2018 (in thousands, except per share data):

| | Three Months Ended | | | |
|---|---|---|---|---|
| | **March 31, 2019** | **June 30, 2019** | **September 30, 2019** | **December 31, 2019** |
| Loss from operations | $ (8,460) | $ (11,814) | $ (12,732) | $ (16,184) |
| Net loss | $ (7,984) | $ (11,385) | $ (12,380) | $ (15,616) |
| Net loss per share attributable to common stockholders, basic and diluted | $ (0.21) | $ (0.31) | $ (0.33) | $ (0.40) |

| | Three Months Ended | | | |
|---|---|---|---|---|
| | **March 31, 2018** | **June 30, 2018** | **September 30, 2018** | **December 31, 2018** |
| Loss from operations | $ (5,547) | $ (5,090) | $ (6,380) | $ (9,357) |
| Net loss and comprehensive loss | $ (8,920) | $ (7,409) | $ (10,452) | $ (14,662) |
| Net loss per share attributable to common stockholders, basic and diluted | $ (1.16) | $ (0.96) | $ (1.33) | $ (0.40) |

## ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURES

None.

## ITEM 9A. CONTROLS AND PROCEDURES

### Management's Evaluation of our Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based upon such evaluation, management concluded that the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level as of December 31, 2019.

*Changes in Internal Control over Financial Reporting*

There has been no change in our internal control over financial reporting during the quarter ended December 31, 2019, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

*Management's Report on Internal Control over Financial Reporting*

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act). Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2019 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in "Internal Control—Integrated Framework" (2013). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2019.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm on our internal control over financial reporting due to an exemption established by the JOBS Act for "emerging growth companies".

## ITEM 9B. OTHER INFORMATION

None.

## PART III

### ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item will be contained in our definitive proxy statement to be filed with the SEC in connection with the Annual Meeting of Stockholders within 120 days after December 31, 2019, or the Proxy Statement, under the caption "Executive Officers" and "Board of Directors and Corporate Governance", and is incorporated in this Annual Report on Form 10-K by reference.

### ITEM 11. EXECUTIVE COMPENSATION

The information required by this item will be contained in the Proxy Statement under the caption "Executive Compensation" and is incorporated in this Annual Report on Form 10-K by reference.

### ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item will be contained in the Proxy Statement under the caption "Security Ownership of Certain Beneficial Owners and Management" and is incorporated in this Annual Report on Form 10-K by reference.

### ITEM 13. CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item will be contained in the Proxy Statement under the caption "Related Person Transactions" and is incorporated in this Annual Report on Form 10-K by reference.

### ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item will be contained in the Proxy Statement under the caption "Ratification of Appointment of Independent Registered Public Accounting Firm" and is incorporated in this Annual Report on Form 10-K by reference.

## PART IV

## ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this report:

(1) FINANCIAL STATEMENTS

The consolidated financial statements are filed as part of this report under Item 8.

(2) FINANCIAL STATEMENT SCHEDULES

All schedules to the consolidated financial statements are omitted as the required information is either inapplicable or presented in the consolidated financial statements.

(3) EXHIBITS

## EXHIBIT INDEX

| Exhibit Number | Description | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| | | Form | File No. | Exhibit | Filing Date |
| 3.1 | Amended and Restated Certificate of Incorporation of Kodiak Sciences Inc. | 10-Q | 001-38682 | 3.1 | 11/16/2018 |
| 3.2 | Amended and Restated Bylaws of Kodiak Sciences Inc. | 10-Q | 001-38682 | 3.2 | 11/16/2018 |
| 4.1 | Form of Common Stock Certificate | S-1/A | 333-227237 | 4.1 | 9/24/2018 |
| 4.2 | Investors' Rights Agreement, dated September 8, 2015, as amended, by and among the registrant and the investors and founders named therein | S-1/A | 333-227237 | 4.2 | 9/24/2018 |
| 4.5 | Form of Class B Share Warrant | S-1/A | 333-227237 | 4.5 | 9/7/2018 |
| 4.6* | Description of Securities | | | | |
| 10.1+ | Form of Director and Officer Indemnification Agreement | S-1/A | 333-227237 | 10.1 | 9/24/2018 |
| 10.2+ | 2009 Options and Profits Interest Plan | S-1 | 333-227237 | 10.2 | 9/7/2018 |
| 10.3+ | 2015 Share Incentive Plan | S-1 | 333-227237 | 10.3 | 9/7/2018 |
| 10.4+ | Form of Notice of Stock Option Grant and Stock Option Agreement under the 2009 Option and Profits Interest Plan | S-1 | 333-227237 | 10.4 | 9/7/2018 |
| 10.5+ | Form of Notice of Stock Option Grant and Stock Option Agreement under the 2015 Share Incentive Plan | S-1 | 333-227237 | 10.5 | 9/7/2018 |
| 10.6+ | 2018 Equity Incentive Plan | S-1/A | 333-227237 | 10.6 | 9/24/2018 |
| 10.7+ | Form of Notice of Stock Option Grant and Stock Option Agreement under the 2018 Equity Incentive Plan | S-1/A | 333-227237 | 10.7 | 9/24/2018 |
| 10.8+ | Form of Notice of Restricted Stock Unit Grant and Terms and Conditions of Restricted Stock Unit Grant under the 2018 Equity Incentive Plan | S-1/A | 333-227237 | 10.8 | 9/24/2018 |
| 10.9+ | 2018 Employee Stock Purchase Plan | S-1/A | 333-227237 | 10.9 | 9/24/2018 |
| 10.10+ | Form of Subscription Agreement under the 2018 Employee Stock Purchase Plan | S-1/A | 333-227237 | 10.10 | 9/24/2018 |
| 10.11+ | Executive Employment Agreement, effective as of September 6, 2018, between the Registrant and Victor Perlroth | S-1/A | 333-227237 | 10.11 | 9/24/2018 |
| 10.12+ | Amended Executive Employment Agreement, effective as of September 6, 2018, between the Registrant and John Borgeson | S-1/A | 333-227237 | 10.12 | 9/24/2018 |
| 10.13+ | Executive Employment Agreement, effective as of September 6, 2018, between the Registrant and Jason Ehrlich | S-1/A | 333-227237 | 10.13 | 9/24/2018 |
| 10.14+ | Amended Executive Employment Agreement, effective as of September 6, 2018, between the Registrant and Hong Liang | S-1/A | 333-227237 | 10.14 | 9/24/2018 |

| | | | | | |
|---|---|---|---|---|---|
| 10.15+ | Executive Incentive Compensation Plan | S-1/A | 333-227237 | 10.15 | 9/24/2018 |
| 10.16+ | Outside Director Compensation Policy | S-1/A | 333-227237 | 10.16 | 9/24/2018 |
| 10.17 | Funding Agreement, dated as of December 1, 2019, between Kodiak Sciences Inc., Kodiak Sciences GmbH and Baker Bros. Advisors, LP | 8-K | 001-38682 | 10.1 | 12/2/2019 |
| 23.1 | Consent of Independent Registered Public Accounting Firm | | | | |
| 24.1* | Power of Attorney (included in signature page) | | | | |
| 31.1 | Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | | | | |
| 31.2 | Certification of Principal Accounting and Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | | | | |
| 32.1† | Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. | | | | |
| 32.2† | Certification of Principal Accounting and Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. | | | | |
| 101.INS | XBRL Instance Document | | | | |
| 101.SCH | XBRL Taxonomy Extension Schema Document | | | | |
| 101.CAL | XBRL Taxonomy Extension Calculation Linkbase Document | | | | |
| 101.DEF | XBRL Taxonomy Extension Definition Linkbase Document | | | | |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase Document | | | | |
| 101.PRE | XBRL Taxonomy Extension Presentation Linkbase Document | | | | |

* Filed herewith.

\+ Indicates management contract or compensatory plan.

† The certifications attached as Exhibits 32.1 and 32.2 are deemed "furnished" and not deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of Kodiak Sciences Inc. under the Securities Exchange Act of 1933 or the Securities Exchange Act of 1934, whether made before or after the date hereof irrespective of any general incorporation by reference language contained in any such filing, except to the extent that the registrant specifically incorporates it by reference.

**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.

KODIAK SCIENCES INC.

Date: March 16, 2020

By: /s/ Victor Perlroth

**Victor Perlroth, M.D.**
**Chairman and Chief Executive Officer**
**(Duly Authorized Officer and Principal Executive Officer)**

## POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Victor Perlroth and John Borgeson, jointly and severally, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place, and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated:

| Signature | Title | Date |
|---|---|---|
| /s/ Victor Perlroth<br>Victor Perlroth, M.D. | Chairman and Chief Executive Officer<br>(Principal Executive Officer) | March 16, 2020 |
| /s/ John Borgeson<br>John Borgeson | Senior Vice President and Chief Financial Officer<br>(Principal Accounting and Financial Officer) | March 16, 2020 |
| /s/ Bassil I. Dahiyat<br>Bassil I. Dahiyat, Ph.D. | Director | March 16, 2020 |
| /s/ Richard S. Levy<br>Richard S. Levy, M.D. | Director | March 16, 2020 |
| /s/ Robert A. Profusek<br>Robert A. Profusek | Director | March 16, 2020 |
| /s/ Taiyin Yang<br>Taiyin Yang, Ph.D. | Director | March 16, 2020 |

# LEADERSHIP TEAM

**Victor Perlroth MD**
Chairman
Chief Executive Officer

**John Borgeson**
Senior Vice President
Chief Financial Officer

**Jason Ehrlich MD, PhD**
Chief Medical Officer
Chief Development Officer

**Hong Liang PhD**
Senior Vice President,
Discovery Medicine

**Almas Qudrat MSC**
Senior Vice President,
Quality Operations

**Laurent Ducry PhD**
Vice President, Biologics
Development & Manufacturing

**Sinette Heys**
Vice President,
Clinical Operations

**Joel Naor MD**
Vice President, Clinical Science
& Development Operations

**Stephen Raillard PhD**
Vice President,
Chemical Development
& Manufacturing

**Pablo Velazquez-Martin MD**
Vice President, Clinical Research
& Translational Medicine

## BOARD OF DIRECTORS

Deep Biotech & Governance Experience

**Victor Perlroth MD**
Chairman & CEO
Kodiak

**Bassil I. Dahiyat PhD**
Chairman & CEO
Xencor Inc.

**Taiyin Yang PhD**
EVP, Pharmaceutical
Develeopment & Manufacturing
Gilead Sciences Inc.

**Felix J. Baker MD**
Managing Director
Baker Brothers Investments

**Richard S. Levy MD**
Former Chief Drug
Development Officer & CMO
Incyte Corporation.

**Charles Bancroft**
Former CFO
Bristol Myers Squibb

**Robert A. Profusek JD**
Partner & Global Chair M&A
Jones Day

## ANNUAL MEETING

***June 8, 2020***
***9AM PST***

Kodiak Offices
2631 Hanover Street
Palo Alto, CA 94304


KODIAK SCIENCES INC.
2631 HANOVER STREET
PALO ALTO, CA 94304

*WWW.KODIAK.COM*

NASDAQ: KOD