KODIAK

THE OPHTHALMOLOGY MEDICINES COMPANY

2020 ANNUAL REPORT

TRAILBLAZING
SCIENCE

Our creative and thoughtful foundation

GENERATION 2.0
MEDICINES

Our challenge to the status quo

SINGULAR FOCUS IN
OPHTHALMOLOGY

Our 24/7/365

TO OUR KODIAK
STOCKHOLDERS, EMPLOYEES AND FRIENDS:

In 2020, the world experienced anew the power of biology. How it can hurt, with the evil serendipity that created SARS-CoV-2. And then how it can heal, with human ingenuity leaning into that same biology to design and develop wholly new vaccines in record time.

At Kodiak, we are privileged to work on the cutting edge of our own science and towards our mission of preventing and treating the leading causes of blindness globally. Despite the disruptions of this past year, we made tremendous progress.

An Inflection Point for Retina

With a singular focus on ophthalmology, the Kodiak team developed the Antibody Biopolymer Conjugate (ABC) platform to answer the call for an innovative, new generation of retina medicines. The ABC platform combines novel chemistry and protein engineering to create medicines designed for durability, safety and efficacy in the eye. Year 1 data from our Phase 1b study of KSI-301, our lead ABC candidate, show two-thirds of patients with wet age-related macular degeneration (wAMD), diabetic macular edema (DME) or retinal vein occlusion (RVO) can achieve treatment-free intervals of six months or longer with strong efficacy and safety. These remarkable data accord with a profile capable of resolving the fundamental challenges with therapeutic durability physicians and patients contend with today.

A Year of Progress for KSI-301 Development

We made significant advances with our KSI-301 pivotal program. Propelled by the enthusiasm generated from our continuing Phase 1b data, we completed patient enrollment into our pivotal study of wAMD (DAZZLE) and initiated pivotal studies in DME (GLEAM and GLIMMER) and RVO (BEACON). With the closing of a secondary offering of stock in the fourth quarter of 2020, we are emboldened to explore new studies that will support a very broad label at launch. Our agreement with Lonza to construct a purpose-built bioconjugation facility is a strong milestone on our path to build commercial manufacturing capacity to supply KSI-301 to millions of patients globally. We are developing KSI-301 to become the medicine for every patient with retinal vascular disease and seek to ensure the label and our manufacturing plans are reflective of this belief.

Looking Towards the Horizon

Kodiak enters this year strengthened by the thoughtful drive of our world-class team, the breakthrough science fueling our research and the support of our investors. Our stewardship of the KSI-301 pivotal program through primary readouts beginning early 2022 and the buildout of our commercial manufacturing framework remain top of mind this year. Our early engagement with retina practices underscores the importance of addressing needs that exist beyond the molecule. We are focused on taking the necessary early steps this year to define the requirements for a commercial organization tailored to service the unique dynamics of the retina community.

With hundreds of patient-years of experience gained with KSI-301, the science underlying our pipeline of ABC medicine candidates continues to be validated. We are eager to advance KSI-501, our bispecific candidate, into the clinic. KSI-501 targets abnormal angiogenesis and concurrent inflammation which potent combination has been implicated in the pathogenesis of several retinal diseases. We also continue to make exciting progress with our triplet medicines that promise to address complex, multifactorial diseases of the retina such as dry AMD.

On behalf of Kodiak's board of directors and leadership team, I want to thank you for your continued investment and support. The Kodiak team remains dedicated to its mission of applying our trailblazing science to resolve the biggest challenges in ophthalmology. It is my honor to be part of this mission and in this role.

Victor Perlroth, M.D.
Chairman of the Board and Chief Executive Officer

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 single BLA submission in wet AMD, DME, RVO and diabetic retinopathy in 2022; the sufficiency of our cash, cash equivalents and marketable securities to fund our planned operations; our platform technology and potential therapies; future development plans; clinical and regulatory objectives and the timing thereof, including the timing of KSI-301 primary readouts, 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; 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.

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, 2020
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from _____ to _____
Commission File Number: 001-38682

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.)**
1200 Page Mill Road 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

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

The aggregate market value of the 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 30, 2020 as reported by the Nasdaq Global Market on such date, was approximately $1.6 billion. 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 February 19, 2021, the registrant had 51,162,424 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 2021 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, 2020.

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Kodiak Sciences Inc.
Annual Report on Form 10-K for the Fiscal Year Ended December 31, 2020

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 estimates regarding the impact of the novel coronavirus, or COVID-19, pandemic on our business and operations, the business and operations of our collaborators, and on the global economy;
- our aspirational goals and objectives related to our human capital resources and workforce objectives;
- 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; and
- our financial performance.

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.

RISK FACTOR SUMMARY

Investing in our securities involves a high degree of risk. Below is a summary of material factors that make an investment in our securities speculative or risky. Importantly, this summary does not address all of the risks that we face. The below summary is qualified in its entirety by that more complete discussion of such risks and uncertainties. You should consider carefully the risks and uncertainties described under "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K.

- We are in the 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 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.
- 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.
- Our prospects are heavily dependent on our KSI-301 product candidate, which is currently in clinical development for multiple indications.
- A failure of KSI-301 in clinical development may require us to discontinue development of other product candidates based on our ABC Platform.
- 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 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.

- We may encounter difficulties enrolling patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected.
- 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.
- 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 manufacture of our product candidates is highly complex and requires substantial lead time to produce.
- 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.
- The regulatory approval processes of the FDA, EMA, NMPA 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.
- We plan to conduct clinical trials for our product candidates outside the United States, and the FDA, EMA, NMPA and applicable foreign regulatory authorities may not accept data from such trials.
- 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.
- 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 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.
- 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.
- 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.
- 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.
- 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.
- 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 business is currently affected and could be materially and adversely affected in the future by the effects of disease outbreaks, epidemics and pandemics, including the ongoing effects of the COVID-19 pandemic. The COVID-19 pandemic continues to impact our business and could materially and adversely affect our operations, as well as the business or operations of our manufacturers, CROs or other third parties with whom we conduct business.

PART I

ITEM 1. BUSINESS

Overview

At Kodiak, we are bringing new science to the design and development of next generation retinal medicines. Our ABC Platform™ uses molecular engineering to merge the fields of antibody-based and chemistry-based therapies and is at the core of Kodiak's discovery engine. Our goal is to prevent and treat the major causes of blindness by developing and commercializing next-generation therapeutics for chronic, high-prevalence retinal diseases.

Throughout 2020 and into 2021, we have generated compelling clinical data with our most advanced product candidate, KSI-301, a novel anti-VEGF antibody biopolymer conjugate, 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. 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 macular edema, or DME, macular edema due to retinal vein occlusion, or RVO, and diabetic retinopathy, or DR, as well as other vision-threatening diseases that are less prevalent but also may be responsive to anti-VEGF therapy.

The ABC Platform and KSI-301 were developed at Kodiak, and we own rights to these assets in key geographies including the US, EU, China and other major countries. 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. In October 2020, we announced that we entered a supplemental research agreement with AbCellera to generate additional therapeutic antibody candidates for novel disease targets in ophthalmology in support of our evolving research pipeline. 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.

Where Kodiak Stands Today

Growing KSI-301 Clinical Experience: We remain very pleased with the current clinical profile of KSI-301. Approximately 2,000 KSI-301 injections have been administered to approximately 500 patients representing approximately 350 patient-years of exposure. When and if we submit our planned single BLA in wet AMD, DME and RVO, we expect to have durability, efficacy and safety data on KSI-301 treatment in over 1,000 patients across our concurrent pivotal studies.

In our ongoing Phase 1b clinical study, we have administered multiple doses of KSI-301 over 52-weeks or more to treatment-naïve patients with wet AMD, DME or RVO, and we continue to observe promising durability, efficacy and safety data in each of the retinal diseases under study. Some patients have been given KSI-301 injections and followed for as long as two years in the Phase 1b study. KSI-301’s clinical durability continues to be supported with maturing data that demonstrate two in every three patients with wet AMD, DME, or RVO achieving six months or longer treatment-free intervals at Year 1. Additionally, KSI-301 continues to demonstrate an efficacy and safety profile that is tracking with standard of care anti-VEGF agents.

Thoughtfully Designed Pivotal Clinical Trials: Our ongoing registrational study program, designed based on an End of Phase 2 meeting we held in 2019 with the FDA, is assessing KSI-301 in four pivotal studies: two Phase 3 studies in DME (the GLEAM and GLIMMER studies), one Phase 2b/3 study in wet AMD (the DAZZLE study) and one Phase 3 study in RVO (the BEACON study). Each study protocol design has been optimized based on Phase 1b data and experience and will include similar treatment-naïve patient populations as in the Phase 1b, as well as tighter dosing interval ranging, tighter disease control criteria, decreased subjectivity for retreatments, high dose level of 2 mg, and each study has high statistical power for non-inferiority (>90%). The DAZZLE study completed recruitment in late 2020 and top-line results are expected in early 2022. Recruitment is underway for the GLEAM, GLIMMER and BEACON trials. We plan to expand the KSI-301 clinical study program in 2021 with one Phase 3 study (GLOW) in NPDR without DME, and potentially one or more additional clinical studies that could be beneficial for product labeling and/or reimbursement and market access purposes.

Investing with Conviction Commensurate with the Opportunity: Kodiak remains focused on thoughtful execution of our KSI-301 pivotal program, the requisite manufacturing efforts, the regulatory strategy and the pre-commercial readiness. As to manufacturing, in line with our "2022 Vision" which sees us submitting our initial BLA in 2022 and potentially commercializing KSI-301 in 2023, it is our intent to be able to supply millions of doses in Year 1 from our Lonza-Kodiak Ibex Dedicate facility designed from inception with Flex Up capabilities and capacity for double digit millions of doses per year to supply a growing market demand.

Poised Commercial Opportunity: We are optimistic for the future care of patients with retinal vascular diseases. The competitive landscape of intravitreally-injected anti-VEGF biologic therapies and therapeutic candidates is clearing, due to the incremental durability of competing molecules, and/or safety challenges that, even if only recently appreciated, have been observed from early in the development of these potential competitors. Adjacent surgical and gene therapy solutions may also face challenges with long-term safety, limited accessibility and the complex economics of surgical implantation.

KSI-301, with its powerful combination of design attributes, has the potential to be a Generation 2.0 anti-VEGF – a first-line anti-VEGF "product for everyone" that may achieve a significant market share.

As a company, we remain independent. This independence provides us with the flexibility to adapt both R&D and commercial decision-making within the ever-changing domestic and global landscapes. We remain well capitalized and supported by a high-quality group of long-term stakeholders who understand what is needed to build, invest and execute commensurate with the opportunity.

Recent Developments

KSI-301 Phase 1b Study

Updated Year 1 durability, efficacy and safety data from our ongoing Phase 1b trial of KSI-301 in patients with treatment naïve wet AMD, DME or RVO were presented at the Angiogenesis, Exudation, and Degeneration 2021 – Virtual Edition meeting in February 2021. The data show 2 in every 3 patients are on a 6-month or longer treatment-free interval at Year 1 in each of the 3 major retinal vascular diseases after only 3 loading doses. Robust vision gains (particularly notable in the context of very good baseline vision) and robust retinal drying (when baseline anatomical characteristics are considered) were seen across all three diseases being studied. Strong anti-VEGF efficacy (achieving at Year 1 approximately 20/40 eye chart vision on average in wet AMD and approximately 20/32 vision on average in DME and RVO) and an encouraging safety profile continue to be observed across all three diseases. We believe the data continue to support the "anti-VEGF Generation 2.0" profile of KSI-301.

KSI-301 Pivotal Program

We saw robust patient enrollment in our DAZZLE pivotal study in wet AMD through the third quarter of 2020 and completed global patient recruitment in November 2020 – a potential reflection of the enthusiasm for KSI-301 on the part of clinical investigators and patients. With a one-year primary endpoint, we remain on track for DAZZLE top-line data readout in early 2022.

In the third quarter of 2020, we initiated two Phase 3 studies in DME (GLEAM and GLIMMER) and one Phase 3 study in RVO (BEACON). The randomization of treatment-naïve patients into these three studies is a critical step to build the clinical evidence for KSI-301 as a safe, effective and highly durable therapy for patients with retinal diseases. The initiation of the additional Phase 3 studies and the robust patient recruitment into DAZZLE represent strong operational progress towards our 2022 Vision of a single BLA filed for KSI-301 in wet AMD, DME, and RVO in 2022. Clinical trial applications for BEACON, GLEAM, and GLIMMER have been submitted and approved in countries across the EU. To date, we are pleased with progress in site activation, patient screening, and recruitment in these studies. We believe we are also on track to begin recruitment of the GLOW study in NPDR without DME in 2021.

Importantly, to date the data emerging in our Phase 1b study remain consistent and provide support for and confidence in our pivotal study designs.

Follow-on Equity Offering

On November 20, 2020, we completed a follow-on equity offering and issued and sold 5,972,222 shares of the Company's common stock at a price to the public of $108.00 per share. The gross proceeds from this offering were $645.0 million, resulting in aggregate net proceeds of $612.0 million after deducting underwriting discounts and commissions and other offering costs.

Proceeds from the equity offering together with our current cash, cash equivalents and marketable securities 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.

Our current cash, cash equivalents and marketable securities which includes the net proceeds from the November 2020 public offering 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.

Commercial Manufacturing

We successfully negotiated a long-term agreement with Lonza for the manufacture of KSI-301. This agreement will provide Kodiak with a custom-built bioconjugation facility with a capacity to supply millions of doses per year. With construction targeted for completion in early 2022, the Lonza-Kodiak Ibex facility will provide Kodiak with the facility needed for commercial-scale manufacturing of KSI-301. The scale is designed to support KSI-301's potential to achieve significant market share as a new first-line agent designed to improve outcomes for patients with common and serious retinal vascular diseases.

COVID-19

We are continuing to monitor the global ongoing COVID-19 pandemic. Since the initial outbreak in early 2020, governments globally have taken preventative and protective actions, including but not limited to, restrictions on non-essential travel, business operations, and gatherings of individuals. The State of California, where our corporate office is located, declared a state of emergency and shelter-in-place order in March 2020. Although certain restrictions have eased, and phased re-openings are underway, it is not certain when such restrictions will be fully lifted, and recent resurgences in number and rates of infections, reactions to increased testing and/or further spreading of the virus may result in the return or implementation of more restrictive measures. Global financial markets have also experienced extreme volatility and as a result, economic uncertainties have arisen which could impact our operations and its financial position. The extent of the impact of the ongoing COVID-19 pandemic will depend on certain evolving developments, including the duration and spread of the outbreak, regulatory and private sector responses, and the impact on our employees, vendors including supply chain and clinical partners, all of which are uncertain and cannot be predicted.

We continue to monitor government responses and may elect to temporarily close our office and/or laboratory space to protect our employees. We continue to assess the potential for supply chain disruptions as the pandemic may impact personnel at third party manufacturing facilities in China, Switzerland and other countries, as well as its impact on the availability and/or cost of materials. We continue to monitor financial markets and the impact on our operations and capital resources.

We and our key clinical and manufacturing partners have been able to continue to advance our operations. Because the diseases under study in the KSI-301 development program are serious, vision-threatening conditions for which patients are still seeking and receiving treatment from retina specialists during the pandemic, we have been able to continue advancing the clinical programs for KSI-301 during the pandemic towards achieving our "2022 Vision."

During this pandemic, we continue to work closely with our clinical sites towards maximal patient safety and the lowest number of missed visits and study discontinuations. We have taken and continue to take proactive measures to maintain the integrity of our ongoing clinical studies. To date, we are seeing low levels of patient missed visits.

In response to the COVID-19 pandemic with regards to business operations, clinical trials, and manufacturing activities:

- We have taken steps in line with guidance from the U.S. Centers for Disease Control and Prevention, or CDC, and the State of California to protect the health and safety of our employees and the community. In particular, we have implemented remote work arrangements for certain employees since March 17, 2020.
- We are working closely with our clinical trial sites to monitor and attempt to minimize the potential impacts of the evolving COVID-19 pandemic on patient enrollment, continued participation of patients already enrolled in our clinical studies, protocol compliance, data quality, and overall study integrity. Some specific actions we have taken in the United States include the use of remote study monitoring, temporarily increasing study site budget overhead rates, providing additional transportation service options for patients to attend study site visits and focusing on new patient enrollment only at study sites with appropriate backup resource plans in place and where the local COVID-19 situation allows. Since the month of March 2020, the rate of missed study visits has remained <5%. As of now, we have not experienced significant delays to our ongoing or planned clinical trials; however, this could change rapidly depending on the dynamics of the pandemic.

- In June 2020, we restarted patient recruitment activities at certain sites in EU countries. DAZZLE study sites in the EU were activated in the first quarter of 2020, but we deferred study patient enrollment until June due to the pandemic.
- To minimize the potential for disruption of our pivotal studies of KSI-301, we have refined our study designs, including sample size and country selection. We began enrollment of our pivotal DME (GLEAM and GLIMMER) and RVO (BEACON) studies in the third quarter of 2020 in the United States and aim to initiate the pivotal study in non-proliferative DR (GLOW) in the first half of 2021, dependent on the continued evolution of the COVID-19 pandemic. Ex-U.S. clinical trial application submissions are underway for GLEAM, GLIMMER and BEACON, and most have already been approved; recruitment activities are now underway in the EU. We believe we are still on track to achieve our "2022 Vision" objective of filing a single BLA in 2022 for KSI-301 in wet AMD, DME and RVO.
- Our supply chain and manufacturing activities remain intact, and we do not currently anticipate disruptions to our clinical supply of KSI-301 due to COVID-19.
- As we work towards commercial scale-up and manufacturing activities to support BLA submission, there is increasing competition with COVID-19 related vaccine and therapeutic programs for manufacturing related (i) materials such as resins, filters, sterile tubesets, pipette tips; (ii) personnel such as facility engineering and construction as well as plant engineers and workers; and (iii) production slots in cGMP facilities. We are carefully monitoring any potential impacts to our manufacturing activities and timelines with the objective to intersect clinical timelines, manufacturing timelines and number of doses available in the first year(s) after commercial launch. We believe we are still on track for a close intersection of these three key elements.

We will continue to monitor the COVID-19 situation closely. The ultimate impact of the ongoing COVID-19 pandemic on our business operations remains 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. See also the section titled "Risk Factors" for additional information on risks and uncertainties related to the evolving COVID-19 pandemic.

Additional Business Highlights

In 2020 and into the first quarter of 2021, additional highlights of our activities included:

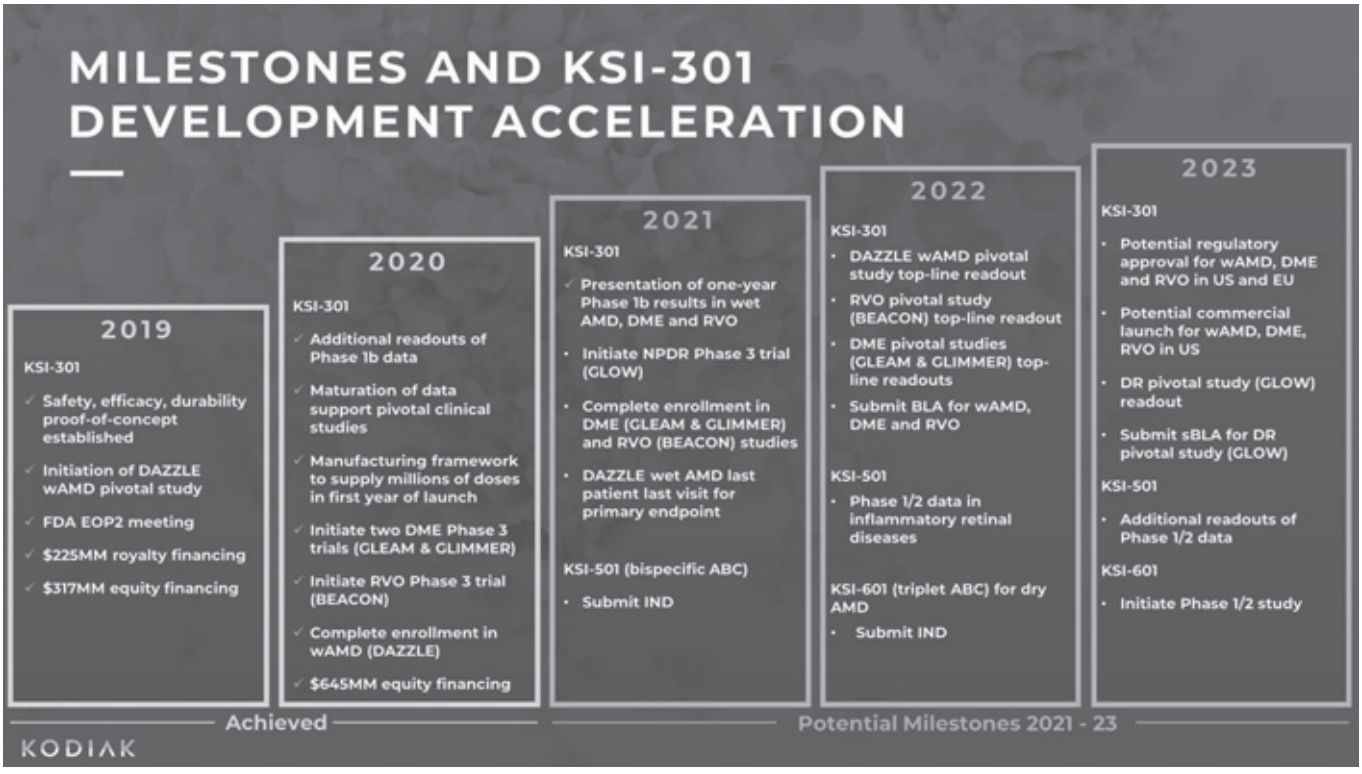
- *Completed Lease Agreement for Kodiak's New U.S. corporate offices:* We have leased approximately 82,662 square feet located at 1200 Page Mill Road, Palo Alto, California and approximately 72,812 square feet located at 1250 Page Mill Road, Palo Alto, California. These newly leased buildings will serve as Kodiak's U.S. corporate offices for office and laboratory space. We also leased approximately 10,750 square feet in Visp, Switzerland, for manufacturing support and supervision.
- *Supplemental Research Agreement with AbCellera:* In October 2020, we announced that we entered a supplemental research agreement with AbCellera to generate additional therapeutic antibody candidates for novel disease targets in ophthalmology in support of our evolving research pipeline. We intend to progress these and other product candidates to address high-prevalence ophthalmic diseases.
- *Appointment of Charles Bancroft to Board of Directors:* Charles Bancroft, formerly Chief Financial Officer of Bristol Myers Squibb (BMS), joined Kodiak's Board of Directors as chair of our audit committee and member of our nominating and governance committee in April 2020. Mr. Bancroft recently retired from a successful career at BMS where he held a number of leadership roles in commercial, strategy and finance. Mr. Bancroft brings financial and management experience that will be vital to Kodiak as the company continues to scale and build its manufacturing and commercial capabilities.

Kodiak's 2022 Vision and KSI-301 Accelerated Development Strategy

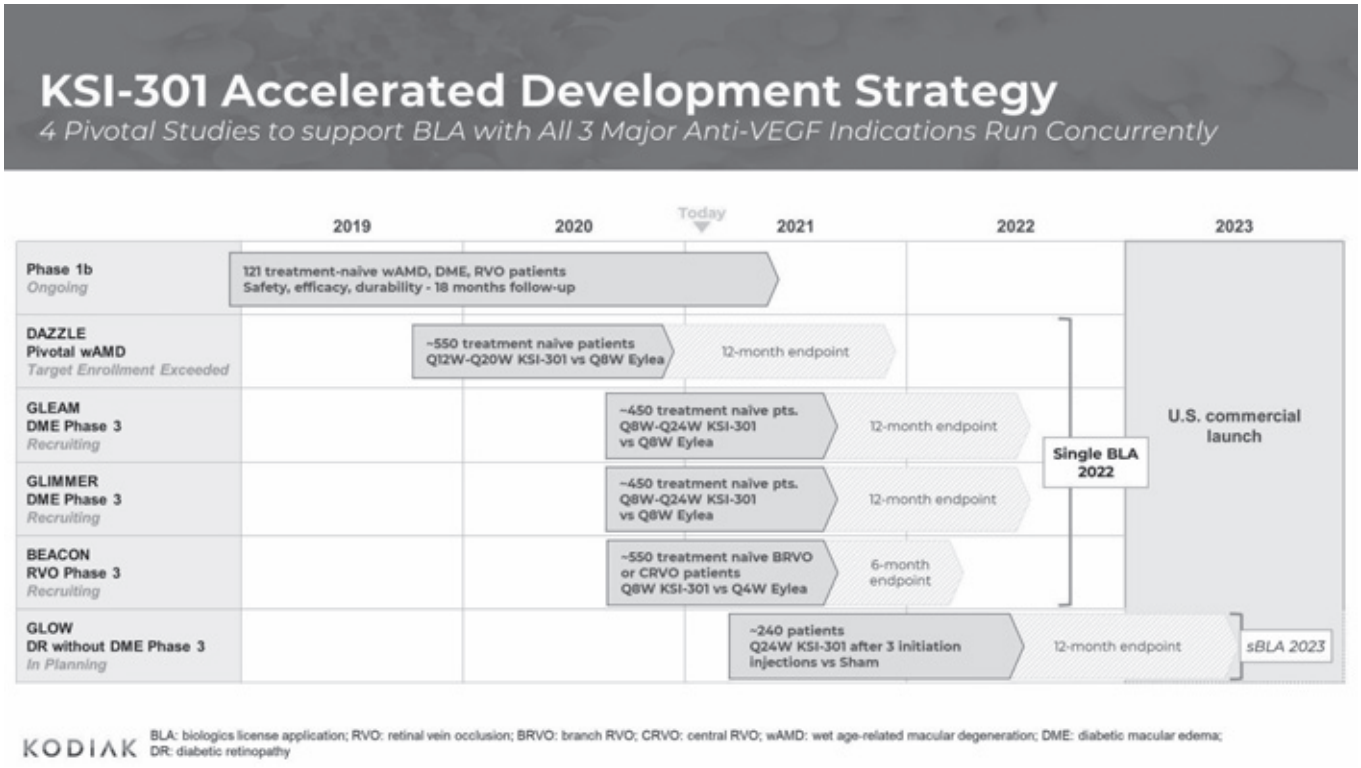
We believe we remain on track to achieve our "2022 Vision" of a single BLA submission and initial FDA approval for KSI-301 in wet AMD, DME and RVO in 2022 with a total of four pivotal trials - two in DME (GLEAM and GLIMMER), one in wet AMD (DAZZLE) and one in RVO (BEACON). These studies, together with our ongoing pivotal study in wet AMD, will be the basis of our intended BLA and supplemental BLA 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 (to be studied in the Phase 3 GLOW trial) in a supplemental BLA in the United States. We may also begin one or more additional KSI-301 clinical studies in 2021 that could be beneficial for product labeling and/or reimbursement and market access purposes.

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 ABC product candidate KSI-601 for the high prevalence multifactorial retinal disease dry AMD.

Our 2022 Vision includes the following potential catalysts and milestones in 2021, 2022 and 2023, along with the important milestones achieved in 2019 and 2020 that support the accelerated development program:



Our "2022 Vision" is built on the following concurrent development strategy. This table incorporates our most recent view of the KSI-301 clinical program and its execution, as described above, and we believe the successful prosecution of this program is achievable based on our currently available information and the evolving effects of the COVID-19 pandemic:



Opportunity for Clinically Meaningful Differentiation

Current intravitreal anti-VEGF agents require frequent eye injections 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 Year 1 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 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 standard of care	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)	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	KSI-301 once every 2 months or longer, after 2 monthly loading doses	KSI-301 once every 6 months, after 3 initiating doses

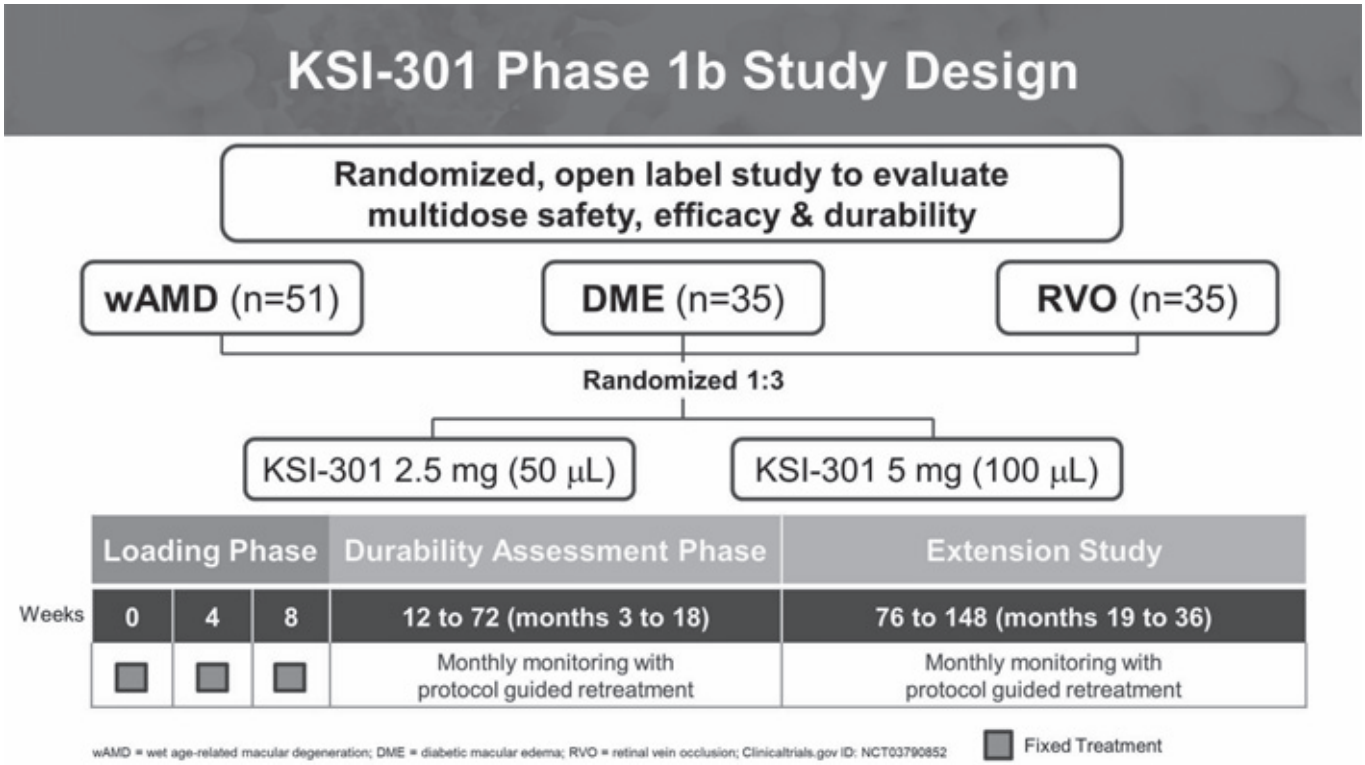
Data From Our Ongoing Phase 1b Trial Continue to Demonstrate KSI-301's Differentiated Profile

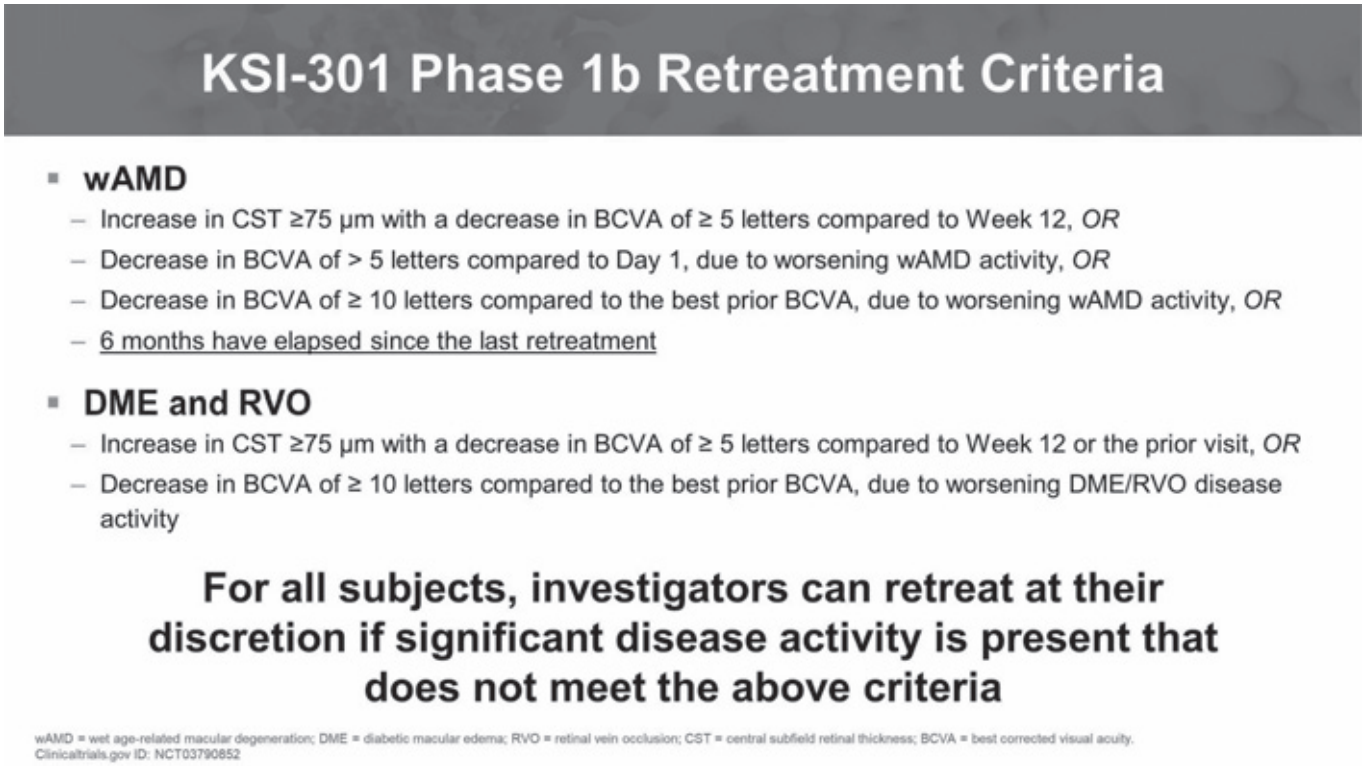
We have continued to make progress with our studies of KSI-301, and the Year 1 durability, efficacy and safety data we observe in the Phase 1b study continue to surpass our expectations. We now have more than 168 patient-years of clinical experience with KSI-301 in the Phase 1b study.

The overall study duration was originally nine and then 18 months, and we have now extended the treatment and follow-up period to 36 months total, to continue generating long-term outcomes data in advance of the pivotal studies. Outcomes include vision, measured as change in best corrected visual acuity or BCVA using the standard ETDRS testing protocol, and retinal anatomy, which is measured as change in retinal central subfield thickness, or CST, using optical coherence tomography imaging, or OCT. We also obtain other images such as fluorescein angiography, color fundus photos, and OCT angiography.

The figures below present the most recent data on durability and efficacy outcomes from the ongoing Phase 1b study presented at the Angiogenesis, Exudation, and Degeneration 2021 - Virtual Edition meeting, held in February 2021. Across all three diseases under study, improvements in vision and retinal anatomy were observed through Year 1 of patient follow-up, with stability in OCT and BCVA over time in the monthly follow-up intervals following the three mandatory loading doses. Year 1 data show 2 in every 3 patients are on a 6-month or longer treatment-free interval at Year 1 in each of the 3 major retinal vascular diseases after only 3 loading doses. Strong anti-VEGF efficacy (achieving at Year 1 ~20/40 eye chart vision on average in wAMD and ~20/32 vision on average in DME and RVO) and an encouraging safety profile continue to be observed across all three diseases. Vision is measured as change in BCVA, on a standardized eye chart, and retinal anatomy is measured as change in retinal CST using OCT imaging.

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.



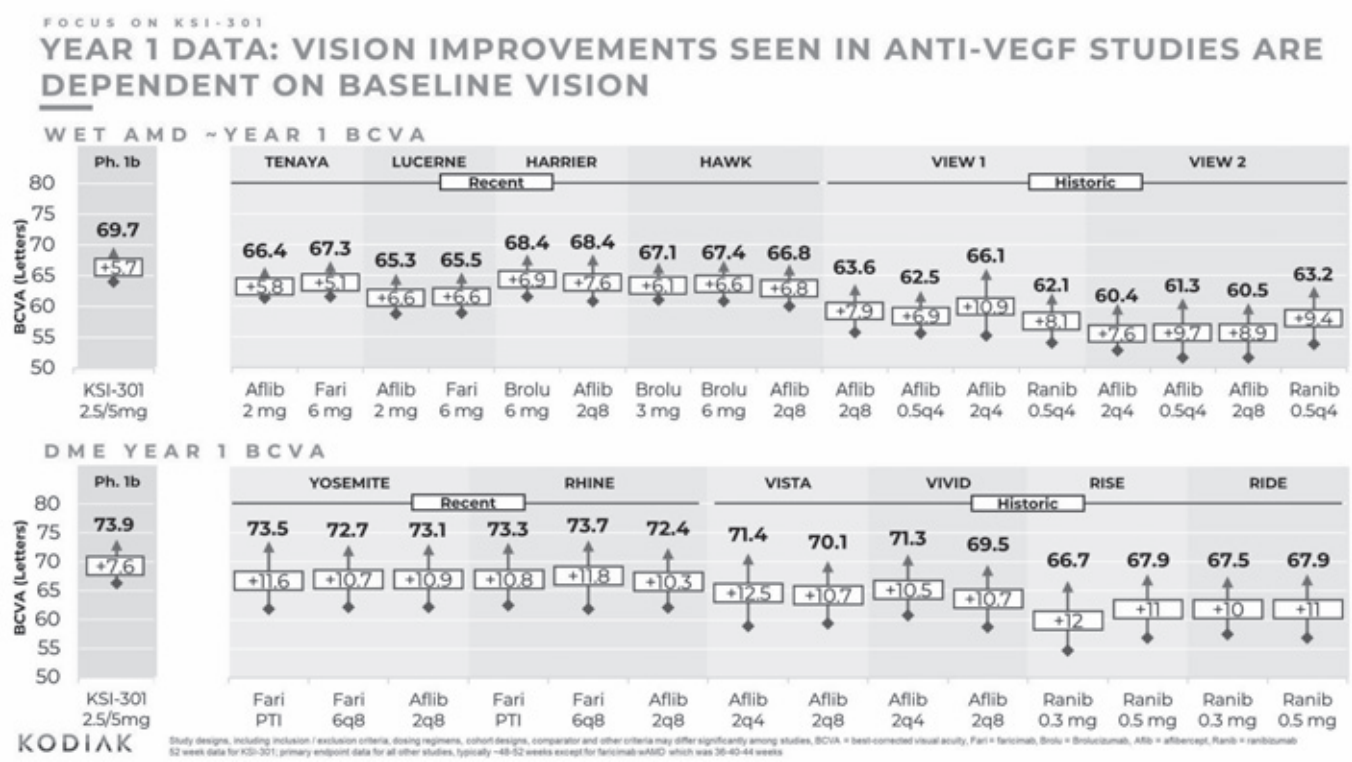


Variable	wet AMD cohort (n=51)	DME cohort (n=35)	RVO cohort (n=35)
Age, mean (SD), years	77.9 (10.5)	59.7 (11.7)	63.6 (12.6)
Gender, n (%), female	32 (62.7)	14 (40.0)	13 (37.1)
Race, n (%), White	48 (94.1)	28 (80.0)	31 (88.6)
BCVA, mean (SD), ETDRS letters	63.3 (13.3)	66.8 (10.2)	54.9 (15.4)
Snellen 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	450 (182)	453 (110)	675 (237)

SD = standard deviation; BCVA = best corrected visual acuity; OCT = optical coherence tomography; CST = central subfield thickness

The Phase 1b data in treatment-naïve patients demonstrate that the observed vision gains of 5.7 letters in wet AMD and 7.6 letters in DME at Year 1 are appropriate for the relatively high baseline vision. After one year of treatment, wet AMD subjects in our Phase 1b study were observed to have an average visual acuity of 69.7 eye chart letters or approximately 20/40 Snellen visual acuity, and DME subjects were observed to have an average visual acuity of 73.9 eye chart letters or approximately Snellen 20/32.

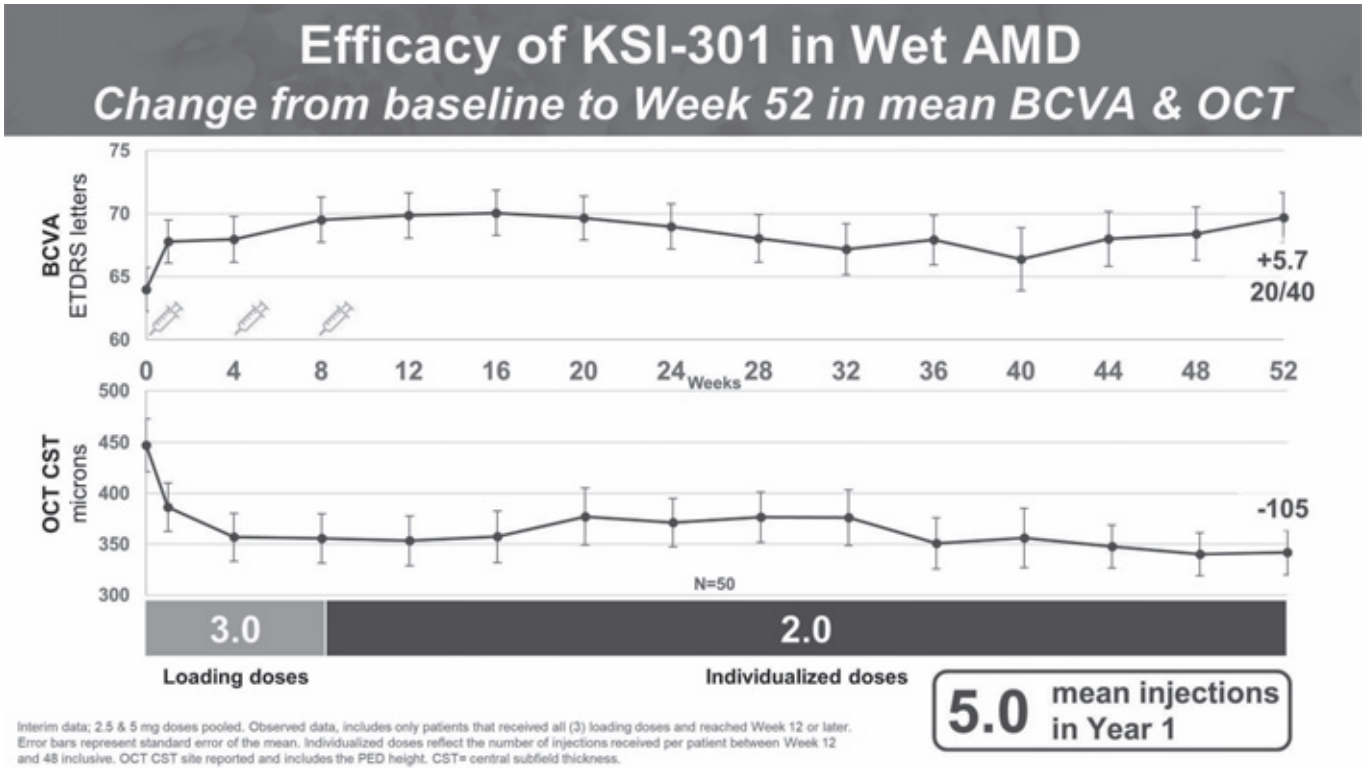
Although out Phase 1b study does not have an active comparator, the chart below places the observed baseline (pre-treatment) and one-year visual acuity outcomes in the context of the starting and one-year visual acuity metrics seen in other recent and historical clinical trials and also demonstrates how post-treatment average visual acuity is dependent on the starting (baseline) visual acuity.



Wet AMD

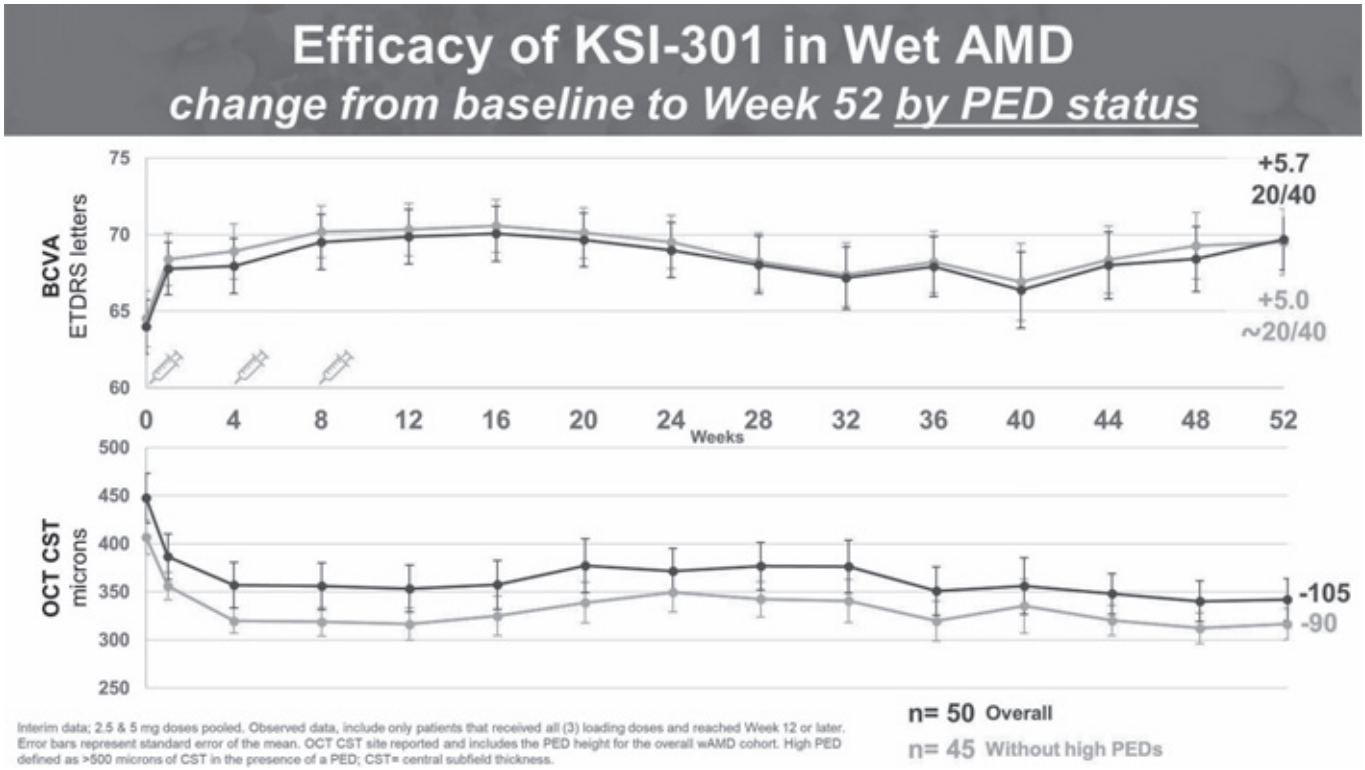
The data below are observed from 50 wet AMD patients who received all loading doses and reached Week 12 or later. These patients had good starting vision, approximately 64 letters. They experienced a visual acuity increase after 3 loading doses and maintained a gain of 5.7 letters, to an average BCVA of 69.7 letters (Snellen ~20/40), achieved with a mean of just 2.0 individualized doses. Supporting the extended durability, we see only a very slow fluctuation in the OCT over time, which compares favorably to the OCT fluctuations observed with existing anti-VEGFs given on shorter dosing intervals. The stability in BCVA over this interval is also consistent with the prolonged duration of KSI-301.

In the Phase 1b study, the average retinal thickness or OCT CST data as reported by our clinical investigators includes the height of pigment epithelial detachments or 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, and whether or how the data are corrected for different OCT machine, among other reasons.

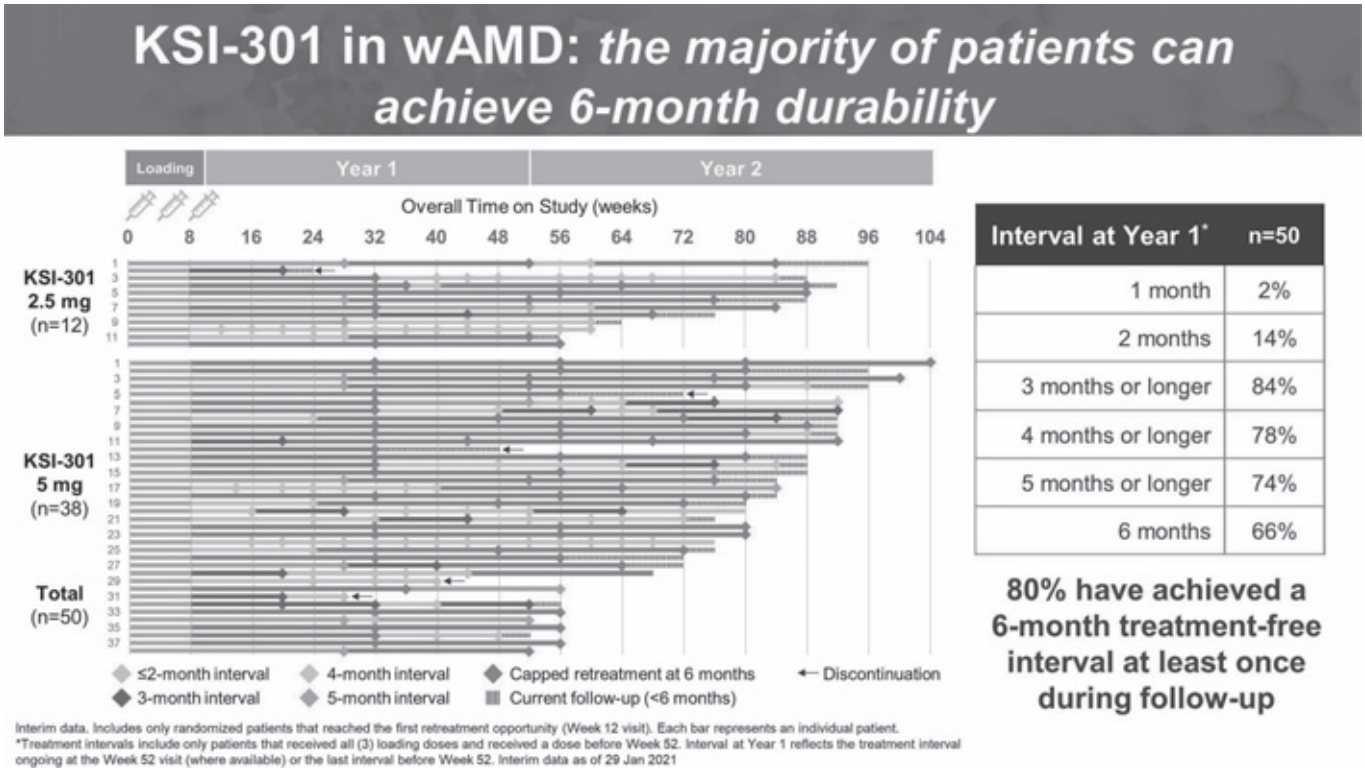


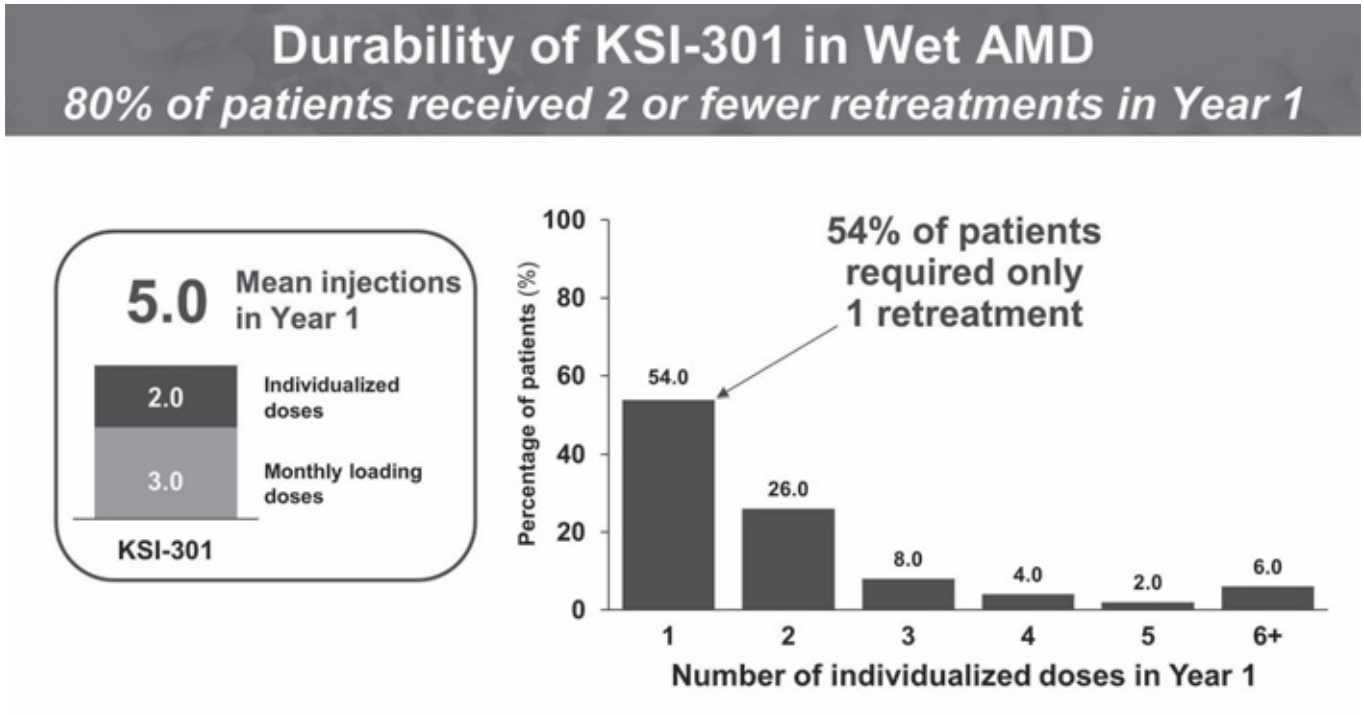
When comparing subjects with and without very high PED at baseline, which we defined as 500 microns or more total CST, the BCVA and OCT CST curves are similar in shape to those of the full cohort. Excluding give patients with high PEDs, the OCT CST values are lower at baseline and over time, and the standard error of the mean (SEM) error bars are narrower. Thus, those five patients with high PEDs thus pull the overall average CST value up.

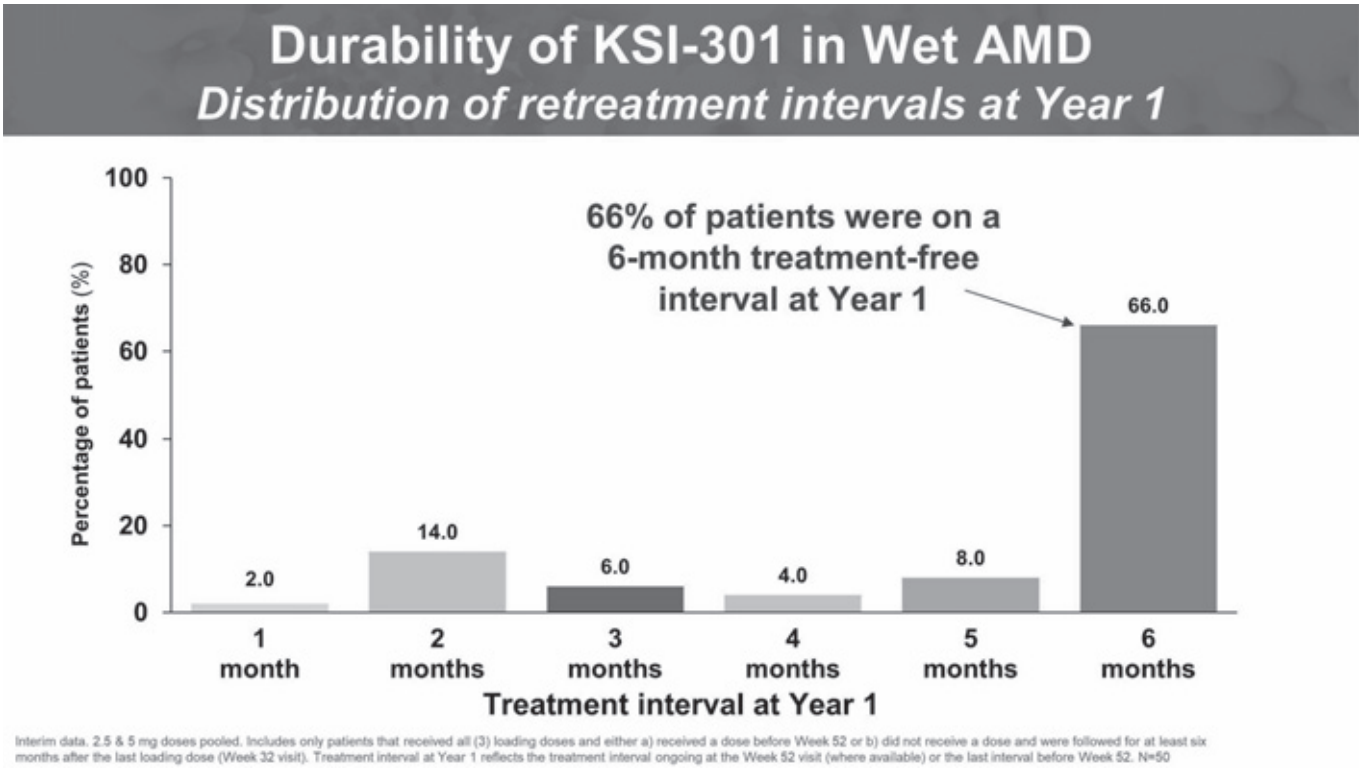
Excluding those patients, the average retinal center subfield thickness is 316 microns after initiation of treatment with KSI-301, as measured using the Heidelberg OCT machine employed by the Phase 1b study sites, in which 305 microns is normal for a healthy (no AMD) female and 315 microns is normal for a healthy male.



Overall, 66% of our wet AMD patients have achieved a 6-months treatment-free interval at Year 1 and 74% of patients achieved a five months or longer treatment-free interval at Year 1. 80% of patients have received two or fewer retreatments in Year 1. Remarkably, 80% of these wet AMD patients have achieved a 6-month treatment free interval at least once during follow-up. As this is an anti-VEGF treatment naïve population, there is no pre-selection for "anti-VEGF responders" or patients who might require or be predicted to require less frequent dosing.





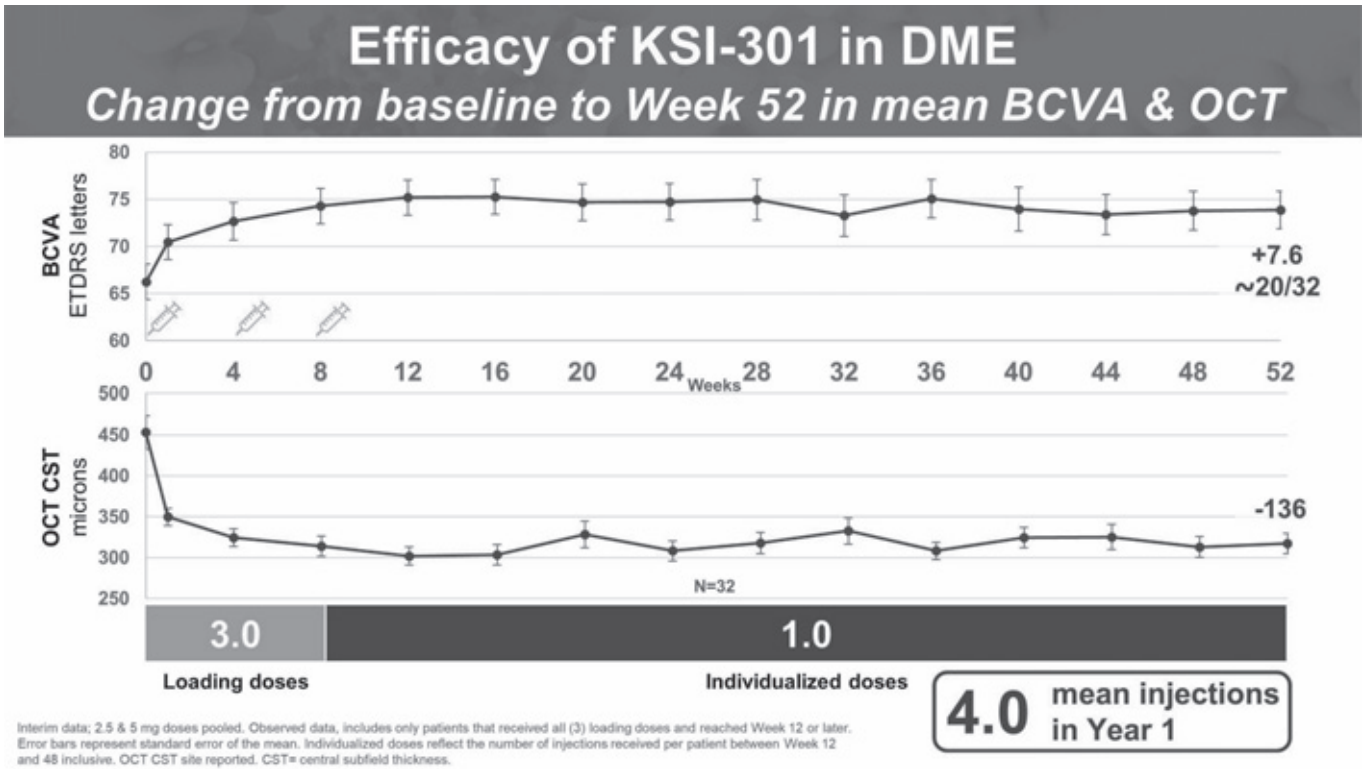


The data generated in wAMD patients in the Phase 1b study form a compelling data package. At Year 1, KSI-301 is achieving remarkable durability, strong efficacy that brings patients to an average ~20/40 vision on the Snellen chart and a favorable safety profile. Together with strong anti-VEGF activity on both vision (BCVA gains) and retinal anatomy (OCT drying) in the DME and RVO cohorts of the Phase 1b, we believe KSI-301 continues to track well towards its "Generation 2.0" profile.

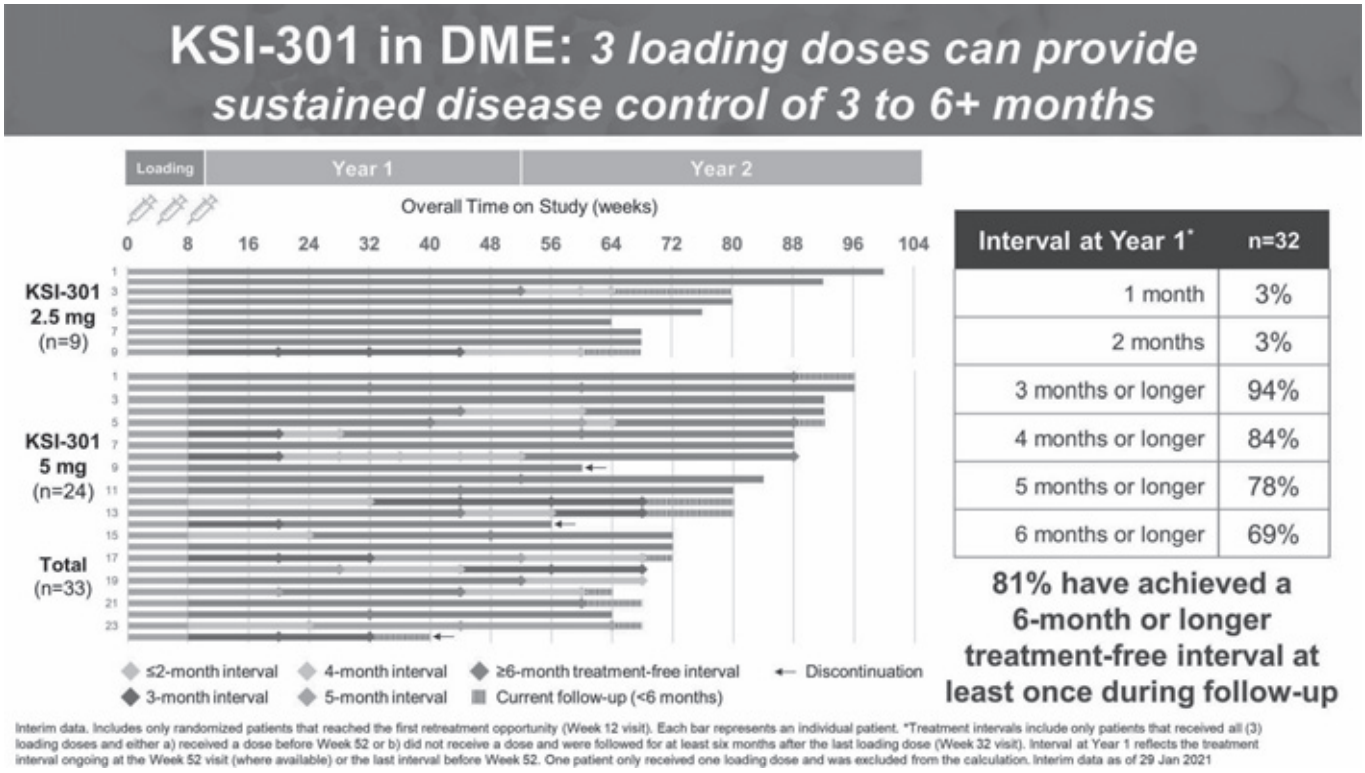
Diabetic Macular Edema (DME)

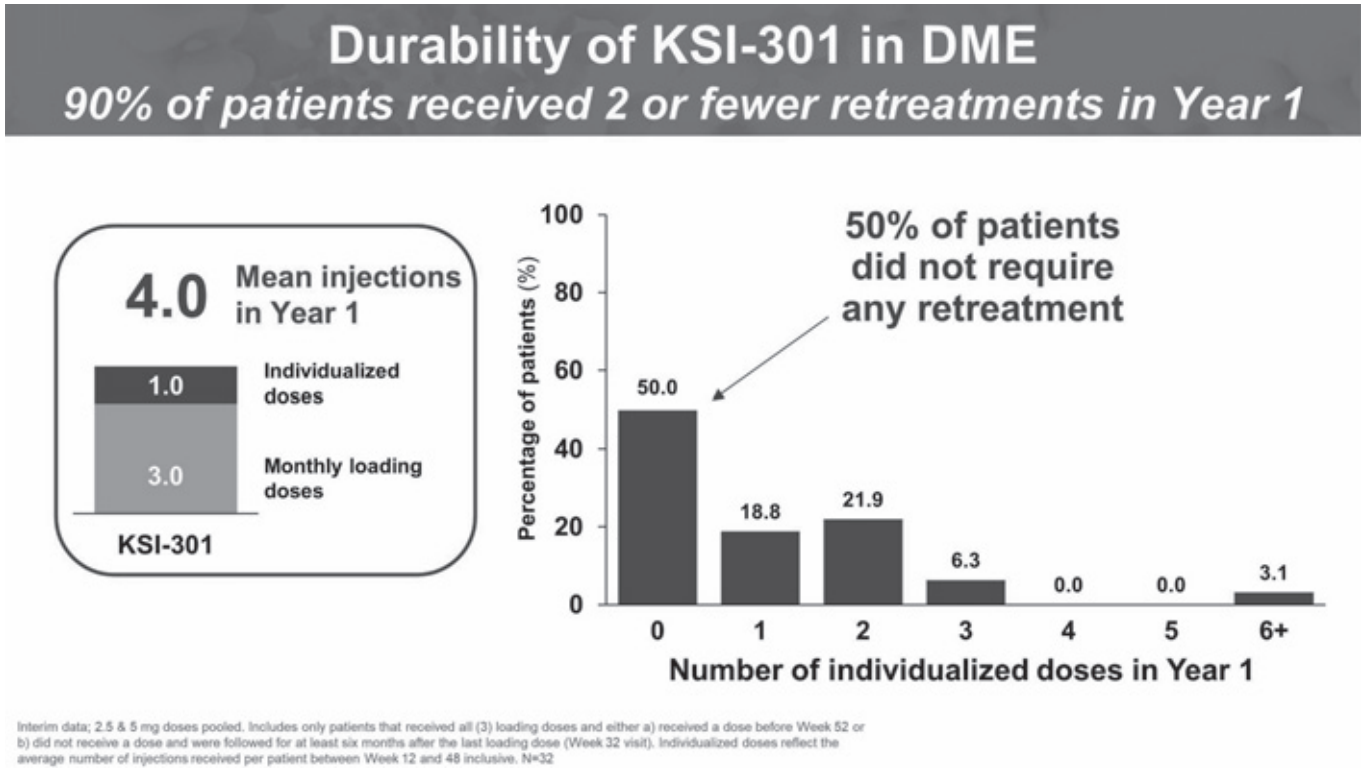
We measure KSI-301 efficacy data in treatment naïve DME as change from baseline in BCVA and OCT CST. Below are data from the 32 DME patients who received all loading doses and reached Week 12 or later. These patients had good starting vision, approximately 66 letters. They experienced a visual acuity increase after three loading doses and maintained a gain of 7.6 letters, to an average BCVA of 73.9 letters (Snellen ~20/32), achieved with a mean of just 1.0 retreatments.

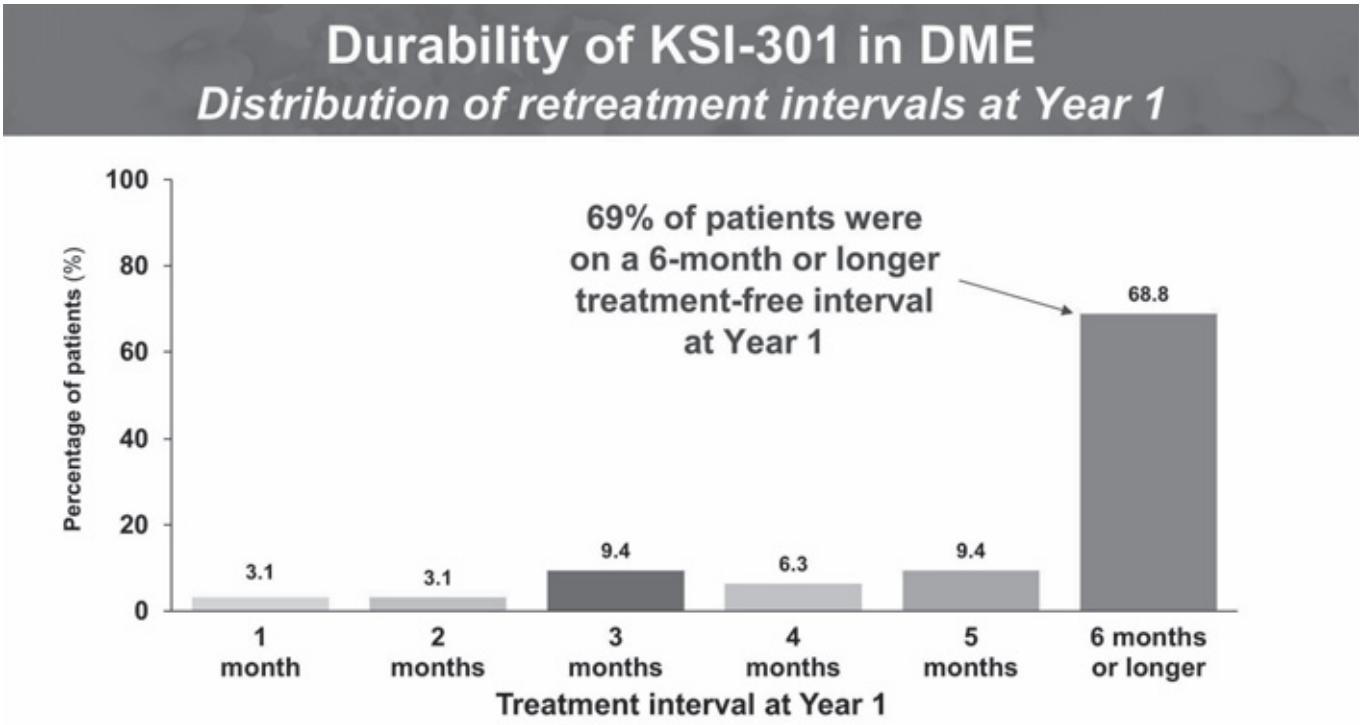
Consistent with the extended durability effect of KSI-301, we see again only slight fluctuations in the OCT over time, which compares favorably to the OCT fluctuations observed with existing anti-VEGF agents that are given on shorter dosing intervals.



The swim lane plot for DME durability is shown below. At Year 1, 94% of DME patients have achieved a three months or longer treatment-free interval. Of these patients, 84% have gone four months or longer, and 78% five months or longer at Year 1. Further, 69% have gone six-months or longer – as there is no cap to the treatment interval in the DME cohort. Half of patients did not require any retreatment at Year 1. 81% of patients have achieved a six months or longer treatment-free interval at least once during follow-up.

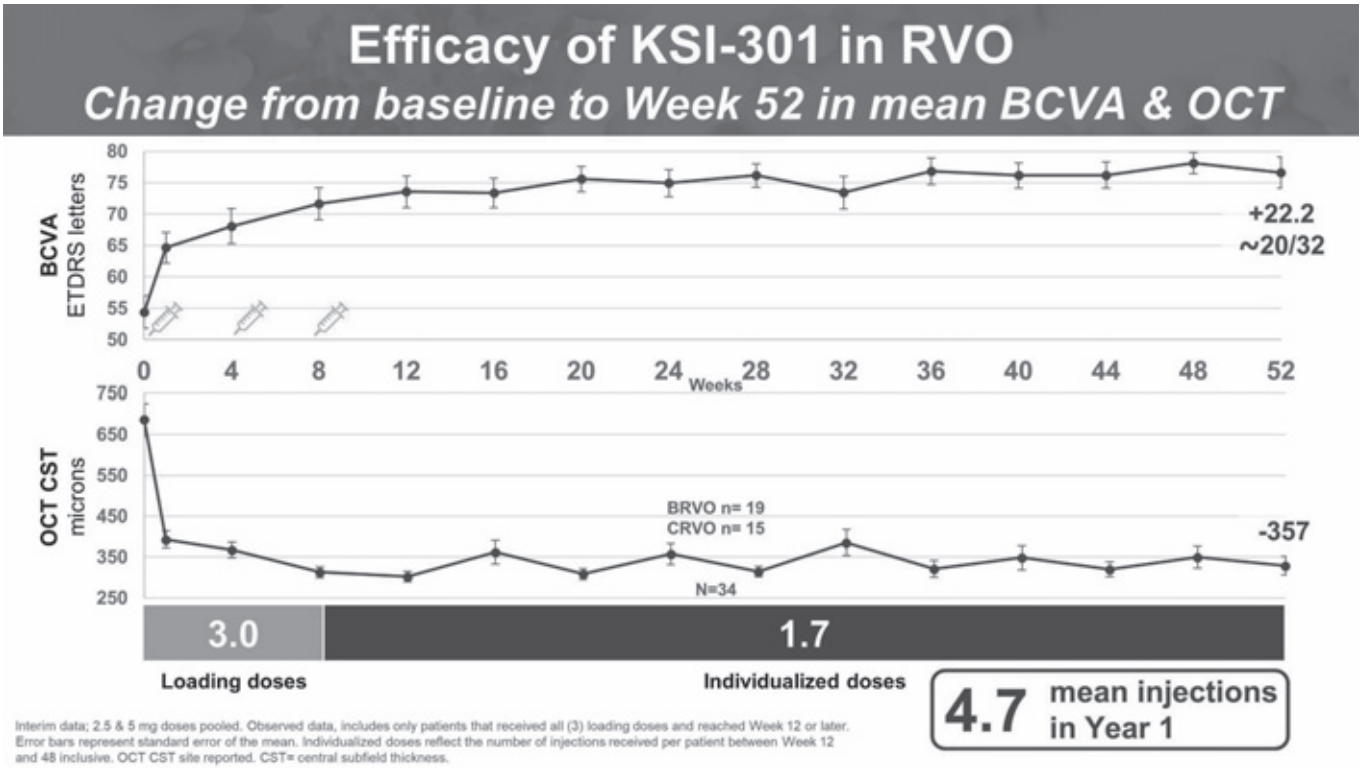




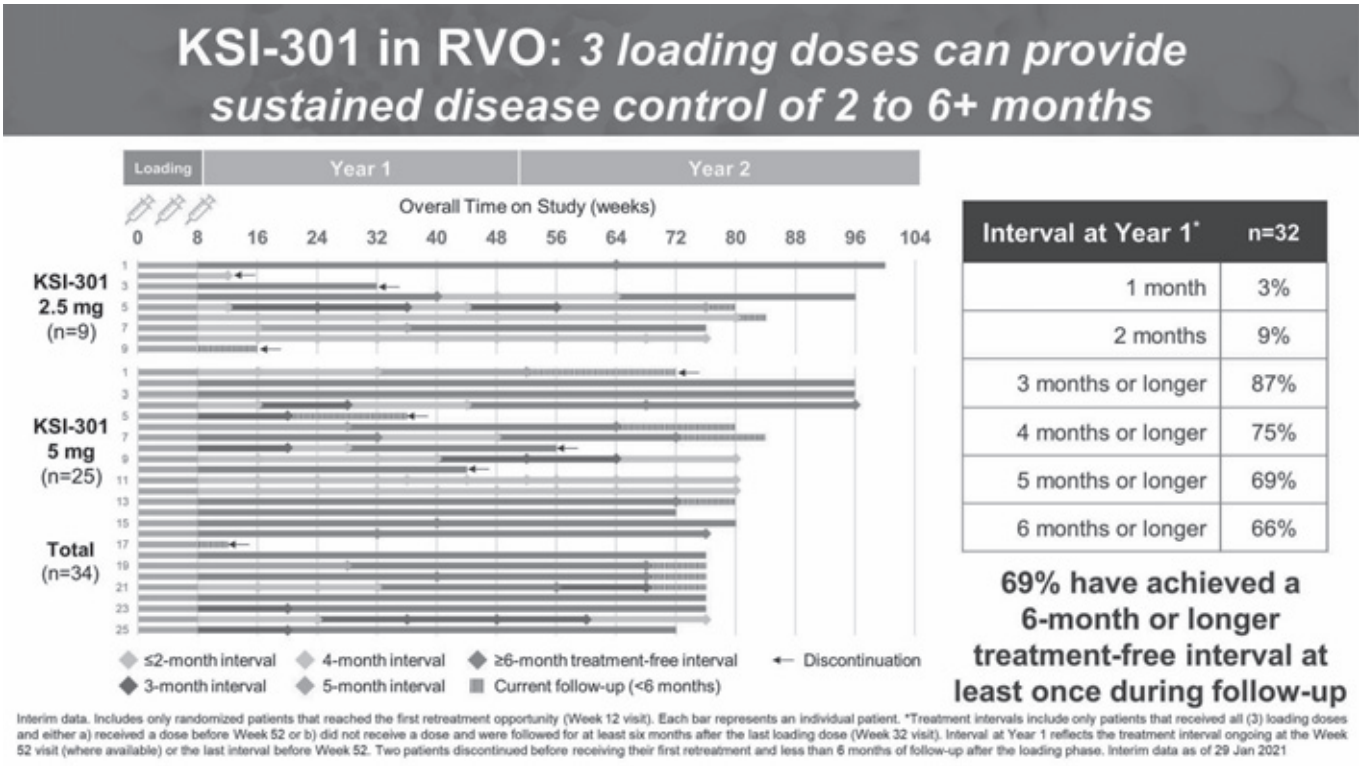


Retinal Vein Occlusion (RVO)

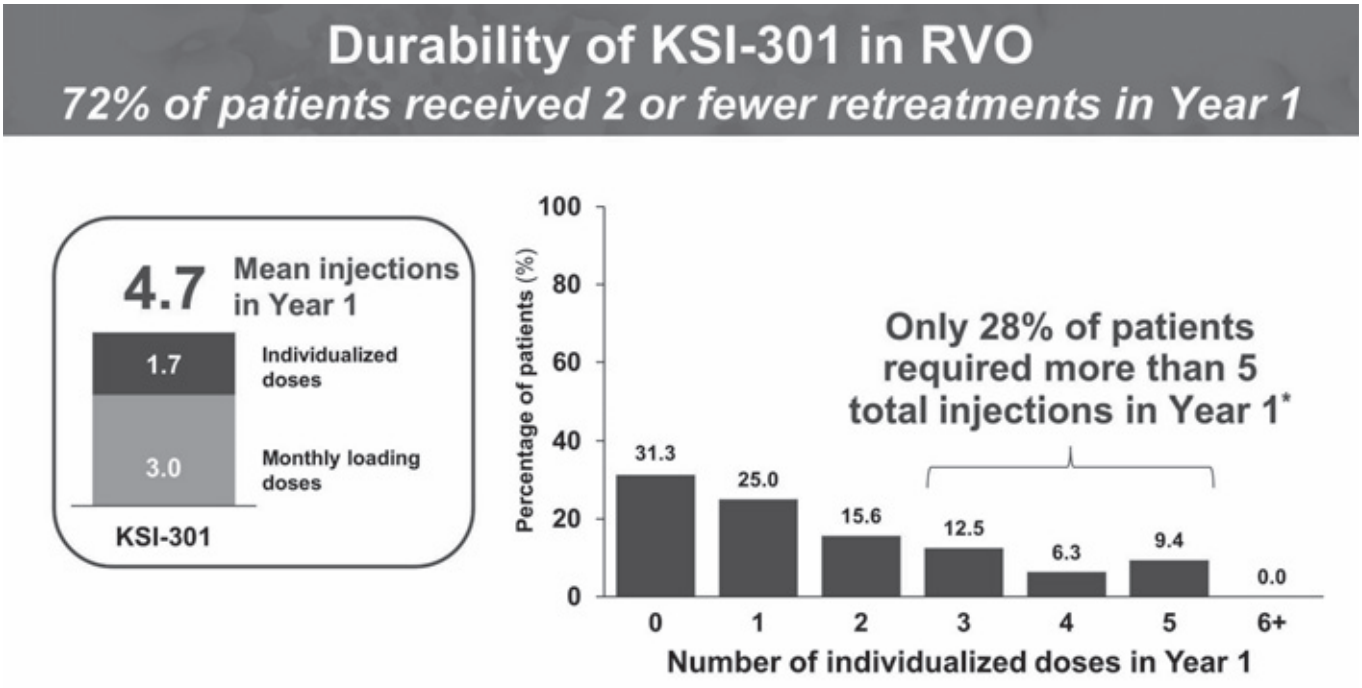
KSI-301 efficacy in treatment naïve RVO is also measured as change from baseline in BCVA and OCT CST. The 34 RVO patients that received all loading doses and reached Week 12 or later began with a lower visual acuity baseline of approximately 54 letters, typical of this disease. After three loading doses, their visual acuity substantially improved, with a 22.2 letter improvement at Year 1, to an average vision of 76.6 letters (Snellen ~20/32). The vision gain was maintained with an average of just 1.7 injections. A sustained OCT response with a decrease of 357 microns was also noted.



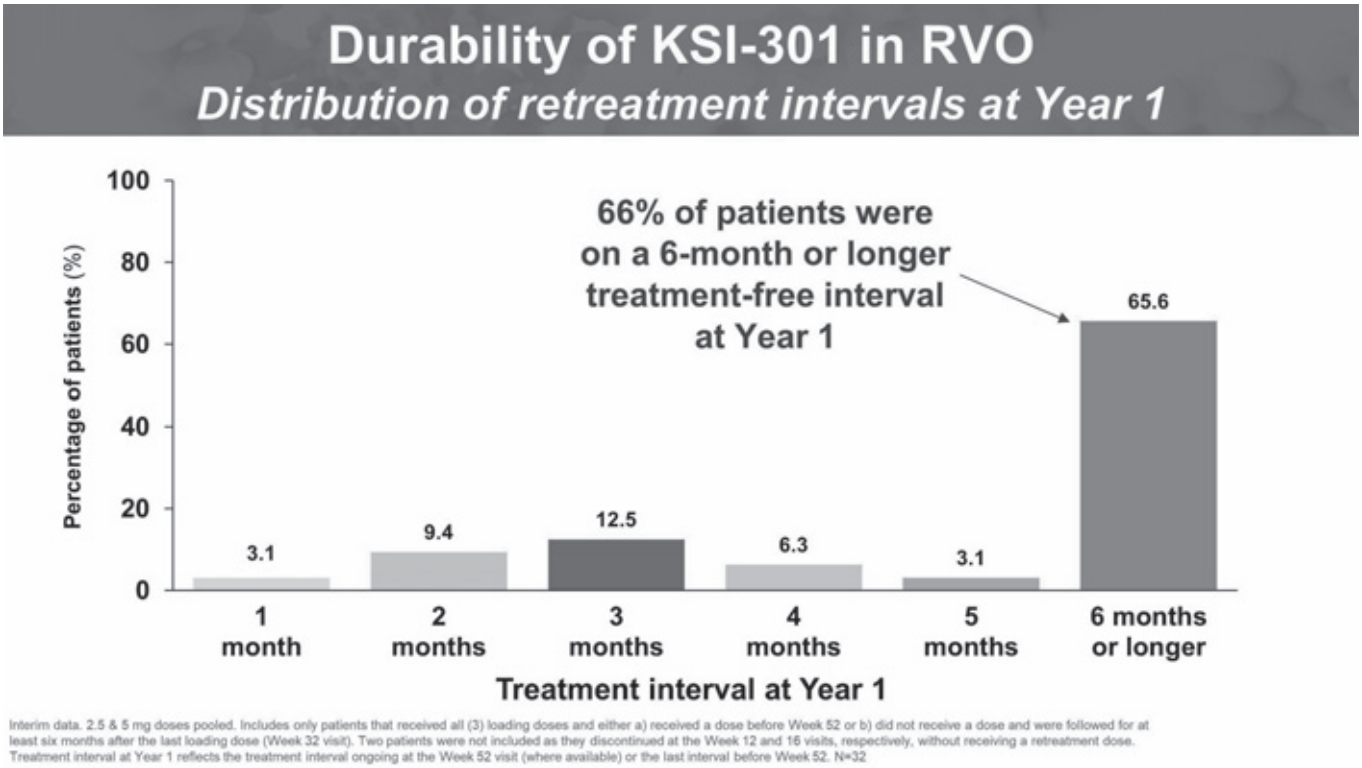
In this swim lane plot of the durability of individual patients with RVO, the disease with arguably the highest VEGF load, the bars in pink and orange now denote retreatment intervals of six months or longer and two months or shorter, respectively. 87% of RVO patients have achieved a three months or longer treatment-free interval at Year 1. Only 3% of patients were on a monthly treatment interval at Year 1. 75% of patients achieved a four months or longer treatment-free interval at Year 1, and 69% achieved a five months or longer interval at Year 1. Remarkably, given that many RVO patients require monthly therapy for the best results with existing medicines, 66% of patients have achieved a six months or longer treatment-free interval at Year 1.



Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit). Each bar represents an individual patient. *Treatment intervals include only patients that received all (3) loading doses and either a) received a dose before Week 52 or b) did not receive a dose and were followed for at least six months after the last loading dose (Week 32 visit). Interval at Year 1 reflects the treatment interval ongoing at the Week 52 visit (where available) or the last interval before Week 52. Two patients discontinued before receiving their first retreatment and less than 6 months of follow-up after the loading phase. Interim data as of 29 Jan 2021



Interim data; 2.5 & 5 mg doses pooled. Includes only patients that received all (3) loading doses and either a) received a dose before Week 52 or b) did not receive a dose and were followed for at least six months after the last loading dose (Week 32 visit). Two patients were not included as they discontinued at the Week 12 and 16 visits, respectively, without receiving a retreatment dose. Individualized doses reflect the average number of injections received per patient between Week 12 and 48 inclusive. N=32
* 3 loading doses plus more than 2 individualized doses

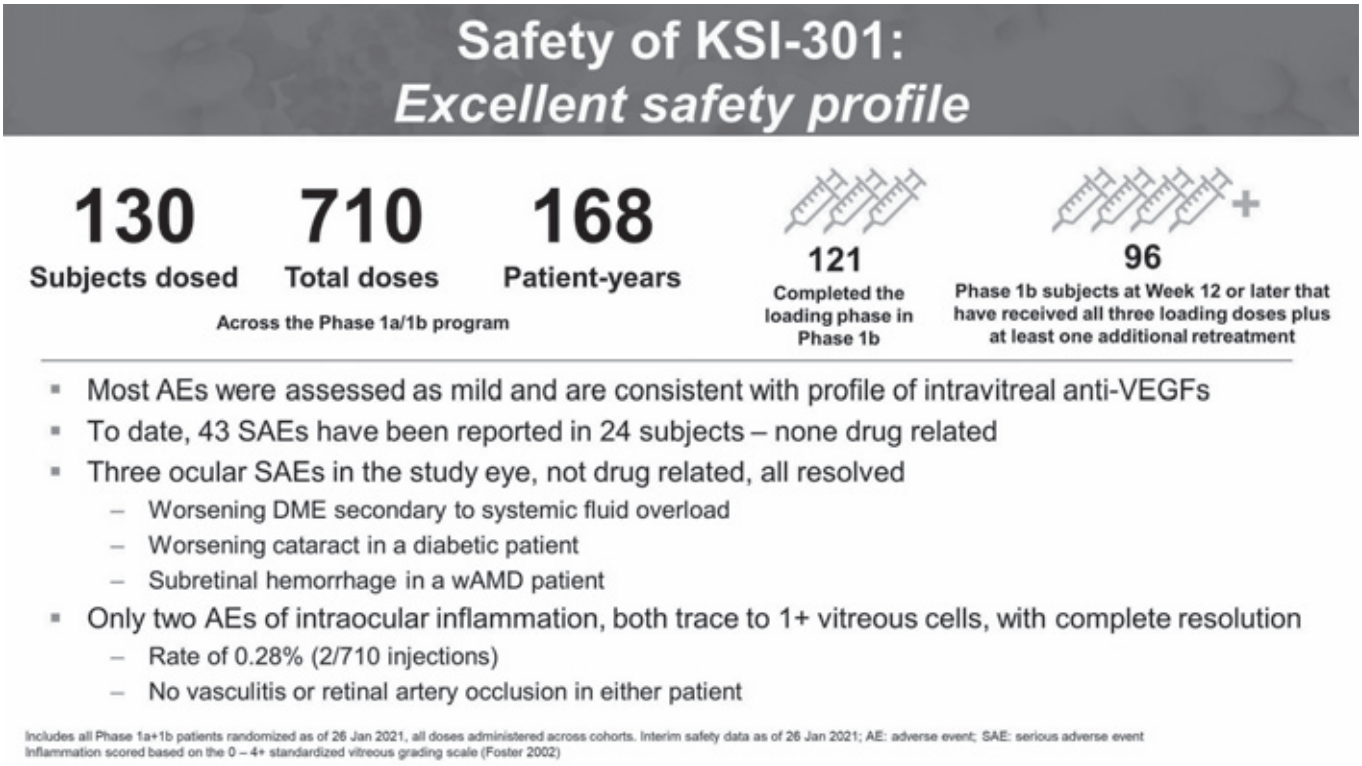


Safety of KSI-301 Injections

We believe the safety profile of KSI-301 continues to be very encouraging. Now with 710 injections given in the Phase 1a/1b program (as of January 26, 2021), and with patients followed for as long as 26 months, we are continuing to track with the expectations set by the safety profile of the current standard of care intravitreal medicines.

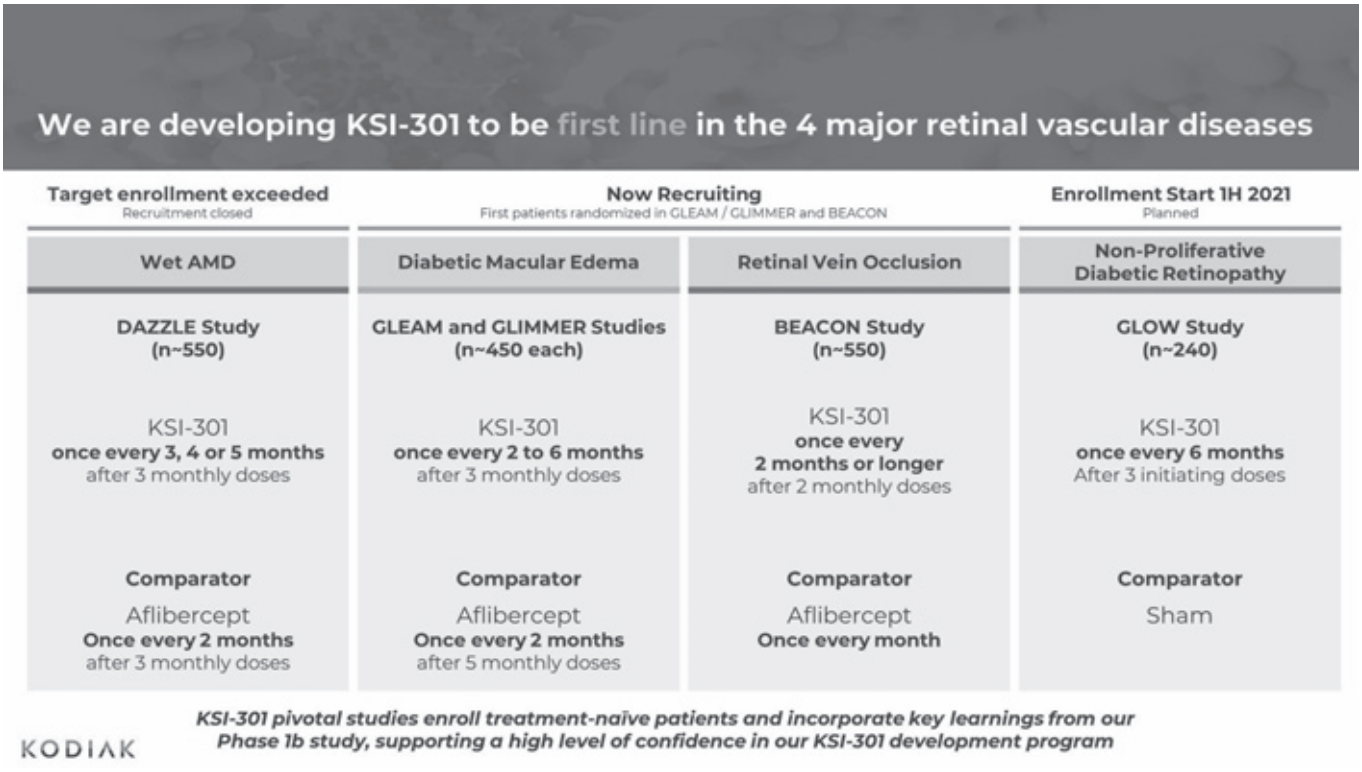
None of the serious adverse events, or SAEs, observed have been reported as or deemed drug-related, and they are typical of the systemic SAEs expected in these patient populations. The ocular SAE of worsening cataract was in a diabetic patient with pre-existing cataract, was not drug-related, and resolved with routine cataract surgery. The ocular SAE of subretinal hemorrhage in a wAMD patient is often found in wAMD patients and was not drug-related.

There have been only two events (previously described) of intraocular inflammation. The events were mild in nature, both trace to 1+ grade cells in the vitreous, on a standardized scale where 0 is none and 4+ is severe. They resolved completely, and there was no vasculitis or retinitis in either patient. Both patients have done very well with substantial improvements in vision from baseline; each of them had gained 30 letters or 6 lines of vision as of their last visits.



KSI-301 Pivotal Study Designs

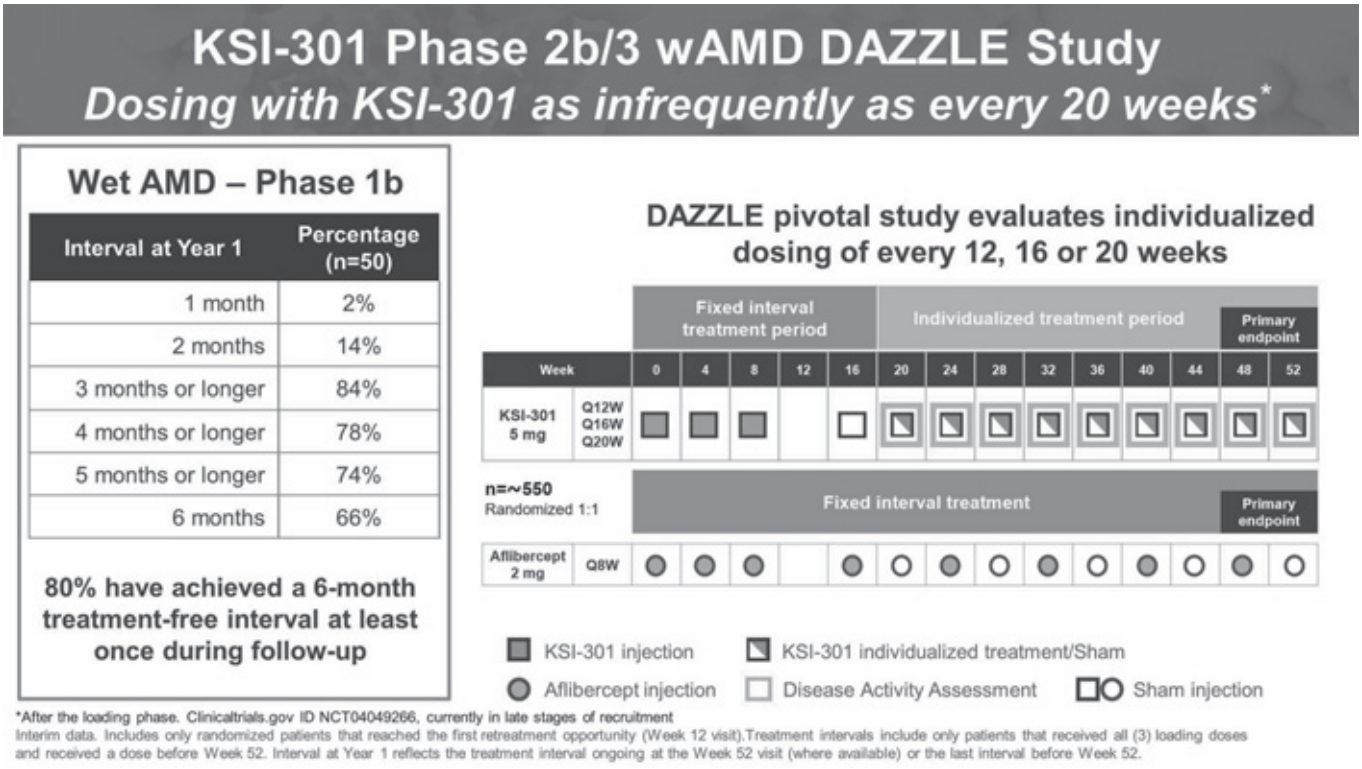
Our pivotal study designs for wet AMD (our ongoing DAZZLE study), DME (our ongoing GLEAM and GLIMMER studies), and RVO (our ongoing BEACON study) have been optimized based on Phase 1b data and experience.



Wet AMD DAZZLE Study

DAZZLE (NCT04049266) assesses patients with treatment naïve wet AMD and are randomized 1:1 to receive KSI-301 every 12 to 20 weeks or Eylea every 8 weeks, each after 3 monthly loading doses. The determination of treatment interval for the patients assigned to KSI-301 is based on disease activity assessments where both OCT and BCVA are measured and compared against prior data, similar to other recent and ongoing Phase 3 studies in the field. By default, patients are on an every 20 week regimen. If disease activity criteria are met before 20 weeks, that is, 12 or 16 weeks after the last dose, then the treatment interval is correspondingly shortened.

The primary endpoint is at one year and is a non-inferiority comparison to Eylea, with a four-letter non-inferiority margin. The one-year endpoint is measured as the average of the BCVA change from baseline to weeks 48 and 52. All of the KSI-301 patients are analyzed together as a single group with respect to the primary comparison to Eylea. In the second year of the study, patients whose disease is stable can have their KSI-301 treatment interval extended, and patients originally randomized to Eylea will be re-randomized 1:1 to either continued Eylea or switched to every eight week KSI-301.



*After the loading phase. Clinicaltrials.gov ID NCT04049266, currently in late stages of recruitment

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit).Treatment intervals include only patients that received all (3) loading doses and received a dose before Week 52. Interval at Year 1 reflects the treatment interval ongoing at the Week 52 visit (where available) or the last interval before Week 52.

Disease assessment criteria are used to determine whether the treatment interval is 12, 16 or 20 weeks. These criteria are tightened, and subjectivity has been reduced, compared to the retreatment criteria used in the Phase 1b study. The DAZZLE criteria, and the overall approach to dosing regimen determination in DAZZLE, are very similar to other recent Phase 3 programs in wet AMD. The aim is to customize the dose interval per patient, in a way that is feasible in a large, multicenter, double-masked trial.

How do DAZZLE Study Disease Activity Assessment Criteria Compare to Phase 1b?

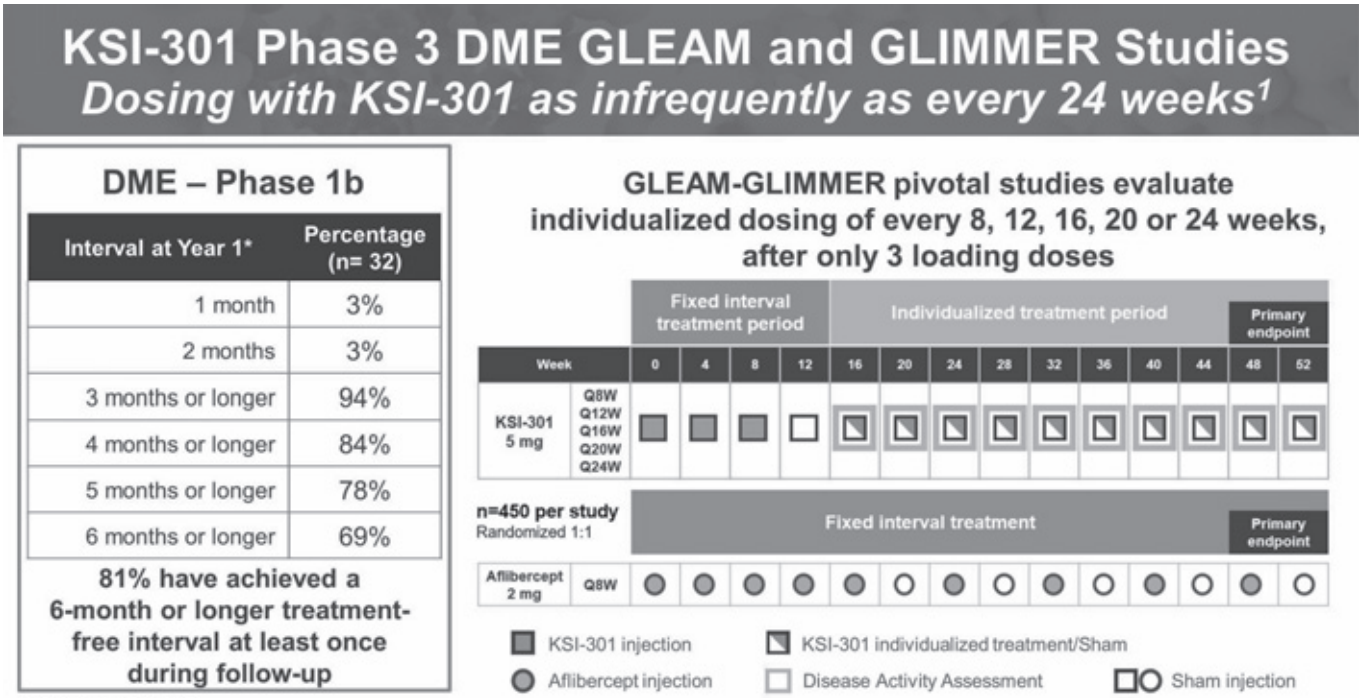
Parameters	Phase 1b Study	DAZZLE study	Change
Visual *and* anatomical	Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12, *OR*	Increase in CST ≥50 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12, *OR*	**Tighter CST control (25 microns)**
Visual only	Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening wAMD activity, *OR*	Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening wAMD activity, *OR*	**No change**
	Decrease in BCVA of > 5 letters compared to Day 1, due to worsening wAMD activity	N/A	**Eliminated to reduce subjectivity and unnecessary retreatments**
Anatomical only	N/A	Increase of ≥ 75 microns compared to Week 12, *OR*	**Added two anatomical-only criteria**
	N/A	New Macular Hemorrhage	

wAMD = wet **age-rhfcelated** macular degeneration; CST = central subfield retinal thickness; BCVA = best corrected visual acuity. Clinicaltrials.gov ID: NCT03790852

Diabetic Macular Edema Paired Studies, GLEAM and GLIMMER

In DME, we are conducting two Phase 3 studies in parallel with identical design. In each of the two studies, called GLEAM (NCT04611152) and GLIMMER (NCT04603937), we will randomize 450 treatment-naïve DME patients to either KSI-301 every 8 to 24 weeks after 3 loading doses, or Eylea every 8 weeks after 5 loading doses. The primary endpoint is the change from baseline in BCVA at one year, again the average of the week 48 and 52 visits. The studies are non-inferiority studies with a margin of 4.5 letters.

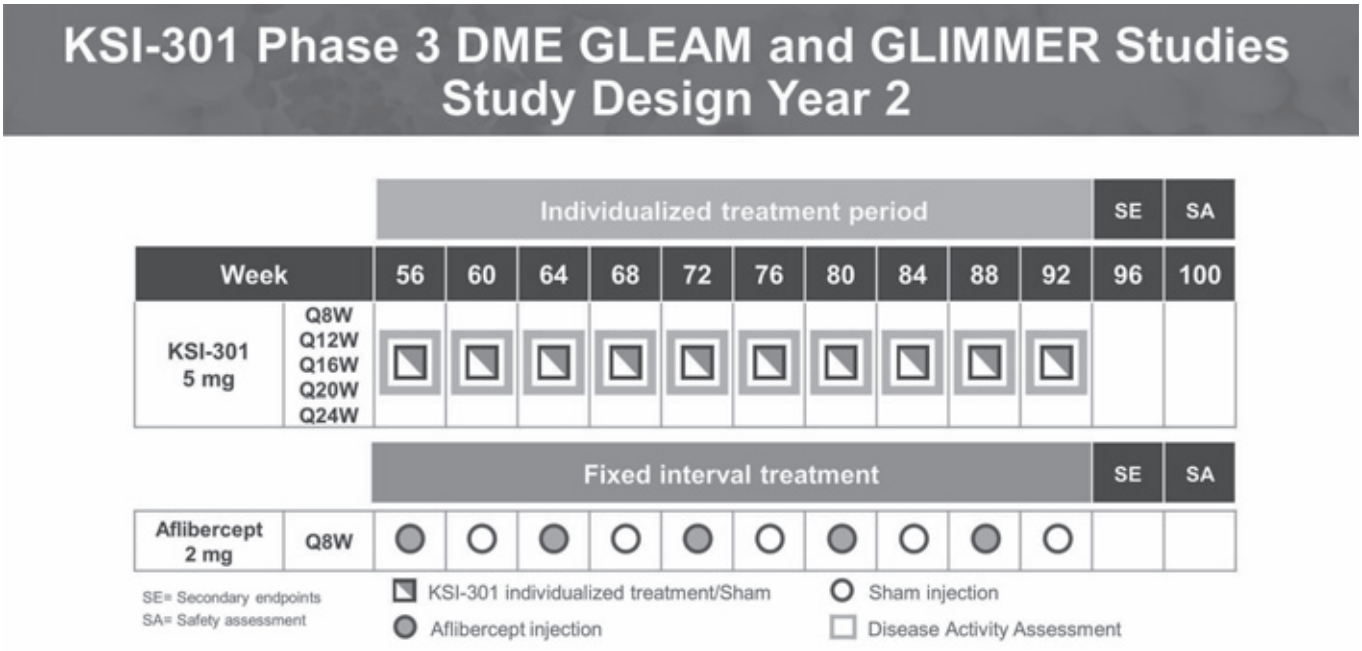
At each monthly study visit, patients who have been randomized to KSI-301 will undergo a disease activity assessment, using data from both BCVA and OCT measurements. Depending on their disease activity status, the dosing interval can be shortened, lengthened, or maintained at the same interval. This is different from the DAZZLE wet AMD study design where the interval can only be maintained or shortened in the first year. In DME, patients may experience disease modification (improvement in the severity of the underlying retinopathy) that curtails the need for therapy over time, an event that has been seen in many DME patients treated with KSI-301 allowing for the treatment interval to be potentially further prolonged after the first retreatment. The minimum KSI-301 treatment interval in GLEAM and GLIMMER is every eight weeks, and the maximum interval is every 24 weeks or six months.



1. After the loading phase

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit). *Treatment intervals include only patients that received all (3) loading doses and either a) received a dose before Week 52 or b) did not receive a dose and were followed for at least six months after the last loading dose (Week 32 visit). Interval at Year 1 reflects the treatment interval ongoing at the Week 52 visit (where available) or the last interval before Week 52. One patient only received one loading dose and was excluded from the calculation

In the second year of both studies, the same approach is maintained. Eylea will stay on its q8 week regimen, and patients on KSI-301 will continue to be on an 8 to 24 week regimen based on disease activity.



To determine the treatment interval for KSI-301 patients, we are employing disease activity assessments and protocol-specified criteria. All patients randomized to KSI-301 are on the longest interval by default. If patients meet any of these disease activity criteria at earlier timepoints, the retreatment interval is shortened. The criteria for shortening the treatment interval are tighter than they are in Phase 1b, and the subjectivity is reduced. Additional anatomic criteria have also been included.

How do GLEAM/GLIMMER Studies Disease Activity Assessment Criteria Compare to Phase 1b?

Parameters	Phase 1b Study[1]	GLEAM/GLIMMER Studies	Change
Visual *and* anatomical	Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12 or the prior visit, *OR*	Increase in OCT CST ≥ 50 µm compared to lowest previous measurement and a decrease in BCVA of ≥ 5 letters compared to the average of the 2 best previous BCVA assessments, due to worsening of DME disease activity, *or*	Tighter and dynamic control of both vision and anatomy
Visual only	Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening DME activity	N/A	Eliminated to reduce subjectivity and unnecessary retreatments
Anatomical only	N/A	Increase in OCT CST ≥ 75 µm compared to lowest previous measurement due to worsening of DME disease activity; *or*	Added two anatomical-only criteria
	N/A	New or worsening proliferative DR (PDR)	

DME = diabetic macular edema; OCT = optical coherence tomography; CST = central subfield retinal thickness; BCVA = best corrected visual acuity.
[1] Clinicaltrials.gov ID: NCT03790852

Retinal Vein Occlusion BEACON Study Design

The Phase 3 BEACON study (NCT04592419) in patients with RVO is a year-long study in which we will randomize 550 patients with treatment-naïve RVO, either branch or central vein type, to either every 8 weeks KSI-301 after two loading doses, or to monthly Eylea, for the first six months. The primary endpoint is at six months, with a non-inferiority margin of 4.5 letters.

In the second six months, patients in both groups will receive treatment on an individualized regimen, again using typical disease activity assessments. This phase of the study will provide a direct, head-to-head comparison of Eylea and KSI-301 on the same criteria-driven regimen. The minimum interval is monthly and there is no upper limit to the retreatment interval in this six-month period.

KSI-301 Phase 3 RVO BEACON Study

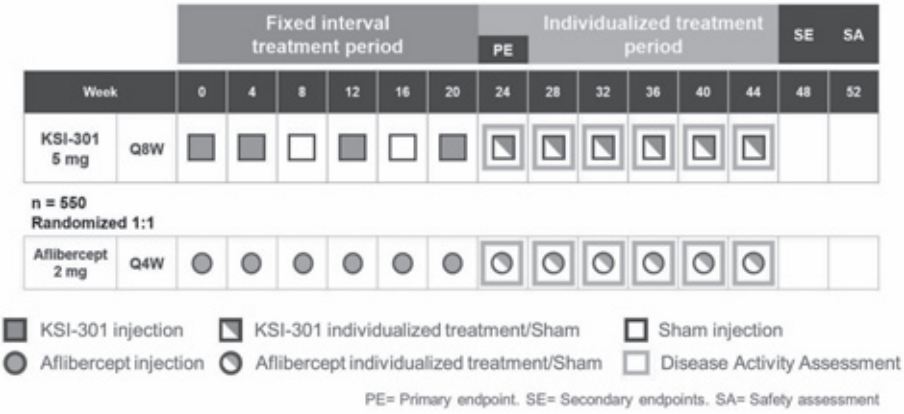
Two loading doses with KSI-301 + every 8 weeks

RVO – Phase 1b

Interval at Year 1*	Percentage (n= 34)
1 month	3%
2 months	9%
3 months or longer	87%
4 months or longer	75%
5 months or longer	69%
6 months or longer	66%

69% have achieved a 6-month or longer treatment-free interval at least once during follow-up

BEACON pivotal study evaluates two loading doses and every 8-week dosing, followed by individualized dosing



PE= Primary endpoint. SE= Secondary endpoints. SA= Safety assessment

Clinicaltrials.gov ID NCT04592419, currently recruiting

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit). *Treatment intervals include only patients that received all (3) loading doses and either a) received a dose before Week 52 or b) did not receive a dose and were followed for at least six months after the last loading dose (Week 32 visit). Interval at Year 1 reflects the treatment interval ongoing at the Week 52 visit (where available) or the last interval before Week 52. Two patients discontinued before receiving their first retreatment and less than 6 months of follow-up after the loading phase.

Because the first six months of the study are fixed-interval dosing, the disease activity assessment criteria are only used to determine dosing in the second six months of the RVO study. The criteria are similar to our DME studies, and tighter than they are in Phase 1b, with the OCT and BCVA measured against the best previous measurements; subjectivity is also reduced.

How do BEACON Study Disease Activity Assessment Criteria Compare to Phase 1b?

Parameters	Phase 1b Study[1]	BEACON Study[2]	Change
Visual *and* anatomical	Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12 or the prior visit, *OR*	Increase in OCT CST ≥ 50 µm compared to lowest previous measurement and a decrease in BCVA of ≥ 5 letters compared to the average of the 2 best previous BCVA assessments, due to worsening of RVO disease activity, *or*	Tighter and dynamic control of both vision and anatomy
Visual only	Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening RVO activity	N/A	Eliminated to reduce subjectivity and unnecessary retreatments
Anatomical only	N/A	Increase in OCT CST ≥ 75 µm compared to lowest previous measurement due to worsening of RVO disease activity; *or*	Added one anatomical-only criteria

RVO = retinal vein occlusion; OCT = optical coherence tomography; CST = central subfield retinal thickness; BCVA = best corrected visual acuity.

[1] Clinicaltrials.gov ID: NCT03790852

[2] Clinicaltrials.gov ID: NCT04592419

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. It is not currently approved for diseases other than wet AMD. 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 branded anti-VEGFs for all indications totaled more than $11.5 billion in 2020. 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 branded anti-VEGFs for all indications were an estimated $11.5 billion in 2020. 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.

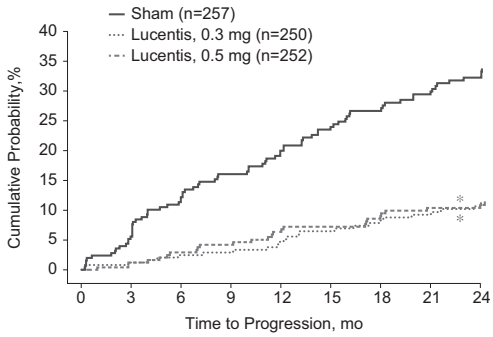


Figure: Time to disease worsening (DR progression as defined by a composite endpoint) from baseline in DME patients with NPDR treated with sham procedures vs. Lucentis.

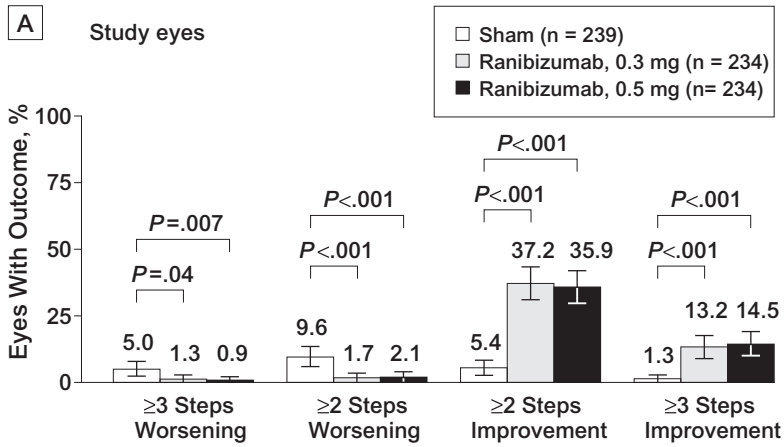


Figure: Proportion of subjects improving or worsening per treatment arm.

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 approximately $11.5 billion in global sales of branded anti-VEGFs in 2020 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.

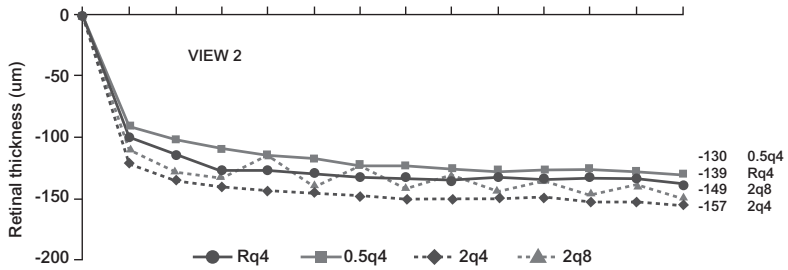


Figure: Retinal thickness (y-axis), measured in microns, decreases upon treatment with Eylea. Rq4 = Lucentis every four weeks; 0.5q4 = Eylea 0.5mg every four weeks; 2q4 = Eylea 2mg every four weeks; 2q8 = Eylea 2mg every eight weeks.

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.

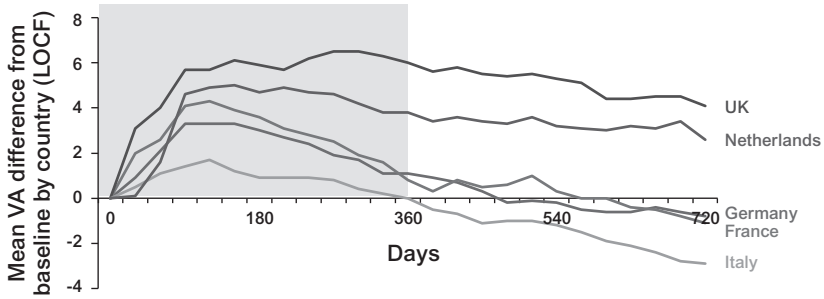


Figure: Vision gains seen in the AURA study over time for all patients by country (adapted from Holz et al).
***Last observation carried forward analysis.**

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.

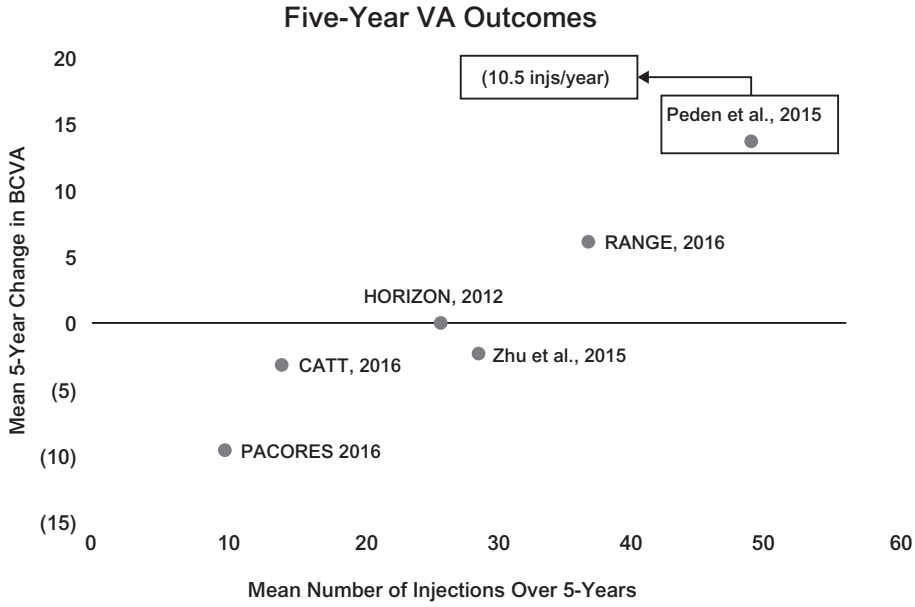


Figure: Five-year visual acuity outcomes versus injection frequency for three or more years in AMD.

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.

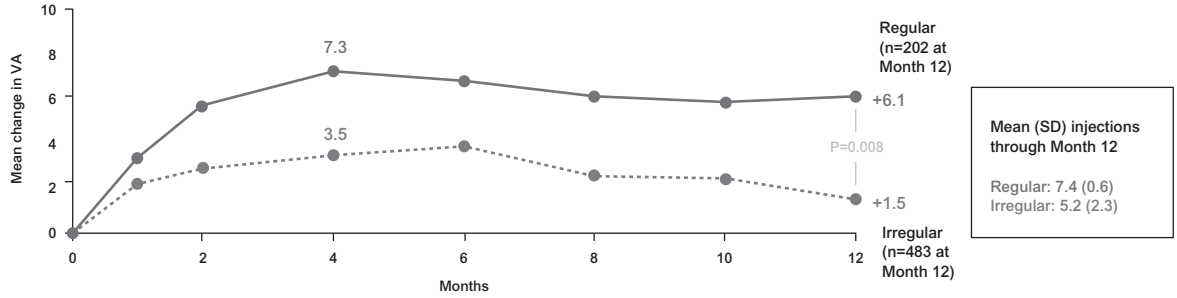


Figure: mean change in visual acuity for regularly and irregularly treated patients in the PERSEUS Study (effectiveness set)

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.

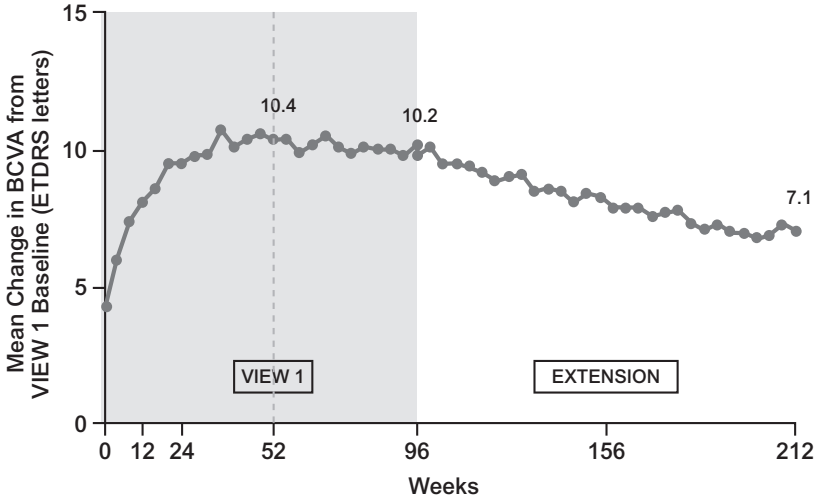


Figure: Mean visual acuity and 95% confidence interval for 647 patients in the Comparison of Age-Related Macular Degeneration Treatments Trials Follow-up Study: (A) overall and by drug assigned in the clinical trial and (B) overall and by dosing regimen assigned in the clinical trial. PRN = "as needed."

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.

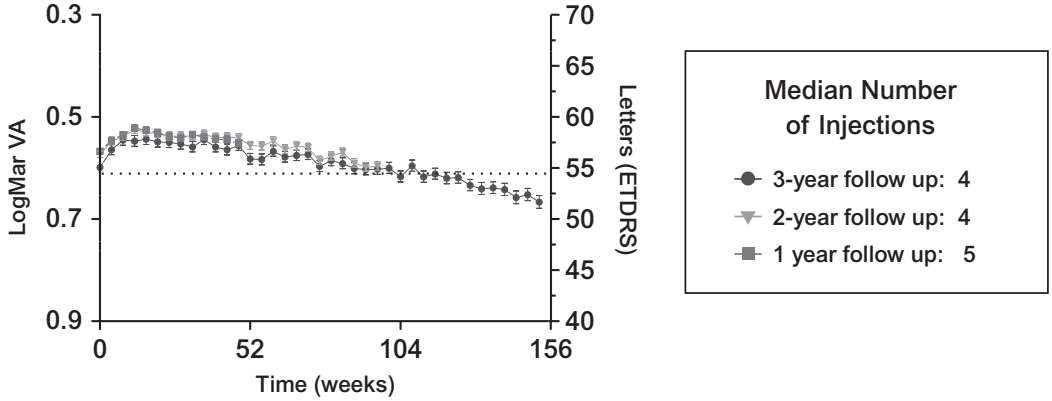


Figure: Mean visual acuity (VA), as measured by letter score, over time comparing patients with follow-up of at least 1, 2 or 3 years.

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.

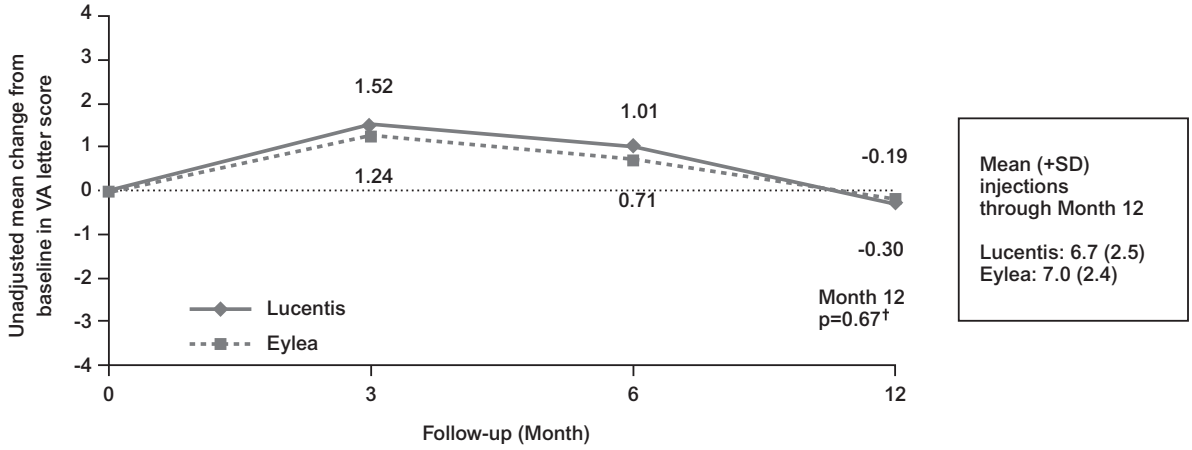


Figure: Mean change in visual acuity (VA) letter score at 3, 6 and 12 months in the first year of treatment. VA was lower at 12 months than at the beginning of treatment.

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.

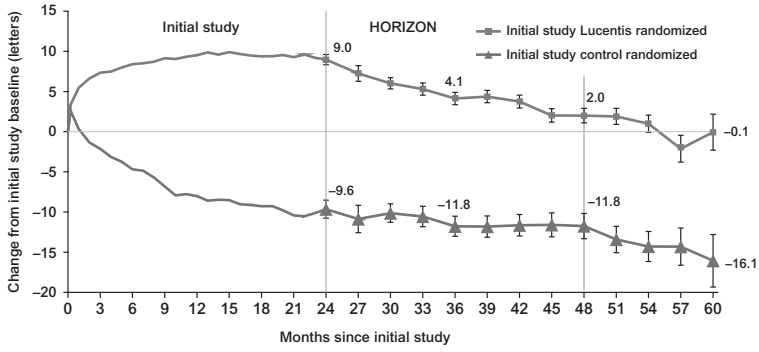
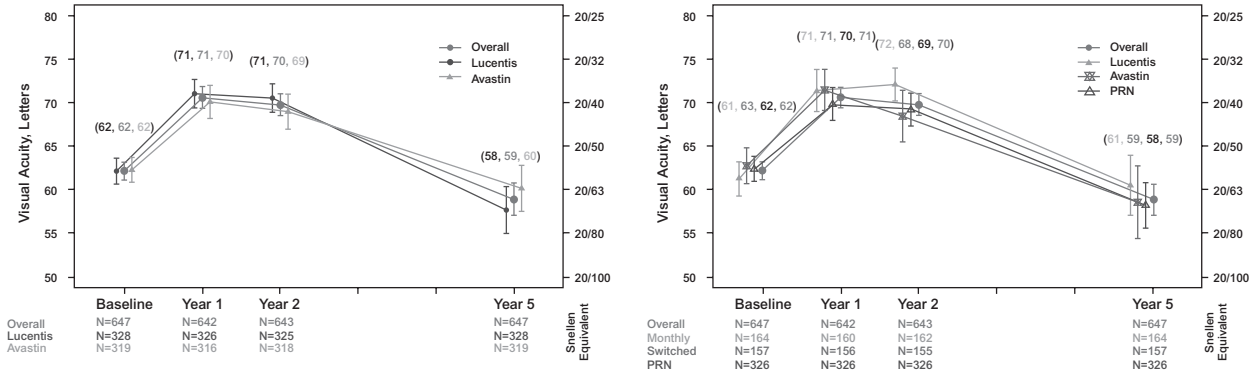


Figure: Mean change in visual acuity (VA) letter score in MARINA and ANCHOR (years one and two) and in HORIZON (years three to five). VA gradually decreased immediately after the patients exited monthly dosing in a clinical trial setting.

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.

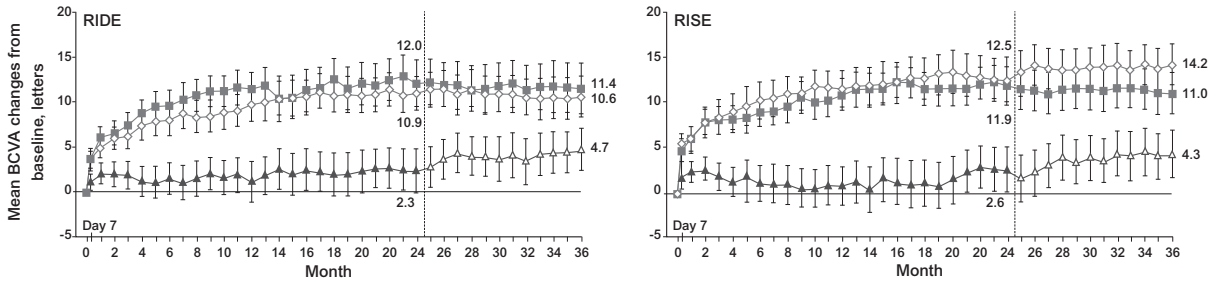


Figure: At 36 months, patients who received Lucentis 0.5mg experienced a mean BCVA change from baseline of 11.4 letters and 11.0 letters in RIDE and RISE, respectively. Patients who received sham treatment for 24 months and then crossed over to Lucentis 0.5mg experienced a diminished benefit in mean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

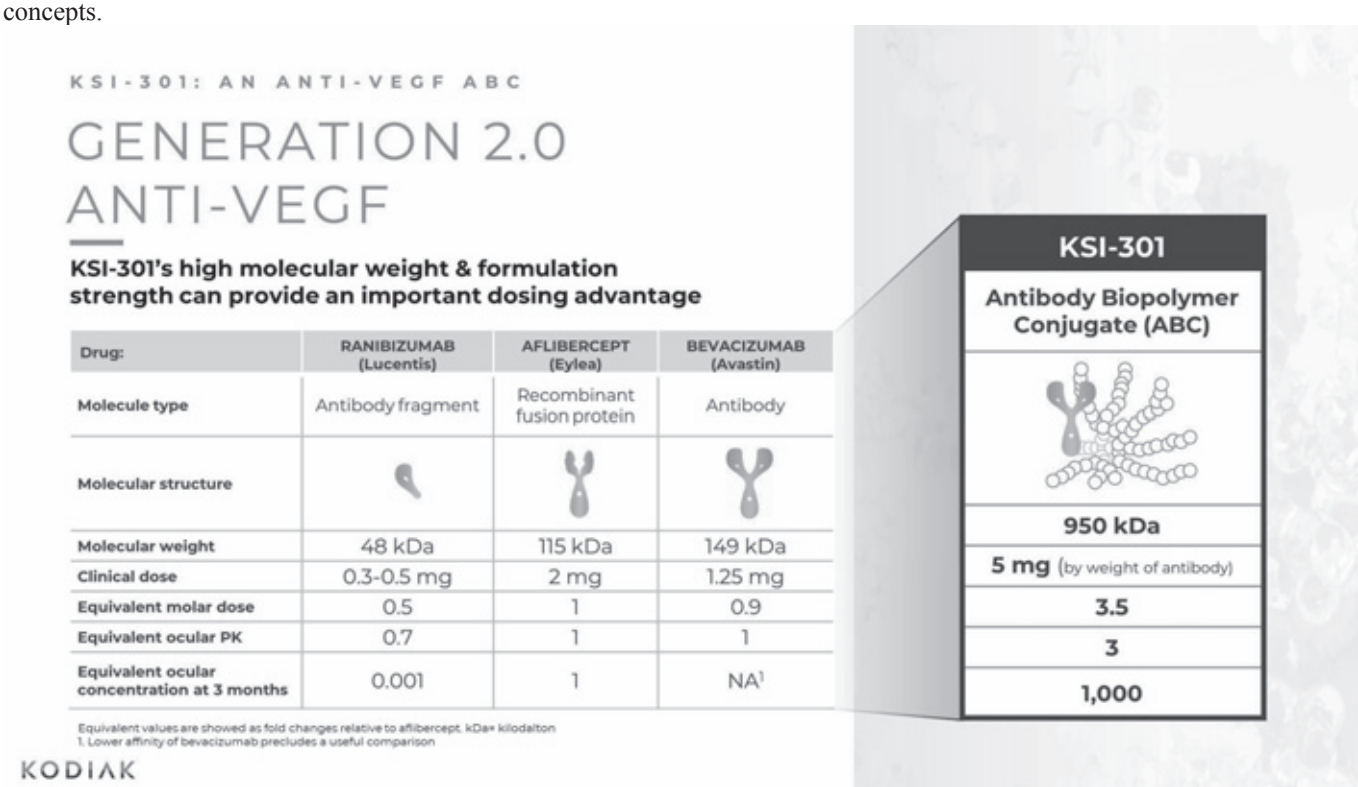
- Design feature: KSI-301's ultra-high molecular weight of 950,000 Daltons as compared to 115,000 for Eylea, 48,000 for Lucentis and 27,000 for brolucizumab
    - Associated performance benefits:
        - 3x improvement in key ocular pharmacokinetic parameters of KSI-301, as compared to Eylea
        - ~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 or other long-term postoperative complications such as implant dislocation. 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 both through high molar doses and the targeting of additional pathways beyond VEGF, 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). 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.

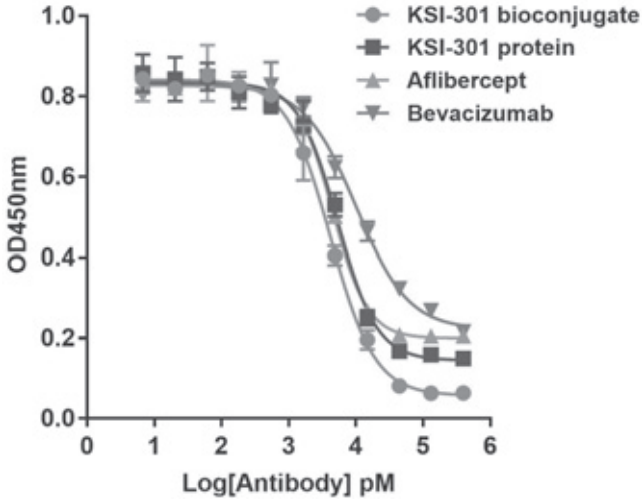


Figure: Inhibition of VEGF binding to VEGF receptors by anti-VEGF agents.

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.

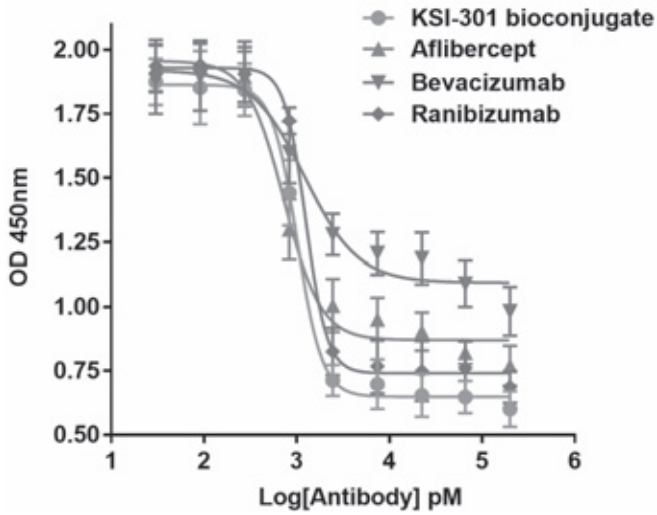


Figure: Effects of KSI-301, Lucentis, Eylea and Avastin on HRMVEC proliferation.

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.

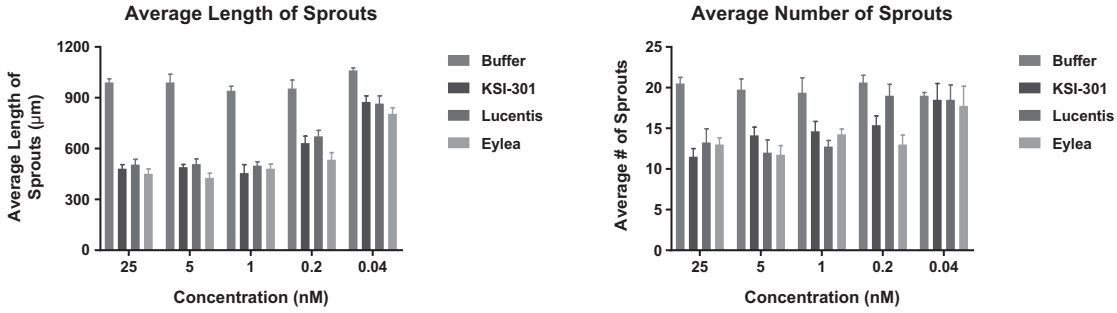


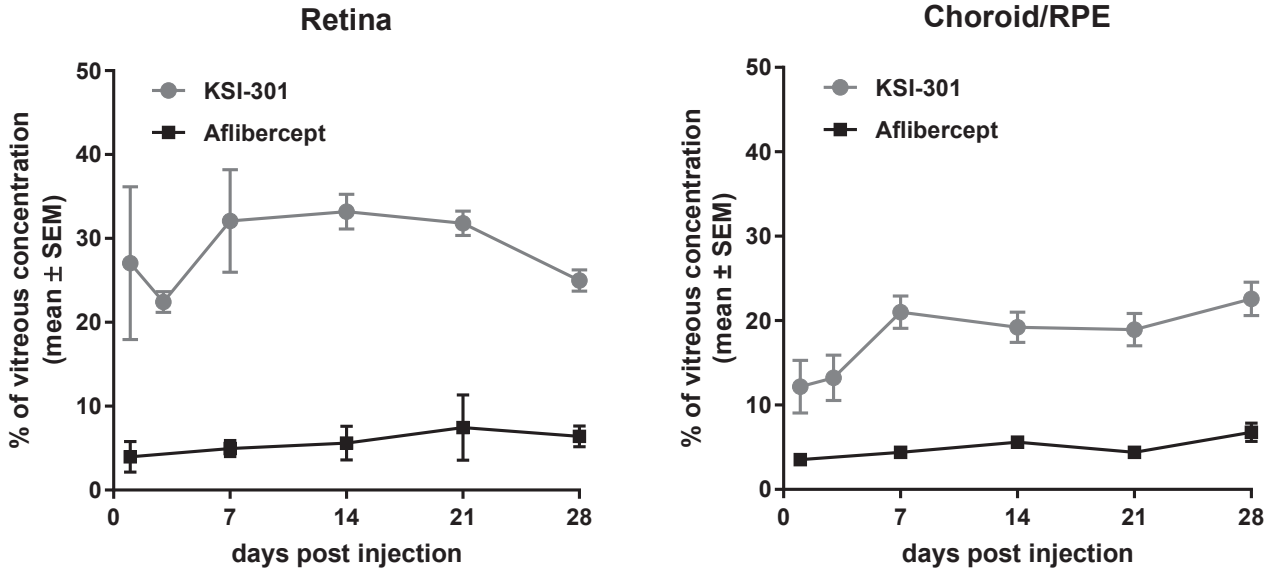
Figure: Effects of KSI-301 and other anti-VEGF molecules on length and number of vascular sprouts in 3-dimensional culture.

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.

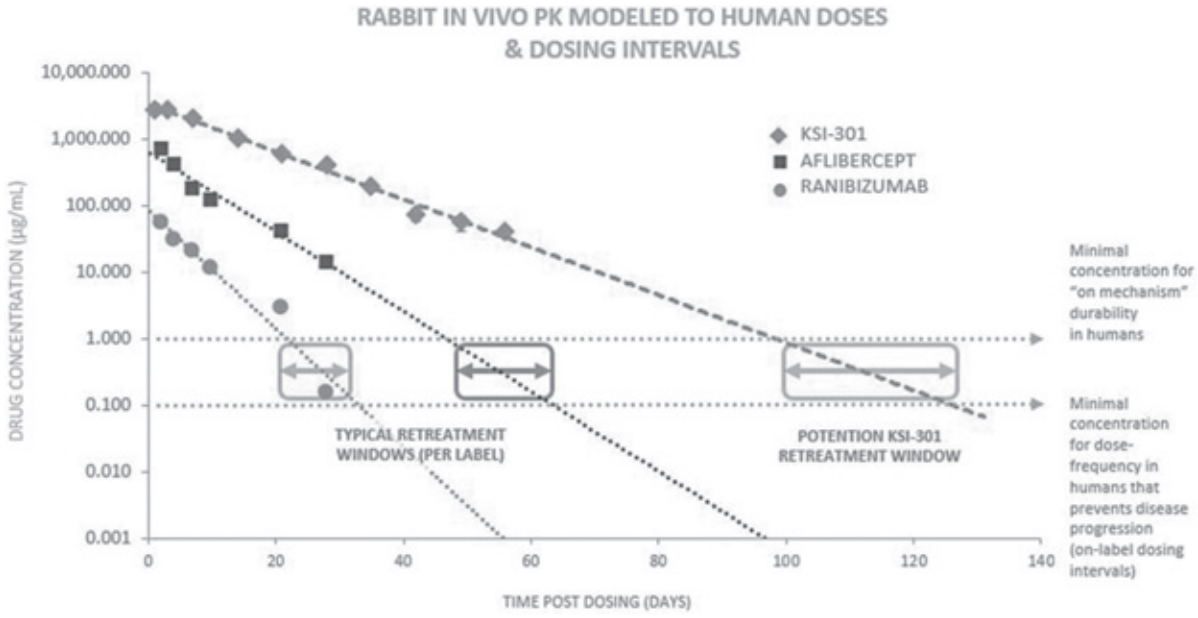
Enhanced Ocular Tissue Bioavailability versus Eylea

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 are currently working towards IND submission in early 2022.

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

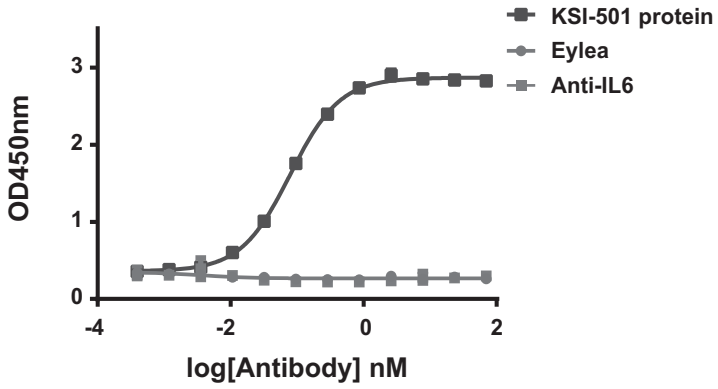


Figure: TAF of KSI-501 simultaneously binds to IL-6 and VEGF by sandwich ELISA, which only shows a signal if a compound binds to both IL-6 and VEGF concurrently.

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.

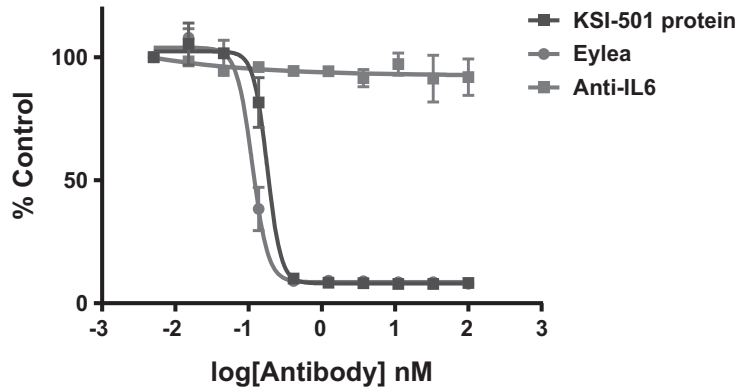


Figure: VEGF stimulated reporter assay with increasing concentrations of anti-VEGF inhibitors

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.

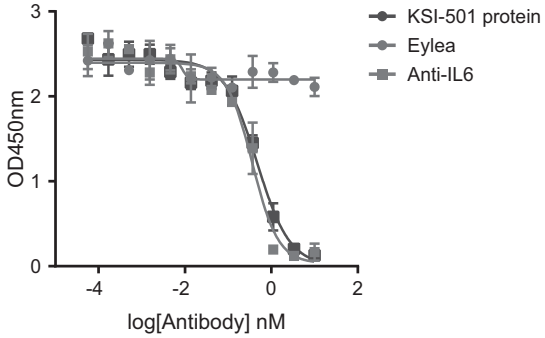


Figure: ELISA measuring IL-6 binding to IL-6R in the presence of increasing concentrations of anti-IL-6 inhibitors

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.

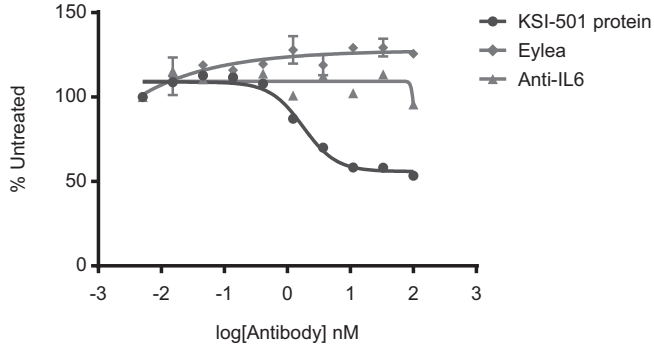


Figure: VEGF/IL-6 mediated HUVEC proliferation in the presence of inhibitors

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.

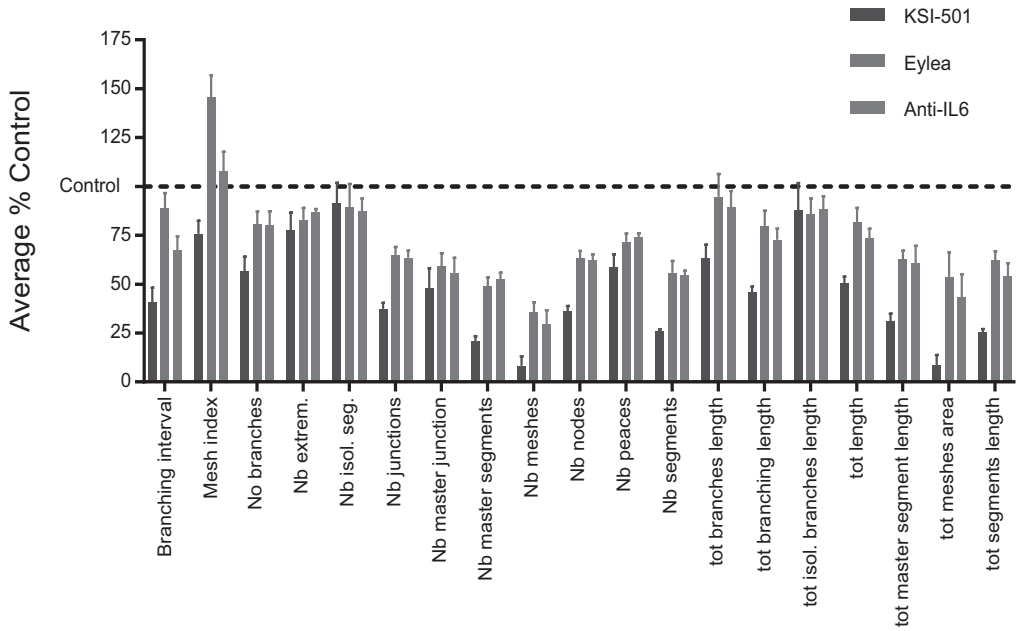


Figure: Quantification of IL-6/VEGF mediated HUVEC tubule formation in the presence or absence of inhibitor molecules using the Angiogenesis Analyzer plugin for ImageJ

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.

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 and biosimilar 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, advanced stages of DR (including DME), and RVO 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; and
- 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 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 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. Roche is developing faricimab, a bispecific antibody targeting VEGF and another mechanism, in wet AMD, DME, and RVO, and recently presented Phase 3 data demonstrating the non-inferiority of faricimab to Eylea in wet AMD and DME. 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, subject to delivery of notice by the Company, payable upon enrollment of 50% of the patients in the RVO clinical program. 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 program fee for approved human 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 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. 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. 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 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.

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 Laws

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, or CMS, other divisions of the Department of Health and Human Services, or HHS, 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. 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.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme or artifice 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, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, 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.

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, the federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act," created under the ACA and its implementing regulations, require certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report

such information related to payments or other transfers of value to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH) and their respective implementing regulations, impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses and their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information as well as their covered subcontractors, relating to the privacy, security, and transmission of such individually identifiable health information. 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 and local jurisdictions 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.

Data Privacy

Privacy laws in the U.S. are also increasingly complex and changing rapidly. For example, the California legislature enacted the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020. The CCPA requires covered companies to provide new disclosures to California residents, and honor their requests to access, delete and opt-out of certain sharing of their personal information. The CCPA provides for civil penalties for violations. Since the enactment of the CCPA, new privacy and data security laws have been proposed in more than half of the states and in the U.S. Congress, reflecting a trend toward more stringent privacy legislation in the U.S. The CCPA itself will expand substantially as a result of California voters approving a November 2020 ballot measure that adopted the California Privacy Rights Act of 2020, or CPRA, which will, among other things, create a new administrative agency to implement and enforce California's privacy laws effective January 1, 2023.

In addition, the processing of personal data in connection with clinical trials in the EU must comply with comprehensive data protection requirements imposed by EU's General Data Protection Regulation, or GDPR. GDPR, which took effect on May 25, 2018, imposes stringent data protection requirements and provides for penalties for noncompliance that can include bans on processing personal data and fines of up to the greater of 20 million euros or four percent of worldwide annual revenues. The GDPR requires organizations to give detailed disclosures about how they collect, use and share personal information; in most cases, obtain explicit consent to process sensitive personal information, such as health or genetic information; contractually require vendors to meet data protection requirements; maintain adequate data security measures; notify regulators and affected individuals of certain data breaches; meet extensive privacy governance and documentation requirements; and honor individuals' data protection rights, including their rights to access, correct and delete their personal information.

European data protection laws, including the GDPR, also restrict the transfer of personal information from Europe, including the European Economic Area, the United Kingdom and Switzerland, to the U.S. and most other countries unless the parties to the transfer have implemented specific safeguards to protect the transferred personal information. One of the primary safeguards allowing U.S. companies to import personal information from Europe has been certification to the EU-U.S. Privacy Shield and Swiss-U.S. Privacy Shield frameworks administered by the U.S. Department of Commerce. However, the Court of Justice of the European Union adopted a decision in July 2020 invalidating the EU-U.S. Privacy Shield. The same decision also raised questions about whether one of the primary alternatives to the EU-U.S. Privacy Shield, namely, the European Commission's Standard Contractual Clauses, can lawfully be used for personal information transfers from Europe to the U.S. or most other countries. Authorities in Switzerland also have issued guidance raising similar questions about the Swiss-U.S. Privacy Shield and the Standard Contractual Clauses.

The failure to comply with any of these laws or regulatory requirements may result in 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.

U.S. Health Care Reform

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 Tax Cuts and Jobs Act of 2017 (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. The United States Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. Although the United States Supreme Court has yet ruled on the constitutionality of the ACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how the United States Supreme Court ruling, other such litigation, and the healthcare form measures of the Biden administration will impact the ACA and our business. 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. For example, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Further, on November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

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 legal framework for the administration of pharmaceutical products in China was established by the Drug Administration Law of the PRC (DAL). The DAL applies to entities and individuals engaged in the development, production, trade, clinical use, as well as supervision and administration of pharmaceutical products by regulatory agencies and provides a framework for regulating pharmaceutical manufacturers, pharmaceutical trading companies, medical institutions, and the research, development, manufacturing, distribution, packaging, pricing, and advertisement activities related to pharmaceutical products. The DAL was revised in 2019 (rDAL) and reflects the regulatory trend of strengthening the lifecycle management of drugs, balancing the development of innovative drugs and generic drugs, and enhancing drug review and enforcement. It also represents legislative efforts to address prominent problems of the pharmaceutical industry, such as high drug prices and counterfeit and substandard drugs.

The rDAL contains a dedicated chapter on the Marketing Authorization Holder (MAH) system. Subject to approval by the NMPA, MAHs will be allowed to transfer their marketing authorizations, although it is uncertain whether the transferability of MAH will offer more flexibility in structuring cross-border transactions. In addition, the implementation of the MAH system was accompanied by a range of new requirements for the MAHs, such as establishing a quality assurance system and being responsible for the whole process including all aspects of preclinical research, clinical trials, manufacturing and distribution, post-marketing research, adverse drug reaction monitoring and reporting.

The rDAL also requires MAHs, manufacturers, distributors, and medical institutions to establish and implement drug track and trace systems. A drug pharmacovigilance system will also be established to monitor, identify, evaluate and control adverse drug reactions and other possible drug-related problems. The NMPA will issue related standards and regulations regarding drug track and trace system.

The rDAL no longer requires the certification for good clinical practice (GCP), good supply practice (GSP), and GMP. Drug manufacturers and drug distributors must still comply with current requirements and the NMPA and its local counterparts are directed to strengthen their surveillance, including through regular and continuous site inspections, to ensure their compliance.

The rDAL creates an expanded access pathway for investigational drugs under which a company sponsor of a clinical trial in China can apply to establish an expanded access treatment program for patients with life-threatening disease who otherwise do not satisfy the inclusion criteria of a clinical trial. To qualify for expanded access: (1) the drug must be used for life-threatening diseases that lack effective treatment; (2) the drug must have demonstrated its potential efficacy based on medical observations; (3) such use is in line with ethical principles; (4) such expanded use has been reviewed and approved (although the approval pathway not clear), and has obtained patients' informed consent; and (5) the drug must be used within the clinical trial institution and used on patients with similar conditions.

The rDAL also significantly increases and expands penalties for violations. Depending on various types of violations, the DAL imposes different penalties, including warnings, confiscation of illegal gains, fines of up to 5 million RMB (about $725,000) or up to 30 times of illegal gains, revocation of required business and operating licenses, certificates or approval documents for drugs, suspension of business, temporary (10 years) or permanent debarment of companies, institutions and responsible persons, and criminal liabilities in the case of serious violations.

There are still uncertainties with respect to the interpretation and implementation of the rDAL. We plan to monitor the implementation of the rDAL in China.

Regulatory Authorities and Recent Government Reorganization

In China, the NMPA is the primary regulator for pharmaceutical products and businesses. The agency was formed from the prior China Food and Drug Administration (CFDA) in 2018 as part of a complete government reorganization. The NMPA is no longer an independent agency and its parent agency is now the newly formed State Administration of Market Regulation (SAMR), into which agencies responsible for, among other areas, consumer protection, advertising, anticorruption, antitrust, fair competition and intellectual property have been merged.

Like the CFDA, the NMPA is still the chief drug regulatory agency and implements the same laws, regulations, rules, and guidelines as the CFDA. The agency regulates almost all of the key stages of the lifecycle 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 Center for Drug Evaluation (CDE), which remains under the NMPA, conducts the technical evaluation of each drug and biologic application for safety and efficacy.

The National Health Commission (NHC), formerly known as Ministry of Health (MOH) and National Health and Family Planning Commission (NHFPC), 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. Furthermore, the NHC and its local counterparts also oversee and organize public medical institutions' centralized bidding and procurement process for pharmaceutical products.. This is the primary way that public hospitals and their internal pharmacies procure drugs and the NHC plays a significant role in drug reimbursement.

Pre-Clinical and Clinical Development

The NMPA requires preclinical data to support registration applications for new drugs, which includes safety assessment studies that meet the GLP standards, issued in 2003 and amended in 2017. The rDAL requires the NMPA to accredit GLP labs, and that nonclinical studies of chemical drug substances and preparations and biologics that are not yet marketed in China be conducted in GLP-certified labs. There are no approvals required from the NMPA to conduct preclinical studies.

Registration Categories

An applicant will need to determine the registration category for its drug candidate, prior to engaging with the NMPA on research and development and approval, 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 innovative or generic drugs that have already been marketed abroad but are not yet approved in China (i.e., imported drugs).

The categories are similar for therapeutic biologics, with Category 1 for new and innovative biologics that have not been approved inside or outside of China. Biosimilars are under Category 3. KSI-301 is classified as Category 1 based on the defined registration category by the NMPA.

Expedited Programs – Priority Evaluation and Approval Programs to Encourage Innovation

The NMPA 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. The NMPA's Drug Registration Rules effective from July 1, 2020 (DRR) provides certain categories of drugs that may be eligible for priority status. 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 NMPA 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 for the purpose of seeking marketing approvals must be approved by the NMPA and conducted at hospitals satisfying GCP requirements. 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 (IMCT). Domestically manufactured drugs are not subject to foreign approval requirements, and in contrast to prior practice, the NMPA has decided to permit those drugs to conduct development via an IMCT as well.

The rDAL has now also adopted an implied approval system for clinical trials of new drugs. Trials can proceed if after 60 business days, the applicant has not received any objections from the CDE, as opposed to the lengthier previous clinical trial pre-approval process in which the applicant had to wait for affirmative approval. In addition, by abolishing the GCP accreditation system, the rDAL also expanded the number of trial sites and simplified the notification procedure followed by trial sites.

Clinical Trial Register

Clinical trials conducted in China must be registered and published through the Drug Clinical Trial Information Platform (http://www.chinadrugtrials.org.cn). Applicants are required to pre-register the trial information within one month after trial approval to obtain the unique trial registration number and to complete registration of certain information before the first subject is enrolled. If the foregoing pre-registration and registration is not obtained within one year after obtaining the clinical trial approval, the applicant shall submit an explanation, and if the procedure is not completed within three years, the clinical trial approval automatically expires.

Human Genetic Resources Regulation

The Regulation on the Administration of Human Genetic Resources (HGR Regulation) became effective on July 1, 2019. The HGR Regulation applies to all human genetic resources (HGR)-related activities for R&D purposes, including sampling, biobanking, use of HGR materials and associated data in China, and the provision or sharing of such materials or data with foreign parties.

The HGR Regulation applies to foreign parties, including foreign entities and entities established or controlled by foreign entities and individuals. Such foreign parties seeking access to China's HGRs for scientific research, including clinical trials intended to support marketing approval of drugs and medical devices in China, must engage in collaborations with Chinese parties, such as Chinese hospitals. The HGR Regulation prohibits foreign parties from independently sampling or biobanking any China HGR in China and requires approval for the sampling of certain HGR and biobanking of all HGR by Chinese parties. Any cross-border transfer of the HGR materials, either under an international collaboration or as a direct export, must be on an as-needed basis and requires approval. In addition, providing HGR data to foreign parties requires a record filing.

The HGR Regulation retains the provision in the Interim Measures for the Administration of Human Genetic Resources issued in 1998 (the Interim Measures) that parties should jointly apply for and own the patent rights arising from the results generated from international collaborations that utilize China HGR. Subject to approval, the parties may contractually agree on how to dispose of their patent rights and non-patent proprietary rights arising from the collaboration. As the joint ownership requirement is rather broad, it is unclear how this requirement will be implemented in practice.

The HGR Regulation also significantly increases and expands penalties for various violations, including warnings, disgorgement of illegal gains, confiscation of illegal HGR, fines up to 10 million RMB($1,450,000) or 5-10 times of illegal gains in the event such illegal gains exceed 1 million RMB ($145,000), and temporary (1-5 years) or permanent debarment of companies, institutions and responsible persons from future HGR projects regulated by the HGR Regulation.

Clinical Trial Process and Good Clinical Practices

As in other parts of the world, clinical trials in China typically 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 a drug registration application. The NMPA requires that the different phases of clinical trials in China receive ethics committee approval and comply with GCP. The NMPA conducts inspections on clinical trials conducted in China to assess GCP compliance and may refuse to approve the drug if it finds substantial issues in the trials. In addition, upon granting the drug registration certificate, NMPA may, at its sole discretion, require a Phase 4 trial to be conducted by MAH within a specified period of time so as to further monitor and obtain safety and efficacy data of the drug.

Pursuant to GCP, sponsors of clinical trials are responsible for proper packaging and labeling of drugs used for clinical trials, including that investigational drugs shall be consistent with the control drug or placebo in appearance, odor, packaging, labeling, and certain other features in double-blinded clinical trials. Pharmaceutical packaging must comply with national and professional standards or obtain approval from the provincial administration for medical products or bureau of standards if these standards are not available and need to be developed and implemented by the sponsors. Changes in such approved packaging standards need to be re-approved. Drugs of which the packaging standards are not approved shall not be released or marketed in China, except for those specifically supplied to the military.

Acceptance of Foreign Clinical Trial Studies

The NMPA may be flexible on the requirements of trials and data generated in China, dependent on the drug and the existing data. The NMPA has granted waivers for all or part of trials and has stated that it will accept data generated abroad (even if not part of a global study), including early phase data, that meets its requirements. In 2018, the NMPA issued the Technical Guidance Principles on Accepting Foreign Drug Clinical Trial Data (the Guidance Principles), as one of the implementing rules for the Opinions on Deepening the Reform of the Evaluation and Approval Systems and Encouraging Innovation on Drugs and Medical Devices (the Innovation Opinion). According to the Guidance Principles, data from foreign clinical trials must meet authenticity, completeness and accuracy requirements and such data must be obtained in compliance with the relevant requirements under the GCP of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Sponsors must be attentive to ethnic differences in the subject population that could be potentially meaningful.

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 domestically manufactured drugs, NDA sponsors must submit data derived from the submitted drugs in support of their approval. Under the rDAL, upon approval of the registration application, the NMPA will issue a drug registration certificate to the applicant which is in fact the marketing approval of the drug, and the applicant is no longer required to be equipped with relevant manufacturing capability.

Manufacturing and Distribution

All facilities that manufacture drugs in China must receive a drug manufacturing license with an appropriate "scope of manufacturing" from the local drug regulatory authority. This license must be renewed every five years, and the manufacturing facility is also required to be in compliance with GMP.

New Drug Monitoring Period

Previously, new varieties of domestically produced drugs approved under Categories 1 or 2 in China could be placed under a monitoring period for three to five years. Category 1 innovative drugs were monitored for five years. During the monitoring period, the NMPA would not approve another CTA from another applicant for the same type of drug, except if another sponsor had an approved CTA at the time that the monitoring period was initiated, it could proceed with its trial and once approved become another drug that was part of the monitoring period. The DRR has abolished these new drug monitoring period programs; however, drugs that had been placed under a monitoring period before the DRR took effect are still entitled to exclusivity before the monitoring periods end.

Post-Marketing Surveillance

Under the rDAL, the MAH of a drug is ultimately 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 the MAH with any product recalls. An MAH for a drug that is currently under the new drug monitoring period must 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 expressly 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.

Regulatory Intellectual Property Protections

In January 2020, the United States and China signed the Economic and Trade Agreement Between the United States of America and the PRC (the Trade Agreement), in which, among other things, China agreed to provide effective protection and enforcement of pharmaceutical-related intellectual property rights, such as patents and undisclosed test or other data submitted as a condition of marketing approval. These provisions of the Trade Agreement will need to be implemented in China. In October 2020, amendments to the PRC Patent Law (the Amended PRC Patent Law) were adopted, effective June 1, 2021, which contains both patent term extension and a mechanism for early resolution of patent disputes, that may be comparable to patent linkage in the United States. There is uncertainty around the scope and implementation of the patent term extension and the early resolution mechanism as the provisions are unclear and/or remain subject to the approval of implementing regulations that are still in draft form or have not yet been proposed.

Regulatory Data Protection

The Innovation Opinion provided a foundation for regulatory data protection to protect innovative drugs and will be available for undisclosed clinical trial data of drugs within the following categories: innovative drugs, innovative therapeutic biologics, drugs that treat orphan diseases, pediatric drugs, and drugs for which there has been a successful patent challenge. According to the Trade Agreement, China has committed to providing for effective protection of undisclosed clinical trial or other data submitted as a condition of marketing approval.

The NMPA has published draft regulations for public comment that would set regulatory data protection for innovative small molecule drugs at six years and for innovative therapeutic biologics at 12 years; pediatric and orphan drugs would receive six years to run concurrently from their approval dates. Full terms of protection would require reliance on local trials or sites of multi-center trials in China and simultaneous submissions of marketing applications in China and other countries. Submissions in China that are up to six years later than those abroad would result in the term being reduced to 1-5 years and submissions over six years later in China may not receive protection.

Patent Linkage

The Innovation Opinion also established the basic elements of a patent linkage system to protect innovators. A follow-on applicant would be required to identify patents that are relevant to its application and notify those relevant patent right holders (including, innovators) within a specified period after filing an application, permitting the patent holders the ability to protect their rights. The system will require that the NMPA continue to review the potentially infringing follow-on application during any lawsuit by the innovator and that the NMPA may not approve the follow-on application pending resolution of the patent litigation in favor of the follow-on application or for a specified period of time, whichever is shorter. Similarly, the Trade Agreement also adopted certain elements of a patent linkage system (notice to the patent right holder of the follow-on application, time and opportunity for that right holder to sue or to seek expeditious remedies, obtain a timely resolution of the patent dispute) but did not explicitly mention a stay of marketing approval of the follow-on application.

The Amended PRC Patent Law provides a cause of action to allow a patent holder to initiate a declarative action during the regulatory review process of a drug to determine whether the drug falls within the patent scope, that may be comparable to the patent linkage system in the United States. There is uncertainty around the scope and implementation of the early resolution mechanism as the provisions are unclear and/or remain subject to the approval of implementing regulations that are still in draft form or have not yet been proposed.

Patent Term Extension

In early 2019, pursuant to the Innovation Opinion, the National People's Congress issued a proposal for patent term extension as part of a proposed amendment to the Patent Law. The Amended PRC Patent Law provides that the China National Intellectual Property Administration shall provide patent term extension, similar to the United States, for the patent term lost during the regulatory review process of a new drug upon the patent holder's request. The extended term shall not exceed five years, and the total patent term after market entry of the new drug shall not exceed 14 years. The Trade Agreement also provides for patent term extension to compensate for unreasonable delay that occurs during pharmaceutical product marketing approvals. There is uncertainty around the scope and implementation of the patent term extension as the provisions are unclear and/or remain subject to the approval of implementing regulations that are still in draft form or have not yet been proposed.

Other PRC national- and provincial-level laws and regulations

Pharmaceutical companies operating in China 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 patient medical information and the circumstances under which patient medical information may be released for inclusion in our information systems or released by us to third parties. 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 working 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 HHS 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. CMS has 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, 2020, we were the assignee of record for approximately five U.S. issued patents, and approximately 13 U.S. pending patent applications directed to certain of our proprietary technology, inventions, and improvements and our most advanced product candidates, as well as 28 patents issued in jurisdictions outside of the United States and 66 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, JP Patent No. 6754749, 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, EP Patent No. 3254678, CN Patent No. ZL201080062252.7, HK Patent No. 1247828, IN Patent No. 319269, JP Patent No. 5760007, JP Patent No. 5990629, JP Patent No. 6416832, JP Patent No. 6777706, MX Patent No. 346423, MX Patent No. 374020, 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 10,702,608, US Appl. No. 16/781869, EP Patent No. 3041513, JP Patent No. 6463361, JP Patent No. 6732056, and foreign applications in certain jurisdictions claiming priority to PCT/US2014/054622	12/21/2034	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
US Appl. No. 17/066856 and PCT Application No. PCT/US2020/055074	10/9/2040	Representative claims include method of treating an eye disorder using the antibody 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 34 trademark applications. These include two applications that have matured to registration in the United States. One application has been abandoned in the United States. Sixteen of our applications have matured to registration, of which ten are in China, and one is in each of Canada, the European Union, Japan, Singapore, Switzerland and the United Kingdom. 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.

Human Capital Management

As of February 19, 2021, we had 72 employees worldwide, of whom 8 were based outside of the U.S. Of these employees, 55 employees were engaged in or support research, development and clinical activities, 19 of whom hold a Ph.D. degree or M.D. (or equivalent) degree. None of our employees are subject to a collective bargaining agreement. Given our expanding operations and need to further grow our headcount to support our business, we continually assess employee turnover, recruitment initiatives, compensation and benefits programs, safety in performing critical laboratory work, diversity and other matters relevant to human capital management, and we review results with our Board of Directors on a periodic basis. We aim to offer competitive compensation (including salary, incentive bonus, and equity) and benefits packages in each of our locations and in each of employee groups at each level around the globe as assessed with internal and external benchmarking data. We aim to build a pipeline for talent to create more opportunities for workplace diversity and to support greater representation within the Company.

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.

Additional Information

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. In addition, the SEC maintains a website at www.sec.gov that contains reports, proxy and information statements, and other information regarding issuers that file electronically with 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 the Discovery, Development and Commercialization of Our Product Candidates

Our prospects are heavily dependent on our KSI-301 product candidate, which is currently in clinical development for multiple indications.

KSI-301 is our only product candidate currently in clinical trials. It may be years before a 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 1/1b clinical trial results for KSI-301 in the respective indications are not necessarily predictive of the results of our ongoing or future discovery programs or any future preclinical or 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 or unobserved adverse events as more patients are treated with KSI-301 and followed for longer periods of time.

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 receive regulatory approval in one or more of our four planned key clinical indications 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 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, China National Medical Products Administration, or NMPA, 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 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, NMPA or any other regulatory authority concerns about risk to patients of the technology broadly; or if the FDA, EMA, NMPA 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, NMPA 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, NMPA 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, NMPA 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, NMPA 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 are studying 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, as attributable to molar dose. 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 REMS 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 effects of health epidemics, including the ongoing COVID-19 pandemic and the resulting shelter-in-place, travel or similar restrictions;
- 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, DME/DR, and RVO. 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, DME/DR, and RVO. These drugs are well established therapies and are widely accepted by physicians, patients and third-party payors, which may make it difficult to educate these parties on the benefits of switching 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, AbbVie/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, NMPA 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. For example, the effects of health epidemics, including the ongoing COVID-19 pandemic and the resulting shelter-in-place, travel or similar restrictions may impact the timing of clinical resupply facing and BLA facing manufacturing activities.

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, NMPA and foreign regulatory authority approval processes and continuous oversight. We will need to contract with manufacturers who can meet all applicable FDA, EMA, NMPA 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, NMPA 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, NMPA 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, NMPA or other regulatory agencies;
- product labeling or product insert requirements of the FDA, EMA, NMPA 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, NMPA 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 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, NMPA 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, NMPA 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, NMPA or comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA, NMPA 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, NMPA 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, NMPA 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 a BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA, EMA, NMPA 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, NMPA 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, NMPA 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, NMPA 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, NMPA 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, NMPA 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 NMPA 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, NMPA 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 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 REMS), 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, NMPA 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 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the 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 several 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 eliminated 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 Act. 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. The United States Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. Although the United States Supreme Court has yet ruled on the constitutionality of the ACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how the United States Supreme Court ruling, other such litigation and the healthcare reform measures of the Biden administration 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 2030 unless additional Congressional action is taken. However, COVID-19 relief support legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2021. 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 included 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. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. 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. On July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals. The FDA also released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. 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. Further, it is possible that additional governmental action is taken in response to the ongoing COVID-19 pandemic.

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, NMPA and other comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA, EMA, NMPA 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 and their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information as well as their covered subcontractors, 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- Beginning in 2022, applicable manufacturers also will be required to report such information related to payments or other transfers of value made to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year;
- 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 foreign laws and regulations apply to the collection, use, retention, protection, disclosure and transfer 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's General Data Protection Regulation, or GDPR, which took effect on May 25, 2018, imposes stringent data protection requirements and provides for penalties for noncompliance that can include bans on processing personal data and fines of up to the greater of 20 million euros or four percent of worldwide annual revenues. The GDPR requires organizations to give detailed disclosures about how they collect, use and share personal information; in most cases, obtain explicit consent to process sensitive personal information, such as health or genetic information; contractually require vendors to meet data protection requirements; maintain adequate data security measures; notify regulators and affected individuals of certain data breaches; meet extensive privacy governance and documentation requirements; and honor individuals' data protection rights, including their rights to access, correct and delete their personal information.

European data protection laws, including the GDPR, also restrict the transfer of personal information from Europe, including the European Economic Area, the United Kingdom and Switzerland, to the U.S. and most other countries unless the parties to the transfer have implemented specific safeguards to protect the transferred personal information. One of the primary safeguards allowing U.S. companies to import personal information from Europe has been certification to the EU-U.S. Privacy Shield and Swiss-U.S. Privacy Shield frameworks administered by the U.S. Department of Commerce. However, the Court of Justice of the European Union adopted a decision in July 2020 invalidating the EU-U.S. Privacy Shield. The same decision also raised questions about whether one of the primary alternatives to the EU-U.S. Privacy Shield, namely, the European Commission's Standard Contractual Clauses, can lawfully be used for personal information transfers from Europe to the U.S. or most other countries. Authorities in Switzerland also have issued guidance raising similar questions about the Swiss-U.S. Privacy Shield and the Standard Contractual Clauses. At present, there are few, if any, viable alternatives to the EU-U.S. Privacy Shield, the Swiss-U.S. Privacy Shield and the Standard Contractual Clauses. Although we and third party service providers rely primarily on individuals' explicit consent to transfer certain information from Europe to the U.S. and other countries, in certain cases we and third parties we work with have relied on the EU-U.S. Privacy Shield and the Standard Contractual Clauses. If we are unable to rely on explicit consent to transfer individuals' personal information from Europe, which can be revoked, or implement other valid compliance solutions, we may face increased exposure to fines under European data protection laws as well as bans on processing personal information from Europe. Inability to import personal information from Europe may also impact our operations in the European Economic Area and Switzerland and require us to incur significant costs to increase our data processing capabilities in Europe.

In addition, it is unclear whether the transfer of personal information from the EU to the United Kingdom will continue to remain lawful under the GDPR in light of Brexit. Pursuant to a post-Brexit trade deal between the United Kingdom and the EU, transfers of personal information from the European Economic Area to the United Kingdom are not considered restricted transfers under the GDPR for a period of up to six months from January 1, 2021. However, unless the EU Commission makes an adequacy finding with respect to the United Kingdom before the end of that period, the United Kingdom will be considered a "third country" under the GDPR and transfers of European personal information to the United Kingdom will require an approved compliance mechanism to render such transfers lawful under the GDPR. Although the United Kingdom's primary data protection legislation is designed to be consistent with the GDPR, uncertainty remains regarding how data transfers to and from the United Kingdom will be regulated after Brexit. Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of delivering our services and operating our business.

Privacy laws in the U.S. are also increasingly complex and changing rapidly. For example, the California legislature enacted the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020. The CCPA requires covered companies to provide new disclosures to California residents, and honor their requests to access, delete and opt-out of certain sharing of their personal information. The CCPA provides for civil penalties for violations. Since the enactment of the CCPA, new privacy and data security laws have been proposed in more than half of the states and in the U.S. Congress, reflecting a trend toward more stringent privacy legislation in the U.S. The CCPA itself will expand substantially as a result of California voters approving a November 2020 ballot measure that adopted the California Privacy Rights Act of 2020, or CPRA, which will, among other things, create a new administrative agency to implement and enforce California's privacy laws effective January 1, 2023. While certain clinical trial activities are exempt from the CCPA's requirements, other personal information that we handle may be subject to the CCPA, which may increase our compliance costs, exposure to regulatory enforcement action and other liabilities.

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 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 and bans on processing personal information, 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 UK 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" and "KODIAK SCIENCES" in the United States. 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 cease and desist letters to two companies and filed a trademark opposition proceeding against one company. 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 U.S. operations at our facilities 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 February 19, 2021, we had 72 employees, all of whom were full-time. As our development plans and strategies develop, and as we continue 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.

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 a cybersecurity incident that could harm our business.

In the course of our business, we collect, store and transmit proprietary, confidential and sensitive information, including personal information. The information and data processed and stored in our technology systems, and those of our research collaborators, CROs, contractors, consultants, and other third parties on which we depend to operate our business, may be vulnerable to security breaches, loss, damage, corruption, unauthorized access, use or disclosure, or misappropriation. Such incidents may also result from errors or malfeasance by our personnel or the personnel of the third parties with which we work, malware, viruses, software vulnerabilities, hacking, denial of service attacks, social engineering (including phishing), ransomware, credential stuffing or other cyberattacks, including attacks by state-sponsored organizations or sophisticated groups of hackers.

While we have developed systems and processes designed to protect the integrity, confidentiality and security of the confidential and personal information under our control, we cannot assure you that our security measures or those of the third parties we depend on will be effective in preventing cybersecurity incidents. There are many different and rapidly evolving cybercrime and hacking techniques, and we may be unable to anticipate attempted security breaches, identify them before our information is exploited, or react in a timely manner.

Additionally, as a result of the ongoing COVID-19 pandemic, certain functional areas of our workforce remain in a remote work environment and outside of our corporate network security protection boundaries, which imposes additional risks to our business, including increased risk of industrial espionage, phishing and other cybersecurity attacks, and unauthorized dissemination of proprietary or confidential information, any of which could have a material adverse effect on our business.

Although to our knowledge, we have not experienced a material system failure or cybersecurity incident 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.

Cybersecurity incidents and any unauthorized access or disclosure of our information or intellectual property could also compromise our intellectual property, expose sensitive business information, expose the personal information of our employees, require us to incur significant remediation costs, disrupt key business operations and divert attention of management and key information technology resources. Such incidents could also subject us to significant liability, harm our competitive position and delay the further development and commercialization of our product candidates.

We cannot be certain that our insurance coverage will be adequate for cybersecurity liabilities, will continue to be available to us on economically reasonable terms, or at all, or that any insurer will not deny coverage as to any future claim. The successful assertion of one or more large claims against us that exceed available insurance coverage, or the occurrence of changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could adversely affect our reputation, business, financial condition and results of operations.

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 connection to the ongoing COVID-19 pandemic, the various quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases, could adversely affect our business, financial condition or results of operations by limiting our ability to manufacture product, 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 ongoing COVID-19 pandemic 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 COVID-19 pandemic and the actions to contain the coronavirus or treat its impact, among others.

Our operations are located at facilities in Palo Alto, California and Switzerland. 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.

Following the result of a referendum in 2016, the United Kingdom, or UK, left the European Union, or EU, on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the UK and the

EU, the UK was subject to a transition period until December 31, 2020, or the Transition Period, during which EU rules continued to apply. A trade and cooperation agreement, or the Trade and Cooperation Agreement, that outlines the future trading relationship between the United Kingdom and the European Union was agreed in December 2020.

Since a significant proportion of the regulatory framework in the UK, is derived from EU directives and regulations, Brexit may have a material impact upon the regulatory regime applicable to our operations, including with respect to our ability to obtain regulatory approvals of our product candidates in the EU. For example, Great Britain is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the European Medicines Agency, or EMA, and a separate marketing authorization will be required to market our product candidates in Great Britain. It is currently unclear whether the Medicines & Healthcare products Regulatory Agency, or MHRA, in the UK is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Any delay in obtaining, or an inability to obtain, any marketing approvals, would delay or prevent us from commercializing our product candidates in the UK or the EU and restrict our ability to generate revenue and achieve and sustain profitability.

While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the UK and the EU there may be additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period. Further, should the UK diverge from the EU from a regulatory perspective in relation to medicinal products, tariffs could be put into place in the future. We could therefore, both now and in the future, face significant additional expenses (when compared to the position prior to the end of the Transition Period) to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the UK It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the EU.

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

Our business is currently affected and could be materially and adversely affected in the future by the effects of disease outbreaks, epidemics and pandemics, including the ongoing effects of the COVID-19 pandemic. The COVID-19 pandemic continues to impact our business and could materially and adversely affect our operations, as well as the business or operations of our manufacturers, CROs or other third parties with whom we conduct business.

Our business could be materially and 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 March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. In response, we delayed initiation of the next set of KSI-301 pivotal studies by one quarter from June to September 2020 in order to assess how best to minimize the impact of COVID-19 on clinical trial conduct. We implemented and continue to implement various enhancements into our ongoing study execution to help ensure the safety of patients, physicians, study site staff and Kodiak operations team members during the ongoing COVID-19 pandemic, including the use of remote study monitoring. To date, we have observed minimal disruption resulting from the evolving effects of the COVID-19 pandemic, and we and our key clinical and manufacturing partners have been able to continue to advance our operations. during the pandemic towards achieving our "2022 Vision."

The COVID-19 pandemic continues to unfold and we will continue to monitor our operations in response. We continue to observe government recommendations and may elect to temporarily close our office and/or laboratory space to protect our employees. Quarantines for COVID-19 or other viruses could impact personnel at third party manufacturing facilities, or the availability or cost of materials, which would disrupt our supply chain. While many of these materials may be obtained by more than one supplier, 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 materially and adversely affected by the COVID-19 outbreak in the future. Site initiation and patient enrollment may be further 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, may 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 and in-person monitoring of study data quality. 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 and/or missed visit rates if these patients are adversely affected by the COVID-19

outbreak. To date, we are seeing low levels of patient missed visits (<5%). Additionally, the pandemic could result in delayed recruitment in some or all of our clinical studies that are currently recruiting patients, for example if as a consequence of the pandemic patients are not willing to be seen by their physician as frequently as our study protocols require.

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.

The extent to which the risks and evolving effects of the COVID-19 pandemic impact our business and our clinical development and regulatory efforts will depend on future developments that are highly uncertain and cannot be predicted with confidence, such as the ultimate duration and severity of the pandemic, government actions, such as travel restrictions, quarantines and social distancing requirements in the U.S. and in other countries, business closures or business disruptions and the effectiveness of actions taken in the U.S. and in other countries to contain and treat the disease, including the effectiveness and timing of vaccine programs in the U.S. and worldwide. The COVID-19 pandemic may also have the effect of heightening many of the other risks described in this "Risk Factors" section.

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

As of December 31, 2020, the Company had $50.1 million of federal and $171.0 million of state net operating loss, or NOLs, that may be available to offset future taxable income. A portion of the federal NOL carryforwards begin to expire in 2035 and the state NOL carryforwards begin to expire in 2035, if not utilized. 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 NOL 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.

The Tax Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act") enacted in March 2020, among other things, includes changes to U.S. federal tax rates and the rules governing NOL carryforwards. Federal NOLs arising in tax years beginning after December 31, 2017 are permitted to be carried forward indefinitely, but carryback of such NOLs is generally permitted to the prior five taxable years only for NOLs arising in taxable years beginning before 2021. In addition, under the Tax Act, as modified by the CARES Act, the deductibility of federal NOLs incurred in taxable years beginning after December 31, 2017 is limited in taxable years beginning after December 31, 2020. For state income tax purposes, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California recently imposed limits on the usability of California state net operating losses to offset taxable income in tax years beginning after 2019 and before 2023. The new limitations on use of NOLs may significantly impact our ability to utilize our NOLs to offset taxable income in the future.

Risks Related to Our Business, Financial Condition and Capital Requirements

We are in the 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 committed to researching, developing and commercializing transformative therapeutics to treat 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. Except for 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 $133.1 million, $47.4 million and $41.4 million for the years ended December 31, 2020, 2019 and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of $291.2 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 current and any future product candidates;
- change or add additional contract manufacturers or suppliers;
- seek regulatory approvals and marketing authorizations for our product candidates, including KSI-301;
- 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.

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 funded our operations primarily through the sale of equity securities. Developing our product candidates is expensive, and we expect to continue to increase our spending as we conduct the Phase 3 clinical trials for our KSI-301 product candidate. 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, 2020, we had cash, cash equivalents and marketable securities of $969.0 million. 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. For example, the ongoing COVID-19 pandemic has significantly disrupted world financial markets, negatively impacted US market conditions, increased the volatility of trading prices for biopharmaceutical companies, and may reduce opportunities for us to seek out additional funding when needed. We currently 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 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, including fluctuations attributable to the ongoing COVID-19 pandemic and other unforeseeable circumstances; 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.

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.

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. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

General Risk Factors

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.

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. Furthermore, 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. 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. Any failure to maintain effective internal controls could also have an adverse effect on our business, financial position and results of operations.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our corporate offices are located in Palo Alto, California, where we lease approximately 155,000 square feet of office, research and development, engineering and laboratory space pursuant to lease agreements commending in June 2020. The initial lease term for 1200 Page Mill Road is 6.5 years and 13 years for 1250 Page Mill Road.

We continue to lease office and laboratory space at 2631 Hanover Street in Palo Alto, California, which commenced in January 2013. 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. The facilities in Palo Alto, California houses substantially all of our personnel.

In April 2020, we entered into a lease agreement for office and laboratory space at Rottenstrasse 5 in Visp, Switzerland. The space is approximately 1,000 square meters. The initial lease term is 5 years, with automatic renewals every 5 years for a maximum lease term of 15 years.

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 trades on the Nasdaq Global Market under the trading symbol "KOD".

Holders of Common Stock

As of February 19, 2021, there were approximately 29 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.

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,				
	2020	2019	2018	2017	2016
	(in thousands, except share and per share data)				
Consolidated Statements of Operations Data:					
Operating expenses					
Research and development	$ 107,389	$ 37,506	$ 18,793	$ 22,022	$ 14,053
General and administrative	28,618	11,684	7,581	3,499	3,098
Total operating expenses	136,007	49,190	26,374	25,521	17,151
Loss from operations	(136,007)	(49,190)	(26,374)	(25,521)	(17,151)
Interest income	2,902	1,568	617	—	—
Interest expense	(25)	(8)	(5,519)	(1,185)	(6)
Other income (expense), net	34	265	(4,688)	(1,230)	25
Loss on extinguishment of debt	—	—	(5,479)	—	—
Net loss	$ (133,096)	$ (47,365)	$ (41,443)	$ (27,936)	$ (17,132)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.91)	$ (1.25)	$ (2.77)	$ (3.72)	$ (2.38)
Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted	45,741,845	37,853,616	14,976,515	7,515,336	7,211,360

	As of December 31,				
	2020	2019	2018	2017	2016
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 968,974	$ 348,177	$ 88,254	$ 1,395	$ 9,622
Working capital	940,583	327,519	85,623	(7,563)	7,682
Total assets	1,067,347	358,866	92,189	3,244	12,114
Total liabilities	206,596	13,507	5,356	21,965	3,180
Accumulated deficit	(291,227)	(158,131)	(110,766)	(69,323)	(41,387)
Total stockholders' equity (deficit)	860,751	345,359	86,833	(68,738)	(41,083)

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

Kodiak Sciences (we or the Company) is a biopharmaceutical company committed to researching, developing and commercializing transformative therapeutics to treat high prevalence retinal diseases in the United States and additional international markets. We are bringing new science to the design and development of next generation retinal medicines. Our ABC Platform™ uses molecular engineering to merge the fields of antibody-based and chemistry-based therapies and is at the core of Kodiak's discovery engine. Our lead product candidate, KSI-301, is a novel anti-VEGF antibody biopolymer conjugate generating compelling data in treatment naïve patients with retinal vascular diseases. Our pivotal program is exploring KSI-301 in wAMD, DME, RVO and non-proliferative diabetic retinopathy. Our hope with KSI-301 is to meaningfully change the treatment paradigm for all patients with retinal vascular diseases. Our pipeline, including product candidates KSI-501 and KSI-601, aims to bring a similar ethos of drug development to other unmet needs in retina such as dry AMD and glaucoma.

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

Product Candidates

KSI-301

Kodiak's lead product candidate, KSI-301, is a novel anti-VEGF antibody biopolymer conjugate being developed for the treatment of retinal vascular diseases including age-related macular degeneration, a leading cause of blindness in elderly patients, and diabetic eye diseases, a leading cause of blindness in working-age patients. We continue to observe promising safety, efficacy and clinical durability data through 52-weeks in our ongoing Phase 1b study of KSI-301 in treatment-naïve patients with wet AMD, DME or RVO. Based on the encouraging data from our Phase 1b study, we have expanded the KSI-301 clinical pivotal program in the third quarter of 2020, and we have entered into the manufacturing-related commitments necessary for KSI-301's commercial scale-up and BLA submission. We successfully recruited patients into both of our paired pivotal studies in DME (GLEAM and GLIMMER) and into our pivotal study in RVO (BEACON) in the third quarter of 2020. The pivotal study for wet AMD (DAZZLE) began recruiting in the third quarter of 2019 and completed patient enrollment in the fourth quarter of 2020. Approximately 2,000 KSI-301 injections have been administered to approximately 500 patients, representing approximately 350 patient-years of exposure. We believe the intersection of these clinical and manufacturing activities remain on track per our "2022 Vision" to submit a single BLA for wet AMD, DME and RVO in calendar year 2022.

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.

Our Pre-Clinical Pipeline

Kodiak has leveraged its ABC Platform to build a pipeline of product candidates in various stages of development including KSI-501, our bispecific anti-IL-6/VEGF biopolymer conjugate for the treatment of neovascular retinal diseases with an inflammatory component, and we are expanding our early research pipeline to include ABC Platform based triplet inhibitors for multifactorial retinal diseases such as dry AMD and glaucoma. The ABC Platform and KSI-301 were developed at Kodiak, and we own worldwide rights to these assets.

Further details of our ongoing KSI-301 Phase 1b trial, our accelerating development strategy, our manufacturing-related commitments, and our pipeline of retinal medicines based on the ABC Platform are described in the "Business" section above.

Financial Operations Overview

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. In November 2020, we completed a second 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 $133.1 million, $47.4 million and $41.4 million for the years ended December 31, 2020, 2019 and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of $291.2 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.

In November 2020, we filed an automatic shelf registration statement (File No. 333-250109), which became effective upon filing. The shelf registration statement allows us to issue certain securities, including shares of our common stock, from time to time. In November 2020, we completed a follow-on offering pursuant to the automatic shelf registration and issued and sold 5,972,222 shares of the Company's common stock, including the underwriters' full exercise of their over-allotment option, at a price to the public of $108.00 per share under our shelf registration statement. The gross proceeds from this offering were $645.0 million, resulting in aggregate net proceeds of $612.0 million after deducting underwriting discounts and commissions and other offering costs.

As of December 31, 2020, we had cash, cash equivalents and marketable securities of $969.0 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 conduct our Phase 3 clinical 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.

Other Income (Expense), Net

Other income (expense), net consists primarily of accretion income and amortization expense on marketable debt securities net of amortized issuance costs from the liability related to the future sale of royalties to BBA in 2019.

Results of Operations

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

	Year Ended December 31,			2020 vs 2019 Change	
	2020	2019	2018	Dollar	Percent
	(in thousands, except percentages)				
Operating expenses:					
Research and development	$ 107,389	$ 37,506	$ 18,793	$ 69,883	186%
General and administrative	28,618	11,684	7,581	16,934	145%
Loss from operations	(136,007)	(49,190)	(26,374)	(86,817)	176%
Interest income	2,902	1,568	617	1,334	85%
Interest expense (includes $nil, $nil and $3,030 attributable to related parties for the years ended December 31, 2020, 2019 and 2018, respectively)	(25)	(8)	(5,519)	(17)	*
Other income (expense), net (includes $49, $nil, and $2,736 expenses attributable to related parties for the years ended December 31, 2020, 2019, and 2018, respectively)	34	265	(4,688)	(231)	*
Loss on extinguishment of debt (includes $1,587 attributable to related parties for the year ended December 31, 2018)	—	—	(5,479)	-	*
Net loss	$ (133,096)	$ (47,365)	$ (41,443)	$ (85,731)	181%

* Percentage is not meaningful

Research and Development Expenses

Research and development expenses increased $69.9 million, or 186%, from the year ended December 31, 2019 to the year ended December 31, 2020.

The following table summarizes our research and development expenses:

	Year Ended December 31,			2020 vs 2019
	2020	2019	2018	Change
	(in thousands)			
ABC Platform external expenses [1]	$ 7,365	$ 2,218	$ 1,397	$ 5,147
KSI-301 program external expenses [2]	58,563	19,285	8,252	39,278
KSI-501 program external expenses [3]	1,573	1,188	—	385
Payroll and personnel expenses [4]	30,434	11,978	6,825	18,456
Other research and development expenses [5]	9,454	2,837	2,319	6,617
Total research and development expenses	$ 107,389	$ 37,506	$ 18,793	$ 69,883

(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.
(2) KSI-301 program external expenses relate 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 relate 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 $5.1 million during the year ended December 31, 2020 as compared to 2019. The increase was primarily driven by manufacturing runs to support our product candidate pipeline.

KSI-301 program external expenses increased $39.3 million during the year ended December 31, 2020 as compared to 2019, primarily due to clinical trial costs to support ongoing trials, as well as manufacturing activities for KSI-301. Our pivotal Phase 2b/3 clinical study in wAMD (DAZZLE) dosed the first patient in October 2019, and patient recruitment completed in the fourth quarter of 2020. We initiated two pivotal Phase 3 clinical studies in DME (GLEAM and GLIMMER) and one pivotal Phase 3 clinical study in RVO (BEACON) in the third quarter of 2020.

KSI-501 program external expenses increased $0.4 million during the year ended December 31, 2020 as compared to 2019, due to ongoing research and development of KSI-501.

Payroll and personnel expenses increased $18.5 million during the year ended December 31, 2020 as compared to 2019, due to increased headcount and stock-based compensation expense.

Other research and development expenses increased $6.6 million during the year ended December 31, 2020 as compared to 2019, primarily due to the allocation of lease costs for Palo Alto and Switzerland. 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 $16.9 million, or 145%, from the year ended December 31, 2020 as compared to 2019. The increase in general and administrative expenses was primarily driven by increased headcount and stock-based compensation expense as well as professional services related to consulting, legal and accounting, as well as the allocation of lease costs for Palo Alto.

Interest Income

Interest income increased $1.3 million from the year ended December 31, 2020 as compared to 2019, which was mainly attributable to interest income earned on increased cash balances from our follow-on offering in December 2019 and November 2020.

Other Income (Expense), Net

Other income (expense), net decreased $0.2 million from the year ended December 31, 2020 as compared to 2019, which was mainly attributable to issuance costs from the liability related to the future sale of royalties to BBA in December 2019.

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, 2020, we had cash, cash equivalents and marketable securities of $969.0 million.

IPO

In connection with our IPO in 2018, 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.

In November 2020, we completed a follow-on offering pursuant to the shelf registration on Form S-3 and issued and sold 5,972,222 shares of common stock at a price to the public of $108.00 per share. The gross proceeds from this offering were $645.0 million, resulting in aggregate net proceeds of $612.0 million after deducting underwriting discounts and commissions and other offering costs.

Future Funding Requirements

We have incurred net losses since our inception. For the years ended December 31, 2020, 2019 and 2018, we had net losses of $133.1 million, $47.4 million, and $41.4 million, respectively, and we expect to continue to incur additional losses in future periods. As of December 31, 2020, we had an accumulated deficit of $291.2 million.

We have based these estimates on assumptions that may prove to be wrong, and we could deplete our available capital resources sooner than we expect. Because of the risks and uncertainties associated with research, development and commercialization of product candidates, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on and could increase significantly as a result of many factors.

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.

The significant uncertainties caused by the evolving effects of the COVID-19 pandemic may also negatively impact our operations and capital resources. We and our key clinical and manufacturing partners have been able to continue to advance our operations, and we continue to monitor the impact of COVID-19 on our ability to continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. This pandemic may ultimately have a material adverse effect on our liquidity and operating plans, although we are unable to make any prediction with certainty given the spread and rapidly changing nature of the pandemic and the evolving global actions taken to contain and treat the novel coronavirus.

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,		
	2020	**2019**	**2018**
		(in thousands)	
Net cash (used in) provided by:			
Operating activities	$ (83,428)	$ (39,146)	$ (29,031)
Investing activities	$ 104,834	$ (136,998)	$ (581)
Financing activities	$ 717,377	$ 299,687	$ 116,471
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 738,783	$ 123,543	$ 86,859

Cash Flows from Operating Activities

Net cash used in operating activities was $83.4 million for year ended December 31, 2020. Cash used in operating activities was primarily driven by the increase in net loss during this period due to increased payroll and personnel expenses and manufacturing and clinical trial costs to support overall growth. Cash used in operating activities was also driven by changes in operating assets and liabilities.

Cash Flows from Investing Activities

Net cash provided by investing activities was $104.8 million for year ended December 31, 2020 and primarily related to purchases of marketable securities, net of maturities, and purchases of property and equipment.

Cash Flows from Financing Activities

Net cash provided by financing activities was $717.4 million for year ended December 31, 2020, which consisted primarily of the net proceeds from our follow-on offering, proceeds from sale of future royalties to BBA, and proceeds from the exercise of stock options.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2020 (in thousands):

	Payments Due by Period				
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	Total
Operating lease obligations	$ 4,288	$ 22,258	$ 30,512	$ 71,462	$ 128,520
Manufacturing agreements	82,576	50,939	36,261	72,523	242,299
Tenant improvement obligations	42	94	110	51	297
Other agreements	470	—	—	—	470
Total	$ 87,376	$ 73,291	$ 66,883	$ 144,036	$ 371,586

For further information, refer to Note 7 of the Notes to Consolidated Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K.

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. The impact of the ongoing COVID-19 pandemic continues to evolve. 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 accrued research and development costs are estimated based on the level of services performed, including the phase or completion of events, and contracted costs. Accrued clinical trial and related costs are estimated using data such as patient enrollment, clinical site activations or information provided by outside service providers regarding their actual costs incurred. Management determined accrual estimates through reports from and discussions with clinical personnel and outside service providers as to the progress of trials, or the services completed. 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 third parties under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other 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, or NOLs, 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.

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, 2020 which concluded no such ownership change had occurred through December 31, 2020.

As of December 31, 2020 and 2019, 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.

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 Part II, Item 8 of this Annual Report on Form 10-K.

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, 2020, we had cash, cash equivalents and marketable securities of $969.0 million, primarily invested in money market funds. As of December 31, 2019, we had cash and cash equivalents of $348.2 million, primarily invested in money market funds, overnight repurchase agreements, U.S. treasury securities, commercial paper and corporate notes. 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, 2020, the net fair value of our interest-sensitive marketable securities would have resulted in a hypothetical decline of less than $0.1 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.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Kodiak Sciences Inc. and its subsidiaries (the "Company") as of December 31, 2020 and 2019, 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, 2020, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

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 Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements 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. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's 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 generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the

company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

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

Accrued Clinical Trial and Related Costs

As described in Notes 2 and 4 to the consolidated financial statements, the Company recorded $11.1 million in accrued clinical trial and related costs as of December 31, 2020. Accrued clinical trial and related costs are estimated using data such as patient enrollment, clinical site activations or information provided by outside service providers regarding their actual costs incurred. Management determined accrual estimates through reports from and discussions with clinical personnel and outside service providers as to the progress of trials, or the services completed.

The principal considerations for our determination that performing procedures relating to accrued clinical trial and related costs is a critical audit matter are the judgment by management in evaluating the data used in developing the accrued clinical trial and related cost estimates, which in turn led to a high degree of auditor judgment and effort in performing procedures to evaluate audit evidence obtained related to patient enrollment, clinical site activations and services rendered by outside service providers used by management in developing the estimates.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to the completeness and accuracy of clinical trial accruals, including controls relating to the reliability of data used in the development of the estimates. These procedures also included, among others, (1) testing management's process for developing the estimated accrued clinical trial and related costs, (2) evaluating the appropriateness of the approach used by management to develop the estimates, (3) testing the completeness and accuracy of the data used in developing the estimates, including data related to patient enrollment, clinical site activations and services rendered by outside service providers, (4) confirming clinical costs and contracted fees with the clinical vendors on a test basis, and (5) examining clinical vendor contracts on a test basis to evaluate the completeness of costs considered in the estimates.

/s/ PricewaterhouseCoopers LLP
San Jose, California
March 1, 2021

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, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 944,396	$ 211,797
Marketable securities	24,578	124,684
Prepaid expenses and other current assets	3,031	2,749
Total current assets	972,005	339,230
Marketable securities	—	11,696
Restricted cash	6,324	140
Property and equipment, net	5,136	996
Operating lease right-of-use asset	73,672	1,790
Other assets	10,210	5,014
Total assets	$ 1,067,347	$ 358,866
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 8,646	$ 2,619
Accrued and other current liabilities	20,402	8,658
Operating lease liability	2,374	434
Total current liabilities	31,422	11,711
Operating lease liability, net of current portion	75,028	1,501
Liability related to sale of future royalties	99,890	—
Other liabilities	256	295
Total liabilities	206,596	13,507
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, 2020 and 2019	—	—
Common stock, $0.0001 par value, 490,000,000 shares authorized at December 31, 2020 and 2019; 51,112,302 and 44,413,404 shares issued and outstanding at December 31, 2020 and 2019, respectively	5	5
Additional paid-in capital	1,151,920	503,475
Accumulated other comprehensive income	53	10
Accumulated deficit	(291,227)	(158,131)
Total stockholders' equity	860,751	345,359
Total liabilities and stockholders' equity	$ 1,067,347	$ 358,866

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, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
Operating expenses			
Research and development	$ 107,389	$ 37,506	$ 18,793
General and administrative	28,618	11,684	7,581
Total operating expenses	136,007	49,190	26,374
Loss from operations	(136,007)	(49,190)	(26,374)
Interest income	2,902	1,568	617
Interest expense (includes $nil, $nil and $3,030 attributable to related parties for the years ended December 31, 2020, 2019 and 2018, respectively)	(25)	(8)	(5,519)
Other income (expense), net (includes $49, $nil, and $2,736 expenses attributable to related parties for the years ended December 31, 2020, 2019, and 2018, respectively)	34	265	(4,688)
Loss on extinguishment of debt (includes $1,587 attributable to related parties for the year ended December 31, 2018)	—	—	(5,479)
Net loss	$ (133,096)	$ (47,365)	$ (41,443)
Net loss per common share, basic and diluted	$ (2.91)	$ (1.25)	$ (2.77)
Weighted-average common shares outstanding used in computing net loss per common share, basic and diluted	45,741,845	37,853,616	14,976,515
Other comprehensive income			
Change in unrealized gains related to available-for-sale debt securities, net of tax	43	10	—
Total other comprehensive income	43	10	—
Comprehensive loss	$ (133,053)	$ (47,355)	$ (41,443)

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	Deficit	(Deficit)
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 in conection with initial public offering, net of offering costs 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 in connection with follow-on offering, net of offering costs 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
Issuance of common stock upon exercise of stock options	—	—	704,675	—	6,248	—	—	6,248
Issuance of common stock in connection with follow-on offering, net of offering costs of $32,984	—	—	5,972,222	—	612,016	—	—	612,016
Vesting of restricted stock units, net of taxes withheld	—	—	22,001	—	(487)	—	—	(487)
Stock-based compensation expense	—	—	—	—	30,668	—	—	30,668
Other comprehensive income	—	—	—	—	—	43	—	43
Net loss	—	—	—	—	—	—	(133,096)	(133,096)
Balance at December 31, 2020	—	$ —	51,112,302	$ 5	$1,151,920	$ 53	$ (291,227)	$ 860,751

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, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
Cash flows from operating activities			
Net loss	$ (133,096)	$ (47,365)	$ (41,443)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	477	538	490
Non-cash interest expense and amortization of debt discount and issuance cost	—	—	5,482
Change in fair value of redeemable convertible preferred stock warrant liability	—	—	2,700
Change in fair value of derivative instrument	—	—	1,988
Extinguishment of debt	—	—	5,479
Stock-based compensation	30,668	6,110	2,665
Amortization (accretion) of premium (discount) on marketable securities	(51)	(241)	—
Amortization of operating lease right-of-use asset	3,731	373	—
Amortization of issuance costs	49	—	—
Changes in assets and liabilities:			
Prepaid expense and other current assets	(218)	(168)	(1,995)
Other assets	(1,814)	(4,511)	—
Accounts payable	5,224	1,569	(2,323)
Accrued and other current liabilities	11,748	4,932	(2,105)
Operating lease liability	(146)	(383)	—
Other liabilities	—	—	31
Net cash used in operating activities	(83,428)	(39,146)	(29,031)
Cash flows from investing activities			
Purchase of property and equipment	(3,814)	(437)	(78)
Deposits on property and equipment	(3,184)	—	(503)
Purchases of marketable securities	(86,317)	(150,961)	—
Maturities of marketable securities	198,149	14,400	—
Net cash provided by (used in) investing activities	104,834	(136,998)	(581)
Cash flows from financing activities			
Proceeds from issuance of common stock in connection with offering, net of offering costs	612,016	297,616	83,755
Proceeds from issuance of common stock upon option exercise	6,248	2,287	49
Payments for restricted stock units, net of taxes withheld	(487)	(132)	—
Proceeds from issuance of convertible notes (includes $9,560 from related parties for the years ended December 31, 2018)	—	—	33,000
Debt issuance cost	—	—	(140)
Proceeds from sale of future royalties, net of issuance costs	99,643	—	—
Principal payments of capital lease	(5)	(48)	(108)
Principal payments of tenant improvement allowance payable	(38)	(36)	(85)
Net cash provided by financing activities	717,377	299,687	116,471
Net increase in cash, cash equivalents and restricted cash	738,783	123,543	86,859
Cash, cash equivalents and restricted cash, at beginning of year	211,937	88,394	1,535
Cash, cash equivalents and restricted cash, at end of year	$ 950,720	$ 211,937	$ 88,394
Reconciliation of cash, cash equivalents and restricted cash to consolidated balance sheets			
Cash and cash equivalents	$ 944,396	$ 211,797	$ 88,254
Restricted cash	6,324	140	140
Cash, cash equivalents and restricted cash in consolidated balance sheets	$ 950,720	$ 211,937	$ 88,394
Supplemental cash flow information:			
Cash paid for interest	$ 25	$ 8	$ 19
Supplemental disclosures of non-cash investing and financing information:			
Operating lease right-of-use asset obtained in exchange for operating lease liability	$ 75,614	$ 2,163	$ —
Purchase of property and equipment under accounts payable	$ 803	$ —	$ —
Unpaid offering costs	$ 238	$ 459	$ 205
Offering costs paid in restricted stock awards	$ —	$ —	$ 91
Derivative instrument related to convertible notes	$ —	$ —	$ 6,603

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 2018, the Company sold and issued 9,400,000 shares of common stock, including the underwriters' full exercise of their over-allotment option, at a price to the public of $10.00 per share for gross proceeds of $94.0 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.

In November 2020, the Company sold and issued 5,972,222 shares of common stock, including the underwriters' full exercise of their over-allotment option, at a price to the public of $108.00 per share for gross proceeds of $645.0 million. The aggregate net proceeds to the Company from the follow-on offering were $612.0 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 and Kodiak Sciences Valais GmbH, the Company's indirect wholly owned subsidiaries, both 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 $0.3 million, less than $0.1 million and $0.3 million for the years ended December 31, 2020, 2019 and 2018, 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. The impact of the ongoing COVID-19 pandemic continues to evolve. As a result, certain estimates and assumptions required increased judgment and carried a higher degree of variability and volatility, including but not limited to, the fair value of marketable securities, performance-based equity awards, and research and development accruals. As events continue to unfold and additional information becomes available, these estimates may change materially in future periods. Actual results could differ from those estimates.

Risk and Uncertainties

In March 2020, the World Health Organization declared a pandemic due to the global COVID-19 outbreak. The significant uncertainties caused by the ongoing COVID-19 pandemic may negatively impact the Company's operations, liquidity, and capital resources and will depend on certain evolving developments, including the duration and spread of the outbreak, regulatory and private sector responses and the impact on employees and vendors including supply chain and clinical partners, all of which are uncertain and cannot be predicted. During this pandemic, the Company continues to work closely with clinical sites towards maximal patient safety and the lowest number of missed visits and study discontinuations. The Company has taken and continues to take proactive measures to maintain the integrity of its ongoing clinical studies. Despite these efforts, the ongoing COVID-19 pandemic could significantly impact clinical trial enrollment and completion of its clinical studies. The Company will continue to monitor the COVID-19 situation and its impact on the ability to continue the development of, and seek regulatory approvals for, the Company's product candidates, and begin to commercialize any approved products.

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, 2020 and 2019, 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, 2020, and 2019, the Company had $6.3 million and $0.1 million, respectively, of long-term restricted cash deposited with a financial institution. The entire amount is held in separate bank accounts to support letter of credit agreements related to the Company's U.S. corporate offices.

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, 2020 and 2019.

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 various third parties, including clinical investigator sites, contract research organizations ("CROs") and contract manufacturing organizations ("CMOs"), to provide research and development activities. The Company's accrued research and development costs are estimated based on the level of services performed, including the phase or completion of events, and contracted costs. Accrued clinical trial and related costs are estimated using data such as patient enrollment, clinical site activations or information provided by outside service providers regarding their actual costs incurred. Management determined accrual estimates through reports from and discussions with clinical personnel and outside service providers as to the progress of trials, or the services completed. 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 third parties under these arrangements in advance of the performance of the related services are recorded as prepaid expenses or other 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.

Liability related to Sale of Future Royalties

On December 1, 2019, the Company and its subsidiary Kodiak Sciences GmbH entered into a funding agreement with Baker Bros. Advisors, LP ("BBA"), which holds more than 5% of the Company's stock, 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. Under the terms of the funding agreement, there is no obligation to repay any funding amount received, other than through the capped royalty payments on future product revenues. The Company recorded the funding amount paid by BBA as a liability on the consolidated balance sheet net of issuance costs, in accordance with ASC 730, *Research and Development*. Under ASC 730, the significant related party relationship between the Company and BBA creates an implicit obligation to repay the funding amount paid to the Company. Once royalty payments to BBA are determined to be probable and estimable, and if such amounts exceed the liability balance, the Company will impute interest to accrete the liability on a prospective basis based on such estimates. If and when the Company makes royalty payments under the funding agreement, it would reduce the liability balance at such time. Refer to Note 14.

Credit Losses – Available-for-Sale Debt Securities

For available-for-sale debt securities in an unrealized loss position, the Company will periodically assess its portfolio for impairment. The assessment first considers the intent or requirement to sell the security. If either of these criteria are met, the amortized cost basis will be written down to fair value through earnings.

If not met, the Company will evaluate whether the decline resulted from credit losses or other factors by considering the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and any adverse conditions specifically related to the security, among other factors. If this assessment indicates that a credit loss exists, the present value of cash flows expected to be collected from the security is compared to the amortized cost basis of the security. If the present value of cash flows expected to be collected is less than the amortized cost basis, a credit loss exists and an allowance for credit losses will be recorded, limited by the amount that the fair value is less than the amortized cost basis. Any impairment that has not been recorded through an allowance for credit losses is recognized in other comprehensive income or loss, as applicable.

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 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 Company assessed the impact of ASU 2016-13 on its available-for-sale debt securities and determined there were no credit losses within the portfolio requiring an allowance upon adoption. The Company adopted this new guidance as of January 1, 2020, which did not impact 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. Among the changes, entities will no longer be required to disclose the amount of and reasons for transfers between Levels 1 and 2 of the fair value hierarchy but will be required to disclose the range and weighted average used to develop significant unobservable inputs for Level 3 fair value measurements. The Company adopted this new guidance as of January 1, 2020, which did not impact 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 Company adopted this new guidance as of January 1, 2020, which did not impact its consolidated financial statements and related disclosures.

New Accounting Pronouncements Not Yet Adopted

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. This guidance is effective for fiscal years beginning after December 15, 2020, including interim periods therein, and early adoption is permitted. The Company has early adopted ASU 2019-12 in 2020; the effect was not material on the Company's financial statements.

3. Property and Equipment, net

Property and equipment, net consists of the following (in thousands):

	December 31, 2020	December 31, 2019
Leasehold improvement	$ 1,285	$ 1,265
Laboratory equipment	3,351	1,125
Furniture and fixtures	214	204
Computer hardware	31	—
Computer software	89	79
Office equipment	107	94
Construction in progress	2,229	—
Total property and equipment	7,306	2,767
Less: Accumulated depreciation	(2,170)	(1,771)
Property and equipment, net	$ 5,136	$ 996

All property and equipment are maintained in the United States and Switzerland. 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, 2020, 2019 and 2018, respectively.

4. Accrued Liabilities and Other Current Liabilities

Accrued liabilities and other current liabilities consist of the following (in thousands):

	December 31, 2020	December 31, 2019
Accrued clinical trial and related costs	$ 11,119	$ 4,056
Accrued research and development	3,082	838
Accrued salaries and benefits	5,094	3,108
Accrued legal fees	252	302
Accrued professional fees	253	195
Accrued other liabilities	602	159
Total accrued and other current liabilities	$ 20,402	$ 8,658

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, 2020			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 917,485	$ —	$ —	$ 917,485
Marketable securities:				
U.S. treasury securities	—	10,006	—	10,006
Corporate notes	—	14,572	—	14,572
Total	$ 917,485	$ 24,578	$ —	$ 942,063

	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

As of December 31, 2020, the fair value of the liability related to sale of future royalties is based on our current estimates of future royalties expected to be paid to BBA, which are considered Level 3 inputs. Refer to Note 14. There were no liabilities measured at fair value on a recurring and non-recurring basis as of December 31, 2019. There were no transfers of assets or liabilities between the fair value measurement levels during the years ended December 31, 2020 and 2019.

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 (in thousands):

	December 31, 2020			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
U.S. treasury securities	$ 10,003	$ 3	—	$ 10,006
Corporate notes	14,522	50	—	14,572
Total marketable securities, current	$ 24,525	$ 53	$ —	$ 24,578

(in thousands, except share and per share data)

	December 31, 2019			
	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, 2020 had effective maturities of less than one year. 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, 2020 and as a result, the Company did not reclassify any amounts out of accumulated comprehensive loss. No marketable securities with unrealized losses as of December 31, 2020. 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.

7. Commitments and Contingencies

Leases

Palo Alto, California Leases

In June 2020, the Company entered into lease agreements for two buildings at 1200 and 1250 Page Mill Road in Palo Alto, California, which are now the Company's U.S. corporate offices. The facilities are approximately 82,662 square feet and 72,812 square feet, respectively and include office and laboratory space. For 1200 Page Mill Road, the monthly rent during the initial 6.5-year term will be approximately $0.6 million, with annual year-over-year increases of 3% plus certain operating expenses and taxes and total rent abatement of approximately $7.2 million. The Company has an option to extend the lease term for a period of 6.5 years. For 1250 Page Mill Road, the monthly rent during the initial 13-year term will be approximately $0.5 million, with annual year-over-year increases of 3% plus certain operating expenses and taxes and total rent abatement of approximately $6.3 million. The Landlord will provide a tenant improvement allowance of approximately $1.2 million and $10.6 million for each building, respectively. The Company has two options to extend the lease term for a period of 5 years each. The Company determined that the renewal options were not reasonably certain at lease inception for the two buildings. The Company executed a $10.9 million cash-collateralized letter of credit, which was subsequently reduced to $6.2 million as a result of meeting certain reduction requirements specified therein. The cash collateralizing the letter of credit is classified as restricted cash on the Company's consolidated balance sheets. Under ASC 842, the Company classified these leases as operating leases and recorded right-of-use assets and lease liabilities on the lease commencement date.

The Company continues to lease office and laboratory space at 2631 Hanover Street in Palo Alto, California. The Company entered into a lease agreement in January 2013 which was amended in March 2016 and extended the lease term until October 2023. The Company classified this lease as an operating lease and recorded a right-of-use asset and lease liability on January 1, 2019 and recognized rent expense on a straight-line basis throughout the remaining lease term.

Switzerland Lease

In April 2020, the Company entered into a lease agreement for office and laboratory space at Rottenstrasse 5 in Visp, Switzerland. The space is approximately 1,000 square meters. The initial lease term is 5 years, with automatic renewals every 5 years for a maximum lease term of 15 years. The monthly rent during the initial 5-year term will be approximately 32 thousand Swiss Francs plus certain operating expenses and taxes. Under ASC 842, the Company classified these leases as operating leases and recorded right-of-use assets and lease liabilities on the lease commencement date.

The maturities of the operating lease liabilities as of December 31, 2020 were as follows (in thousands):

Year ending December 31,	As of December 31, 2020
2021	$ 4,288
2022	7,660
2023	14,598
2024	15,037
2025	15,475
Thereafter	71,462
Total undiscounted lease payments	128,520
Less: imputed interest	(51,118)
Total operating lease liabilities	$ 77,402

The minimum lease payments above do not include any related common area maintenance charges or real estate taxes. The weighted-average remaining lease terms and weighted-average discount rates were as follows:

	December 31, 2020	December 31, 2019
Weighted-average remaining lease term (in years)	9.5	3.8
Weighted-average discount rate	6.7%	8.5%

Embedded lease

In August 2020, the Company and its subsidiary Kodiak Sciences GmbH entered into a manufacturing agreement with a contract manufacturing organization for the clinical and commercial supply of drug substance for KSI-301, the Company's proprietary therapeutic candidate for the treatment and prevention of retinal vascular diseases. A custom-built manufacturing suite is planned to be completed and dedicated to the manufacture of the Company's drug substance with an estimated capital contribution of 40 million Swiss Francs from the Company. Construction of the manufacturing suite is targeted for completion in 2021. The Company will be required to pay annual suite fees of 12 million Swiss Francs for 2021 and 16 million Swiss Francs for each year thereafter, which covers the manufacturing fees for a specified number of batches, and the Company may pay for additional batches to be manufactured. The manufacturing agreement has an initial term of eight years, and the Company has the right to extend the term up to a total of 16 years.

The Company concluded that this agreement contains an embedded lease as the custom-built manufacturing suite will be dedicated for the Company's use. As of December 31, 2020, the Company did not have control of this manufacturing space and therefore, did not record a right-of-use asset and corresponding lease liability. These commitments are not included in the above table.

Manufacturing Agreement

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 or obligate the Company to the binding amount regardless of whether such planned activities are in fact performed. 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 amount dependent on the agreement or the work order. Under these agreements, the total amount of contractual obligations, over a period of ten years, are cancellable and subject to varying levels of cancellation fees, were $242.3 million and $4.7 million, including accrued amounts, as of December 31, 2020 and 2019, respectively. Purchases under this agreement for the years ended December 31, 2020, 2019 and 2018 were $16.8 million, $7.9 million and $2.8 million, respectively. As of December 31, 2020, the Company had not incurred any cancellation fees for the work performed by Lonza.

Other Funding Commitments

In the normal course of business, the Company enters into agreements with third-parties for services to be provided to the Company. Generally, these agreements provide for termination upon notice, with specified amounts due upon termination based on the timing of termination and the terms of the agreement. The actual amounts and timing of payments under these agreements are uncertain and contingent upon the initiation and completion of services to be provided to the Company. As of December 31, 2020 and 2019, the total amount of noncancellable purchase commitments, including potential cancellation fees were $0.5 million and $0.7 million, 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.

The Company has also entered into various cancellable license agreements for certain technology. The Company may be obligated to make payments on future sales of specified products associated with such license agreements. Such payments are dependent on future 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, 2020 and 2019, 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, 2020 and 2019, 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 provision (benefit) for income taxes consists of the following (in thousands):

	Year Ended December 31, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
Current:			
Federal	$ —	$ —	$ —
State	—	—	—
Foreign	14	—	—
Total current	$ 14	$ —	$ —
Deferred:			
Federal	$ —	$ —	$ —
State	—	—	—
Foreign	—	—	—
Total deferred	$ —	$ —	$ —
Provision (Benefit) for income taxes	$ 14	$ —	$ —

The components of loss before income taxes were as follows (in thousands):

	Year Ended December 31, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
United States	$ (17,273)	$ 2,633	$ (17,273)
Foreign	(115,809)	(49,998)	(24,170)
Total loss before income taxes	$ (133,082)	$ (47,365)	$ (41,443)

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, 2020	December 31, 2019	December 31, 2018
Deferred tax assets:			
Net operating loss carryforwards	$ 28,451	$ 18,523	$ 11,044
Intangible assets	12,088	12,112	7,588
Research and development tax credits	10,527	4,037	1,559
Stock-based compensation	8,405	1,539	394
Accruals	1,367	885	700
Operating lease liability	22,276	577	-
Property and equipment	127	143	109
Total deferred tax assets	83,241	37,816	21,394
Valuation allowance	(62,005)	(37,249)	(21,394)
Net deferred tax assets	21,236	567	—
Deferred tax liabilities:			
Operating lease right-of-use asset	(21,234)	(534)	—
Capitalized legal fees	(2)	(33)	—
Total deferred tax liabilities	(21,236)	(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, 2020, 2019 and 2018 was an increase of approximately $24.8 million, $15.9 million and $8.2 million, respectively.

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, 2020 which concluded no such ownership change had occurred through December 31, 2020.

As of December 31, 2020, the Company had $50.1 million of federal and $171.0 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. $32.0 million of the federal net operating loss are not subject to expiration.

As of December 31, 2020, the Company also had federal and state research and development credit carryforwards of $10.2 million and $4.9 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, 2020	December 31, 2019	December 31, 2018
Federal statutory income tax rate	21.0%	21.0%	21.0%
State taxes	4.3	11.0	5.6
Foreign tax rate differential	(7.9)	(12.4)	(3.8)
Change in valuation allowance	(17.3)	(30.5)	(18.3)
Stock-based compensation	6.7	7.7	(0.6)
Research tax credit	3.8	3.3	1.3
Other	—	(0.1)	(0.1)
Sale of future royalties	(9.4)	—	—
Section 162(m)	(1.2)	—	—
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, 2020, 2019 and 2018, 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 penalties and interest expense related to income taxes as a component of other expense, net as necessary.

The beginning and ending unrecognized tax benefits amounts are as follows (in thousands):

	December 31, 2020	December 31, 2019	December 31, 2018
Unrecognized tax benefits at beginning of period	$ 1,838	$ 398	$ 357
Increases related to prior year tax positions	—	—	-
Increases related to current year tax positions	2,812	1,440	41
Unrecognized tax benefits at end of period	$ 4,650	$ 1,838	$ 398

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.

(in thousands, except share and per share data)

9. Preferred Stock

As of December 31, 2020 and 2019, 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, 2020, there are no holders of the Company's preferred stock.

10. Common Stock

As of December 31, 2020 and 2019, 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, 2020	December 31, 2019
Exercise of options outstanding and release of restricted shares	7,257,221	6,830,442
Exercise of common stock warrants outstanding	399,999	399,999
Issuance of common stock under the 2018 Equity Incentive Plan	2,742,183	2,118,877
Issuance of common stock under the 2018 Employee Share Purchase Plan	460,000	460,000
Total	10,859,403	9,809,318

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 number of shares available for issuance increased by 1,776,761 shares in 2020 and there were 2,742,183 shares available for grant under the 2018 Plan as of December 31, 2020.

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, 2020 and 2019, there are no early exercised stock options that remained subject to the Company's right of repurchase.

Stock Options

Stock option activity under the 2018 Plan and 2015 Plan is summarized as follows:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2019	6,671,542	$ 17.90	8.73	$ 362,081
Granted	1,068,335	$ 55.27		
Exercised	(704,675)	$ 8.89		
Forfeited or canceled	(137,926)	$ 25.07		
Outstanding at December 31, 2020	6,897,276	$ 24.52	8.07	$ 841,704
Shares exercisable December 31, 2020	3,769,990			
Vested and expected to vest December 31, 2020	6,897,276			

The weighted-average grant date fair value of the stock options granted for 2020, 2019 and 2018 was $32.44, $34.11 and $4.36 per share, respectively. The aggregate intrinsic value represents the value of the Company's closing stock price on the last trading day of the period in excess of the weighted-average exercise price multiplied by the number of options outstanding or exercisable.

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.

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, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
Expected volatility	66%	68%	59%
Risk-free interest rate	0.39%	1.65%	2.82%
Dividend yield	0%	0%	0%
Expected term	6.00	5.78	6.06

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. As the Company does not have sufficient trading history for its common stock, our approach to estimating expected volatility is to phase in our own common stock trading history and supplement the remaining historical information with an average historical stock price volatility of a peer group of publicly traded companies to be representative of its expected future stock price volatility. 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.

(in thousands, except share and per share data)

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, 2020, 2019 and 2018 was $19.7 million, $4.6 million and $1.2 million, respectively. Stock-based compensation expense recognized during the years ended December 31, 2020, 2019 and 2018 for options granted to employees was $20.8 million, $5.7 million and $2.0 million, respectively.

Non-Employee Stock Options

The Company granted 41,500, 15,000 and 215,000 stock options to non-employees during the years ended December 31, 2020, 2019 and 2018, 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, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
Expected volatility	67%	73%	68%
Risk-free interest rate	0.36%	1.61%	2.71%
Dividend yield	0%	0%	0%
Expected term	5.56	6.08	9.30

Stock-based compensation expense recognized during the years ended December 31, 2020, 2019 and 2018 for options granted to non-employees was $0.7 million, $0.1 million and $0.4 million, respectively.

Restricted Shares

Restricted share activity, including restricted stock awards ("RSAs"), restricted stock units ("RSUs"), and performance-based restricted stock units ("PSUs"), under the 2018 Plan and 2015 Plan is summarized as follows:

	Number of Restricted Shares		Weighted Average Grant Date Fair Value
Unvested at December 31, 2019	160,747	$	60.81
Granted	236,045	$	52.18
Vested	(23,848)	$	9.21
Shares withheld related to net share settlement of RSUs	(7,999)	$	9.90
Canceled	(5,000)	$	72.46
Unvested at December 31, 2020	359,945	$	59.54

Restricted Stock Awards

Under the terms of the restricted stock agreements, the awards vest 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 Company did not grant any RSA to employees in 2020. The total fair value of RSAs vested during the years ended December 31, 2020, 2019 and 2018 was $nil million, less than $0.1 million and $0.2 million, respectively. Stock-based compensation expense recognized during the years ended December 31, 2020, 2019 and 2018 for RSAs was $nil million, less than $0.1 million and $0.2 million, respectively.

Restricted Stock Units

RSUs will vest in four equal annual installments over four years, which is the requisite service period after that date.

The Company granted 236,045 RSUs to employees in 2020. The total fair value of RSUs vested during the year ended December 31, 2020 and 2019 was $0.3 million and $0.3 million, respectively. Stock-based compensation expense recognized during the years ended December 31, 2020, 2019 and 2018 for RSUs was $1.9 million, $0.3 million, and less than $0.1 million, respectively.

Performance-Based Stock Options and Restricted Stock Units

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 are recorded as expense beginning when vesting events are determined to be probable.

The Company did not grant performance-based equity awards to employees in 2020. None of these performance-based equity awards vested during 2020 or 2019. The Company believes that the achievement of the requisite performance condition continues to be probable. Stock-based compensation expense recognized during the years ended December 31, 2020, 2019 and 2018 for the performance-based equity awards was $7.2 million, less than $0.1 million and $nil million, respectively.

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.

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 initial offering period of the ESPP was authorized by the Company's board of directors and commenced on January 4, 2021.

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, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
Research and development	$ 16,957	$ 3,496	$ 1,535
General and administrative	13,711	2,614	1,073
Total stock-based compensation	$ 30,668	$ 6,110	$ 2,608

As of December 31, 2020, the Company had $91.4 million of unrecognized compensation expense related to unvested stock options and unvested restricted stock awards and units that is expected to be recognized over a weighted-average period of 2.9 years.

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, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
Numerator:			
Net loss attributable to common stockholders	$ (133,096)	$ (47,365)	$ (41,443)
Denominator:			
Weighted-average shares outstanding	45,741,845	37,869,291	15,136,197
Less: weighted-average unvested restricted shares and shares subject to repurchase	—	(15,675)	(159,682)
Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted	45,741,845	37,853,616	14,976,515
Net loss per share attributable to common stockholders, basic and diluted	$ (2.91)	$ (1.25)	$ (2.77)

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, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
Exercise of options outstanding	6,897,276	6,671,542	5,135,267
Unvested restricted shares	359,945	160,747	50,450
Total	7,257,221	6,832,289	5,185,717

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, 2020 and 2019, the expense related to the matching contributions was $0.6 million and $0.3 million, respectively.

14. Liability related to Sale of Future Royalties

On December 1, 2019, the Company and its subsidiary Kodiak Sciences GmbH entered into a funding agreement with BBA, which holds more than 5% of the Company's stock, 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 royalty terminates upon the date that BBA has received an aggregate amount equal to 4.5 times the funding amount paid to the Company, unless earlier terminated or repurchased by the Company. Under the terms of the funding agreement, there is no obligation to repay any funding amount received, other than through the capped royalty payments on future product revenues. The Company has the option, exercisable at any point during the term of the funding agreement, to repurchase 100% of the royalties due to BBA for a purchase price equal to 4.5 times the funding amount paid to the Company as of such time, less amounts paid by the Company to BBA.

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, subject to delivery of notice by the Company, payable upon enrollment of 50% of the patients in the RVO clinical program.

The Company recorded the initial $100.0 million payment as a liability on the consolidated balance sheet net of issuance costs. Once royalty payments to BBA are determined to be probable and estimable, and if such amounts exceed the liability balance, the Company will impute interest to accrete the liability on a prospective basis based on such estimates. If and when the Company makes royalty payments under the funding agreement, it would reduce the liability balance at such time. As of December 31, 2020, royalty payments are not probable and estimable.

For the year ended December 31, 2020, no interest expense was recognized for the liability related to the sale of future royalties.

15. Selected Quarterly Financial Data (unaudited)

The following table provides the selected quarterly financial information for the years, 2020 and 2019 (in thousands, except per share data):

	Three Months Ended			
	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
Loss from operations	$ (25,723)	$ (26,779)	$ (36,663)	$ (46,842)
Net loss	$ (24,392)	$ (25,999)	$ (36,122)	$ (46,583)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.54)	$ (0.58)	$ (0.80)	$ (0.97)

	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)

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. Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of the Company's disclosure controls and procedures as of December 31, 2020. Based upon such evaluation, our principal executive officer and principal financial officer concluded that the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level as of December 31, 2020.

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 Rules 13a-15(f) and 15d-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, 2020 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, 2020.

Our independent registered public accounting firm, PricewaterhouseCoopers LLP, has audited the effectiveness of our internal control over financial reporting as of December 31, 2020, as stated in their report included in Item 8 of this Annual Report on Form 10-K.

Limitations on the Effectiveness of Controls

Because of inherent limitations, internal control over financial reporting may not prevent or detect misstatements and projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

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, 2020, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

We are currently party to an Investors' Rights Agreement, dated September 8, 2015, as amended (the "Investors' Rights Agreement") which provides registration rights to entities affiliated with Felix Baker, a member of our board of directors, and Dr. Perlroth, our board chair and chief executive officer. The Investors' Rights Agreement expires this year, and on March 1, 2021, we entered into a registration rights agreement (the "Registration Rights Agreement") with 667, L.P., Baker Brothers Life Sciences, L.P. (collectively, the "Baker Entities") and Victor Perlroth (together with the Baker Entities, the "Investors") which is intended to supersede the expiring Investors' Rights Agreement and pursuant to which the Investors are entitled to certain resale registration rights with respect to shares of common stock of the Company held by the Investors. The rights of the Investors under the Registration Rights Agreement will continue in effect for up to ten years.

The foregoing is only a brief description of the terms of the Registration Rights Agreement and the transactions contemplated thereby, and is qualified in its entirety by reference to the Registration Rights Agreement that is filed as Exhibit 4.7.

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, 2020, 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-K	001-38682	4.6	3/16/2020
4.7*	Registration Rights Agreement, dated March 1, 2021, by and among the registrant and the investors named therein				
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
10.18	Lease Agreement for 1200 Page Mill Road, Building 3, by and between the Registrant and 1050 Page Mill Road Property, LLC, dated June 19, 2020	10-Q	001-38682	10.1	8/10/2020
10.19	Lease Agreement for 1250 Page Mill Road, Building 4, by and between the Registrant and 1050 Page Mill Road Property, LLC, dated June 19, 2020	10-Q	001-38682	10.2	8/10/2020
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 Financial and Accounting 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 Financial and Accounting Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
101.INS	Inline XBRL Instance Document				
101.SCH	Inline XBRL Taxonomy Extension Schema Document				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document				
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				

104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

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* 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 1, 2021

By: /s/ Victor Perlroth

Victor Perlroth, M.D.
Chairman and Chief 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 Victor Perlroth, M.D.	Chairman and Chief Executive Officer *(Principal Executive Officer)*	March 1, 2021
/s/ John Borgeson John Borgeson	Senior Vice President and Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 1, 2021
/s/ Felix J. Baker Felix J. Baker, Ph.D.	Director	March 1, 2021
/s/ Charles Bancroft Charles Bancroft	Director	March 1, 2021
/s/ Bassil I. Dahiyat Bassil I. Dahiyat, Ph.D.	Director	March 1, 2021
/s/ Richard S. Levy Richard S. Levy, M.D.	Director	March 1, 2021
/s/ Robert A. Profusek Robert A. Profusek, J.D.	Director	March 1, 2021
/s/ Taiyin Yang Taiyin Yang, Ph.D.	Director	March 1, 2021

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LEADERSHIP TEAM

VICTOR PERLROTH MD
Chairman
Chief Executive Officer

JASON EHRLICH MD, PHD
Chief Medical Officer
Chief Development Officer

ALMAS QUDRAT MSC
Senior Vice President,
Quality Operations

SINETTE HEYS
Vice President,
Clinical Operations

STEPHEN RAILLARD PHD
Vice President, Chemical
Development & Manufacturing

JOHN BORGESON
Senior Vice President
Chief Financial Officer

HONG LIANG PHD
Senior Vice President,
Discovery Medicine

BERND JANDELEIT PHD
Vice President, Chemistry

LAURENT DUCRY PHD
Vice President, Biologics
Development & Manufacturing

JOEL NAOR MD
Vice President, Clinical Science
& Development Operations

PABLO VELAZQUEZ-MARTIN MD
Vice President, Clinical Research
& Translational Medicine

BOARD OF DIRECTORS

DEEP BIOTECH & GOVERNANCE EXPERIENCE

Victor Perlroth MD
Chairman & CEO | Kodiak

Felix J. Baker MD
Managing Director |
Baker Brothers Investments

Charles Bancroft
Former CFO | Bristol Myers Squibb

Bassil I. Dahiyat PhD
Chairman & CEO | Xencor Inc.

Richard S. Levy MD
Former Chief Drug Development
Officer & CMO | Incyte Corporation

Robert A. Profusek JD
Partner & Global Chair M&A | Jones Day

Taiyin Yang PhD
EVP, Pharmaceutical Development &
Manufacturing | Gilead Sciences Inc.

ANNUAL MEETING

June 7, 2021 | 9 am PST

Virtual meeting. Please visit
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