UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 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, 2021

OR

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

Commission File Number 001-39538

GRAYBUG VISION, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**45-2120079**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

203 Redwood Shores Parkway, Suite 620
Redwood City, CA 94065

(Address of principal executive offices, including zip code)

Registrant's telephone number, including area code: (650) 487-2800

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 per share	GRAY	The Nasdaq Global Market

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

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

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

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

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

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the Registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the Registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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

As of June 30, 2021, the last business day of the Registrant's most recently completed second fiscal quarter the aggregate market value of common stock held by non-affiliates of the Registrant computed by reference to the closing price of the Registrant's common stock on June 30, 2021 was approximately $57.7 million. Shares of common stock held by each executive officer, director and their affiliated holders have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares of the Registrant's common stock outstanding as of March 4, 2022 was 21,357,773.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement relating to the 2022 Annual Meeting of Shareholders are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein. The Definitive Proxy Statement will be filed within 120 days of the Registrant's fiscal year ended December 31, 2021. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements, other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our future financial condition, business strategy and plans, and objectives of management for future operations, are forward-looking statements. In some cases you can identify these statements by forward-looking words such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “could,” “would,” “project,” “plan,” “expect” or the negative or plural of these words or similar expressions. These forward-looking statements include, but are not limited to, statements concerning the following:

- the potential of our technologies and our ability to execute on our corporate strategy;
- our ability to fund our working capital needs;
- our ability to develop and commercialize our product candidates;
- our ability to use and expand our technologies to build a pipeline of product candidates;
- our ability to secure a partnership for GB-102;
- our ability to obtain and maintain regulatory approval of our product candidates;
- the strength and breadth of our patent portfolio;
- the potential for receipt of additional milestone payments;
- our ability to obtain and adequately protect intellectual property rights for our product candidates;
- our continued reliance on third parties for manufacturing our product candidates, conducting our clinical trials and certain research activities;
- our ability to in-license, acquire or invest in complementary businesses, technologies, products or assets to further expand or complement our portfolio of product candidates;
- expected timing of our clinical trials;
- the timing and availability of results of our clinical trials and those of our collaborators; and
- our ability to extend our operating capital.

These statements are only current predictions and are subject to known and unknown risks, uncertainties and other factors that may cause our or our industry’s actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements. We discuss many of these risks in greater detail under the heading “Risk Factors” and elsewhere in this Annual Report on Form 10-K. You should not rely upon forward-looking statements as predictions of future events. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risks and uncertainties.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, after the date of this report, we are under no duty to update or revise any of the forward-looking statements, whether as a result of new information, future events or otherwise.

We obtained industry, market and competitive position data in this report from our own internal estimates and research as well as from industry and general publications and research surveys and studies conducted by third parties. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such information or estimates.

PART I

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company focused on developing transformative medicines for the treatment of ocular diseases. Our novel proprietary technologies are designed to release drugs in ocular tissue at a controlled rate for up to 12 months in order to improve patient compliance, reduce healthcare burdens and, ultimately, deliver better clinical outcomes. Our lead product candidate, GB-102, is an intravitreal injection of a microparticle depot formulation of sunitinib, a potent inhibitor of neovascular growth and permeability, which are leading causes of retinal disease. We are developing GB-102 as a once-every-six month intravitreal injection for the treatment of wet age-related macular degeneration, or wet AMD. In our Phase 1/2a clinical trial, GB-102 administered as a single 1 mg dose was well-tolerated in wet AMD patients and demonstrated durable clinical evidence of disease control of at least six months in approximately 88% of patients in this cohort. Subsequently, GB-102 completed a dose-ranging, standard-of-care controlled and masked safety and efficacy Phase 2b clinical trial in previously-treated patients with wet AMD (the ALTISSIMO trial). Of the 56 patients enrolled in our Phase 2b clinical trial, 50 patients completed the 12-month treatment phase (the Core Study), while the remaining six withdrew for reasons unrelated to their treatment. We reported topline data from the Phase 2b clinical trial in March 2021. Following the 12-month Core Study, 28 of the 50 patients who completed their Month 12 visit and met the eligibility criteria agreed to continue clinical monitoring in a six-month monitoring extension of the trial (the Extension Study). The goal of the Extension Study was to observe further durability of GB-102 in wet AMD patients. We reported topline data from the Extension Study in September 2021. Based on the durability observed in the ALTISSIMO trial, we are evaluating the possibility of also developing GB-102 for the treatment of diabetic retinopathy, or DR. Furthermore, we are using our proprietary technologies to develop GB-401, an intravitreally injected implant formulation of a beta-adrenergic blocking agent prodrug with a target dosing regimen of once every six months or longer for the treatment of primary open-angle glaucoma, or POAG. We believe that our product candidates could significantly improve clinical outcomes versus the respective standards of care for several ocular diseases.

Age-related macular degeneration, or AMD, is a chronic, progressive disease, a leading cause of vision loss in the elderly and estimated to affect approximately 15 million people in North America. The disease prevalence is approximately 85 to 90% nonexudative, or dry, AMD and 10 to 15% wet AMD. The therapeutic market for wet AMD in 2020 was estimated to be $9.0 billion worldwide and has historically grown by approximately 8% as a consequence of an aging population and the lack of preventative measures.

There is no cure for wet AMD. To maintain vision, patients must receive frequent intravitreal injections, up to 12 times per year, with short-acting anti-vascular endothelial growth factor, or VEGF, agents. Although the use of anti-VEGF treatments has revolutionized visual outcomes for patients, the need for frequent injection visits combined with the increasing prevalence of this disease puts an enormous pressure on healthcare systems and represents a severe burden for patients, caregivers and physicians. These dynamics often lead to a reduced frequency of treatment and result in suboptimal visual outcomes in real-world practice.

Damage to the retina as a result of DR includes a number of vision-threatening complications and has been an important cause of acquired vision loss in the young and middle-aged adult population. It is estimated that the number of patients with DR will increase globally to over 190 million by 2030. One-third of DR patients over 40 years of age in the United States are at risk of developing vision-threatening complications. Multiple clinical trials have shown that anti-VEGFs are also beneficial for the treatment of patients with DR without diabetic macular edema (DME); however, the need for frequent injections and follow-up for this often-asymptomatic population leads to inadequate compliance and suboptimal clinical benefit.

GB-102, our lead product candidate, is designed to provide pan-VEGF inhibition for six months or longer while minimizing fluctuations in retinal thickness in between treatments, which is emerging as predictive of visual outcomes. We believe durable and sustained drug delivery with dosing every six months or longer offered by GB-102 could provide improved visual outcomes for patients with wet AMD, better patient quality-of-life and reduced disease-monitoring requirements.

In the ALTISSIMO trial, disease control was achieved in 48% of patients for 6 months following a single intravitreal injection, and for 12 months in 55% of the patients who agreed to enter the 6-month Extension Study. This potentially longer duration of clinical benefit and consequently less frequent need for intravitreal injections may be more conducive to maintaining a typically asymptomatic patient with DR on an effective anti-VEGF therapy regimen. If approved for DR, GB-102 could provide a paradigm shift in the treatment of patients with DR who are currently managed either by observation alone, pan-retinal laser photocoagulation or, in rare instances, with short-acting anti-VEGF injections.

Our second product candidate, GB-401, is an intravitreally administered, proprietary implant formulation containing a prodrug of a beta-adrenergic receptor inhibitor designed to provide a controlled release of the active drug to maintain reduced intraocular pressure, or IOP, for six months or longer after a single injection, thus addressing the patient compliance problem and improving outcomes.

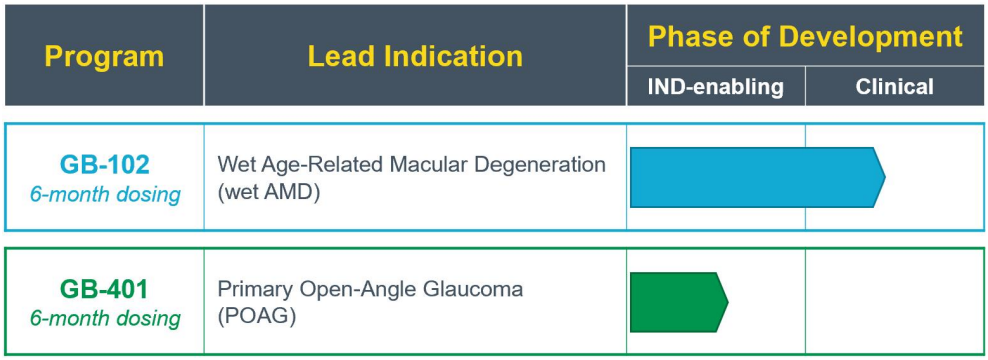
Glaucoma is an optic neuropathy that is characterized by the progressive degeneration of the optic nerve that leads to visual impairment. It is a leading cause of irreversible vision loss that is projected to affect approximately 76 million people worldwide in 2020, including approximately 2.7 million people in the United States. The most common type of glaucoma is POAG, which is characterized by an increase in IOP because fluid, which is continuously generated by cells inside the front of the eye, cannot drain properly. The global POAG therapeutics market is estimated to reach approximately $3.8 billion in 2026, of which the United States represents approximately $2.9 billion.

The most common treatment options for glaucoma are topical eye drops, which must be administered daily, or invasive medical procedures. Topical eye drops can lower IOP and have been shown to both delay and prevent the progressive degeneration associated with POAG. However, these medications must be administered up to four times per day, and approximately 30% of patients often require more than one class of drug to control IOP. It is estimated that approximately 50% of patients stop using their glaucoma medications in the first six months post-diagnosis due to various reasons, including forgetfulness, lack of disease awareness and/or cost, thus leading to uncontrolled IOP and progressive loss of peripheral vision. A sustained-release implant containing the IOP-lowering medicine bimatoprost was recently approved by the US Food & Drug Administration, or FDA, for only one injection in the front of the eye, limiting its potential use for this chronic disease. Laser-based or surgical treatments to permanently reduce IOP are invasive and achievement of IOP targets may require multiple surgeries. If approved, GB-401 could represent a significant paradigm shift in the way physicians treat POAG.

We have acquired intellectual property that will enable us to expand our pipeline into additional disease areas, including geographic atrophy as well as inherited retinal and corneal diseases.

Our pipeline

The following chart summarizes the status and development plan for the disclosed product candidates in our pipeline. We own worldwide rights to each of our programs.



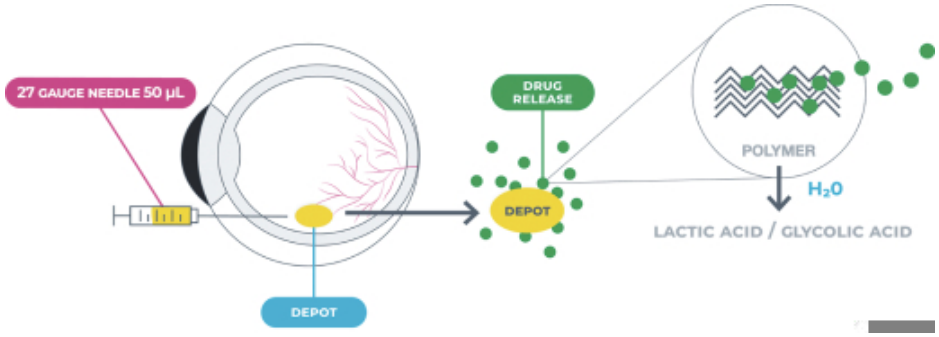
Our proprietary technologies

Our proprietary technologies are designed to allow sustained delivery of pharmacologic agents to the eye in a well-tolerated and controlled manner to achieve extended duration of effectiveness. Our proprietary technologies utilize microparticle depot and implant formulations each containing biodegradable polymers such as poly (lactic-co-glycolic acid), or PLGA.

The microparticles are engineered to carry a hydrophilic coating such as polyethylene glycol, or PEG, that helps eliminate or minimize inflammation typically associated with intraocular administration of conventional PLGA microparticles. Our preclinical studies and Phase 1, 2a, and 2b clinical trials provided preliminary evidence that our microparticles are well-tolerated in the eye.

Furthermore, our microparticles are designed to aggregate after intravitreal injection upon exposure to the vitreous fluid at body temperature to form a depot near the bottom of the eye, outside of the visual axis. Our biodegradable microparticles then gradually release the active ingredient at a rate dependent on the composition of the polymers and biodegrade into lactic acid, glycolic acid and

PEG that are naturally cleared from the body. Our implants are designed to be injected near the bottom of the eye and are expected to remain in place due to their geometry and the structure of the vitreous humor.



Some molecules, due to their physicochemical properties, are difficult to integrate into polymer formulations and deliver in a controlled manner. For that purpose, we have developed a proprietary prodrug technology to enable sustained delivery of these therapeutics. Our research and development team has developed our product candidates with different pharmacologic agents using these prodrug technologies. For example, GB-401 has been developed using this approach.

We have also developed intravitreally-injected implant formulations containing biodegradable polymers such as poly(lactic-co-glycolic acid), or PLGA, in the form of a rod, that we intend to use in our upcoming Phase 1/2a clinical trial for our GB-401 program.

Our lead program GB-102

We are developing our lead product candidate, GB-102, as a once-every-six months intravitreally delivered microparticle depot formulation of sunitinib for the treatment of wet AMD. Sunitinib is a pan-VEGF inhibitor that targets several neovascular pathways (VEGF-A, B, C and D). We believe that GB-102 is differentiated from the current standard of care, which requires more frequent dosing, up to 12 times per year, and primarily targets one neovascular pathway (VEGF-A).

In January 2019, we completed a Phase 1/2a trial in 32 patients with wet AMD (the ADAGIO trial). This trial met its primary endpoint of safety and tolerability. No ocular serious adverse event, or SAE, or dose-limiting toxicity was reported, and the majority of patients had no drug-related adverse events, or AEs. The most common AE was the presence of medication in the anterior chamber. These AEs were reversible and with no long-term sequelae. In this trial, 88% of patients who were previously treated with an average of eight injections annually were able to maintain stable central retinal thickness and visual acuity for six months or more with a single injection of 1 mg of GB-102.

Based on the data from the ADAGIO trial, we initiated the Phase 2b ALTISSIMO trial in September 2019 to evaluate an improved product formulation that would minimize the presence of medication within the anterior chamber. This trial was designed to compare two doses of GB-102 (1 or 2 mg) administered every six months to aflibercept administered every two months in up to 56 patients with anti-VEGF-responsive wet AMD. On the basis of a safety analysis of the Phase 2a clinical trial of GB-102 in macular edema (ME), described below, and the interim safety data in the ALTISSIMO trial, we terminated the development of the GB-102 2 mg dose in all of our clinical trial programs. The primary endpoint of the ALTISSIMO trial was to determine time-to-additional anti-VEGF supportive therapy. Of the 56 patients originally enrolled in the study, 50 completed the 12-month Core Study and six withdrew for reasons unrelated to their treatment. Furthermore, 28 of the 50 patients who completed their Month 12 ALTISSIMO visit were eligible and agreed to continue masked clinical monitoring until the point at which they required additional supportive therapy, up to a maximum of six months. ALTISSIMO topline results were released in March 2021, and the topline results of the 6-month Extension Study were released in September 2021.

In September 2019, we initiated a Phase 2a clinical trial of GB-102 in 21 patients with ME secondary to DME and branch or central retinal vein occlusion (RVO). This trial was designed to be a six-month, single injection, multicenter, open-label, parallel arm trial with a primary endpoint of safety and tolerability of two dose levels of GB-102 (1 and 2 mg) in patients with ME secondary to DME or RVO who had been previously treated with anti-VEGFs. All patients have completed the study and the final safety analysis has been performed. An interim data analysis from the ALTISSIMO and ME trials identified 1 mg of GB-102 as the optimal dose for future clinical trials. In 2021, we decided to prioritize development of GB-102 in wet AMD.

Additional pipeline programs

We are also applying our proprietary technologies to develop GB-401, a proprietary implant formulation containing a prodrug of a beta-adrenergic receptor inhibitor, designed to be injected once every six months or longer to reduce IOP in POAG patients. We expect to submit an investigational new drug application, or IND, for GB-401 and initiate a dose-escalating Phase 1/2a clinical trial of GB-401 in patients with POAG in the first half of 2023.

We believe our proprietary technologies and our acquired intellectual property will allow us to develop other novel therapeutics, either alone or in combination, that can treat additional diseases, achieve extended durations of effectiveness, and improve the care and quality of life for patients with chronic diseases and disorders of the eye.

Our executive leadership team

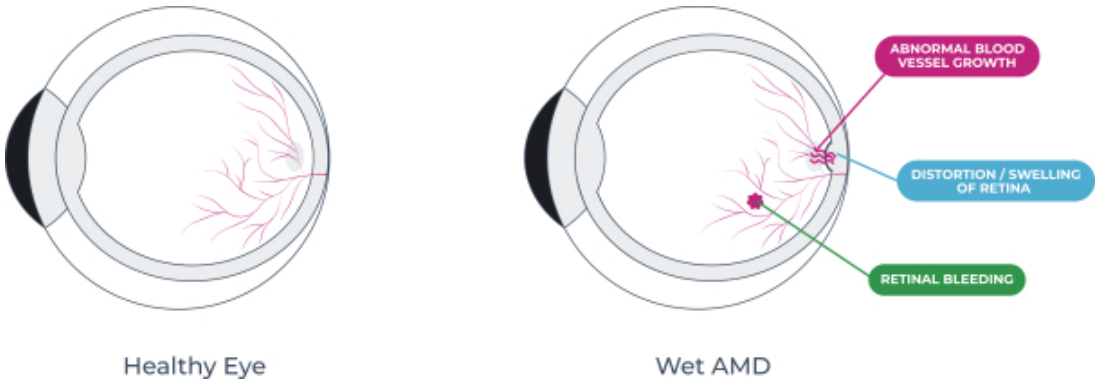
We are led by a team of experienced pharmaceutical industry executives with significant experience in ophthalmology:

- Frederic Guerard, Pharm.D., our Chief Executive Officer, has 20 years of leadership, strategic and commercial pharmaceutical experience, including as Worldwide Business Franchise Head of Ophthalmology at Novartis AG and Global Franchise Head of Pharmaceuticals at Alcon Laboratories, Inc.
- Parisa Zamiri, M.D., Ph.D., our Chief Medical Officer, is an ophthalmologist and was previously Vice President, Global Head of Clinical Development and Therapeutic Area Head for Ophthalmology at Novartis AG.
- Robert S. Breuil, our Chief Financial Officer, has over 20 years of experience in the biopharmaceutical and drug delivery industries, and previously served as Chief Financial Officer of Corium, Inc. and Codexis, Inc.
- Bettina Maunz, our Chief People Officer, has over 20 years of experience across the pharmaceutical, biotechnology, and medical device industries, and previously served as VP, Group Head of Enterprise Communications at Novartis AG.
- Ming Yang, Ph.D., our Senior Vice President of R&D, has over 20 years of R&D experience in developing novel therapeutics and drug delivery systems, including past experience at Genentech focused on ocular drug delivery.

Wet AMD

Wet AMD is a common ocular disease caused by the growth of abnormal blood vessels under the central portion of the retina, or macula. This growth is triggered by VEGF, a protein produced by cells that stimulates the formation of new abnormal blood vessels, a process called neovascularization, and induces vascular permeability, leading to leakage and swelling of the retina. Anti-VEGF treatment has been shown to improve vision in patients with wet AMD when compared to either no treatment or laser alone.

According to the American Academy of Ophthalmology, it is estimated that 15 million people in North America have AMD. The prevalence of the disease is approximately 85 to 90% nonexudative, or dry, AMD and 10 to 15% wet AMD. As a greater percentage of Americans are living well beyond 60 years of age, more patients will become visually impaired from AMD than from glaucoma and diabetic retinopathy combined. Early intervention is essential to treat wet AMD; without treatment, vision rapidly declines. The figure below illustrates the primary effects of wet AMD.



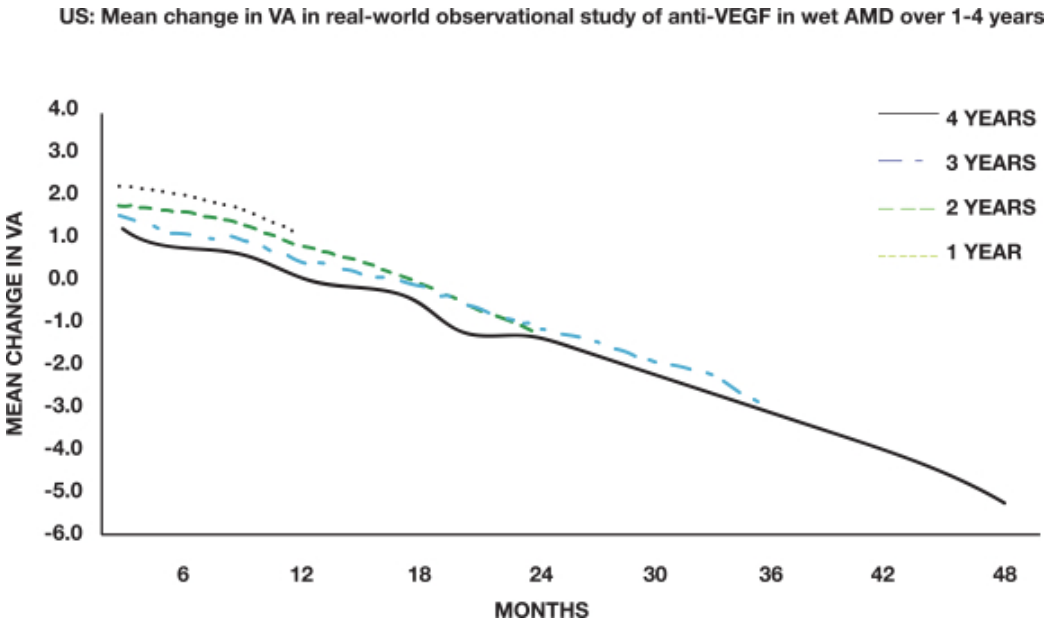
Our market opportunity in wet AMD

In 2020, annual anti-VEGF sales reported for the treatment of retinal diseases exceeded $15 billion in 2020 globally. We believe a substantial majority of these sales were in connection with the treatment of wet AMD and DME. Avastin is also used off-label in over 50% of the wet AMD patients in the United States, therefore the potential therapeutic market is greater than reported. The wet AMD market has historically grown by approximately 8% because of an aging population and lack of preventative procedures.

Despite the significant benefits of existing therapeutic options, the need for frequent intravitreal injections is burdensome for both patients and retinal specialists. Retinal practitioners surveyed by the American Society of Retinal Specialists responded that their three greatest unmet needs are availability of long-acting sustained drug delivery, therapies that reduce treatment burden and new treatment mechanisms of action. According to a 2019 study of patient interviews in the United States, France and Australia, the factors affecting adherence from the patient perspective included the psychological burden of repeated intravitreal injections, the time burden of both treatment and monitoring visits for both patients and caregivers, which could take up to 12 hours per visit including travel time.

In clinical trials, intravitreal injections of anti-VEGF drugs resulted in significant gains in visual acuity for patients with retinal diseases. However, in settings outside of clinical trials, patients often receive less frequent injections than in clinical trial settings. Long-term observational studies in the United States, Europe and Japan have demonstrated that many patients with wet AMD lose visual acuity due to the challenges associated with receiving anti-VEGF injections at an optimal frequency.

The diagram below shows the declining visual acuity, or VA, results over four years after the first anti-VEGF injection in patients with wet AMD in the United States.



Most recently, it was shown that fluctuations between injections in retinal thickness in eyes receiving treatment for wet AMD is adversely associated with visual outcomes.

Diabetic retinopathy

Diabetic retinopathy, or DR, is the leading cause of acquired vision loss in the young and middle-aged adult population. Of an estimated 463 million people with diabetes mellitus, or DM, worldwide, approximately one-third have signs of DR and of these, a further one-third experience vision-threatening DR. Mild, or non-proliferative diabetic retinopathy (NPDR) is the first stage of diabetic retinopathy which is often asymptomatic but shows blocked or abnormal blood vessels, such as microaneurysms. Without good control of diabetes, patients can develop diabetic macular edema, or DME, and/or proliferative diabetic retinopathy (PDR). DME affects central vision and can lead to a decline in vision ranging from slight visual blurring to blindness, substantially affecting independence and quality of life. If left untreated, DME is the most common cause of vision loss in patients with DR. The abnormal blood vessels (neovascularization) in PDR can lead to reduction of vision and, if left untreated, eventually to retinal detachment and blindness.

The figure below illustrates the primary effects of diabetic retinopathy with diabetic macular edema compared to a healthy eye.

Our market opportunity in DR

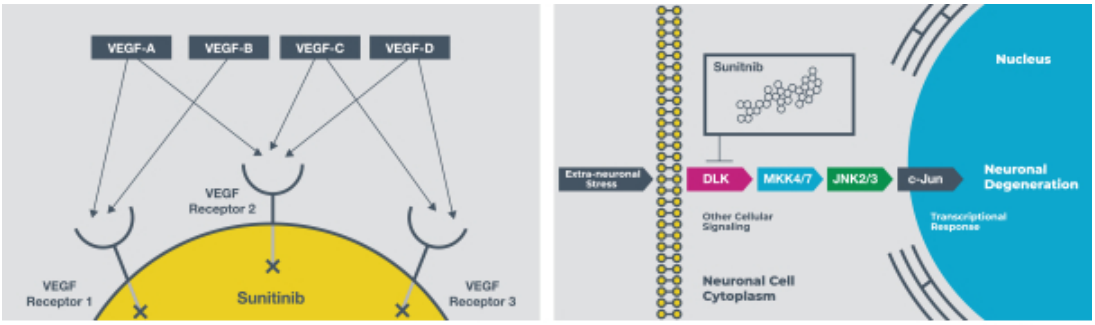
Approximately 30 million people in the United States have diabetes, 10 million of whom suffer from DR, including 1.5 million with DME. DME is the second largest market for anti-VEGF therapies, accounting for approximately $3.8 billion of sales worldwide and approximately $1.1 billion in the United States in 2020. It is estimated that there are three times as many DR patients as there are DME patients, which illustrates the commercial attractiveness of the DR indication for which short-acting anti-VEGFs have been recently approved. Multiple trials have shown that anti-VEGFs are also beneficial for the treatment of DR without DME; however, the need for frequent injections and follow-up in this often asymptomatic population leads to inadequate compliance and subsequent vision loss.

Our product candidates

GB-102

GB-102 is a potent small molecule multiple receptor tyrosine kinase inhibitor sunitinib malate, or sunitinib, formulated in our proprietary microparticles and designed to be administered intravitreally once every six months. Prior to administration, GB-102 is suspended in a buffered diluent and injected intravitreally in a manner similar to the standard in clinical practice with anti-VEGFs. After injection, sunitinib is gradually released from the microparticle formulation into the vitreous chamber and is designed to sustain therapeutic drug levels in the ocular tissues for up to six months. Sunitinib also has a high binding affinity to the natural melanin pigment granules in the retina that allows the retinal pigmented epithelium, or RPE, to serve as a potential secondary drug reservoir and extend duration of action.

Sunitinib is an orally administered treatment for advanced renal, gastric and pancreatic malignancies that was originally approved in 2006. Oral sunitinib has demonstrated efficacy in murine laser choroidal neovascularization, or CNV, models and in wet AMD patients for the treatment of their cancers. However, because of a boxed warning related to hepatotoxicity for cancer indications, oral sunitinib has not been used for retinal indications. There are no reported cases of retinal toxicities in patients receiving continuous oral sunitinib for up to six years for the management of primary malignancies. In our preclinical and clinical studies, we have demonstrated that there are no detectable levels of sunitinib in the plasma after intravitreal injections of GB-102. Sunitinib's mechanism of action is the inhibition of receptor tyrosine kinases, specifically of VEGF receptors 1, 2 and 3, blocking all VEGF signals, including VEGF-A, -B, -C and -D and placental growth factor, or PlGF, which are ligands implicated in pathologic neovascularization in patients with wet AMD. Moreover, sunitinib is a DLK-inhibitor, which may result in a neuroprotective effect.



Siu (2018) Zack (2011 2012)

Our clinical trials

Phase 1/2a trial of GB-102 in patients with wet AMD

In January 2019, we completed our Phase 1/2a clinical trial of GB-102 in patients with wet AMD, or our ADAGIO trial. This trial enrolled patients with wet AMD diagnosed less than 18 months prior to enrollment who had received at least three prior injections of any anti-VEGF treatment and demonstrated a response to anti-VEGF treatment, defined as physician-reported improvement in vision or reduction in macular thickness. Eligible patients received a single injection of GB-102 and were followed for eight months. Monthly assessments included adverse events, best-corrected visual acuity, or BCVA, using the Early Treatment of Diabetic Retinopathy Study, or ETDRS, protocol letter score, central sub-field thickness, or CST, slit-lamp biomicroscopy, dilated fundoscopy and plasma blood samples to detect systemic levels of sunitinib. Patients were eligible for supportive anti-VEGF treatment if any of the following criteria were met: ≥ 10 letter loss in BCVA (ETDRS) with new or increasing intra- or sub-retinal fluid judged to be the cause in the reduction in BCVA; an increase of ≥ 75 µm in CST from baseline; new onset vitreous hemorrhage.

In the ADAGIO trial, GB-102 met its primary endpoint of safety and tolerability with no ocular SAEs or dose limiting toxicities. Our data demonstrated that for patients who required an average of eight injections per year to control their disease, a single injection of GB-102 at various doses was able to maintain their central retinal thickness and visual acuity for six months or more, while significantly reducing the frequency of injection. The overall best performing dose was the 1 mg, which controlled the disease in seven out of eight patients for six months, and in four out of eight patients beyond eight months.

Since the most commonly reported ocular AE was presence of medication in the anterior chamber, we optimized the manufacturing process for GB-102 to enhance the binding affinity of the microparticles' surface, thus improving their ability to aggregate post injection. This optimized version of the microparticles was used for the Phase 2a Macular Edema and Phase 2b ALTISSIMO trials.

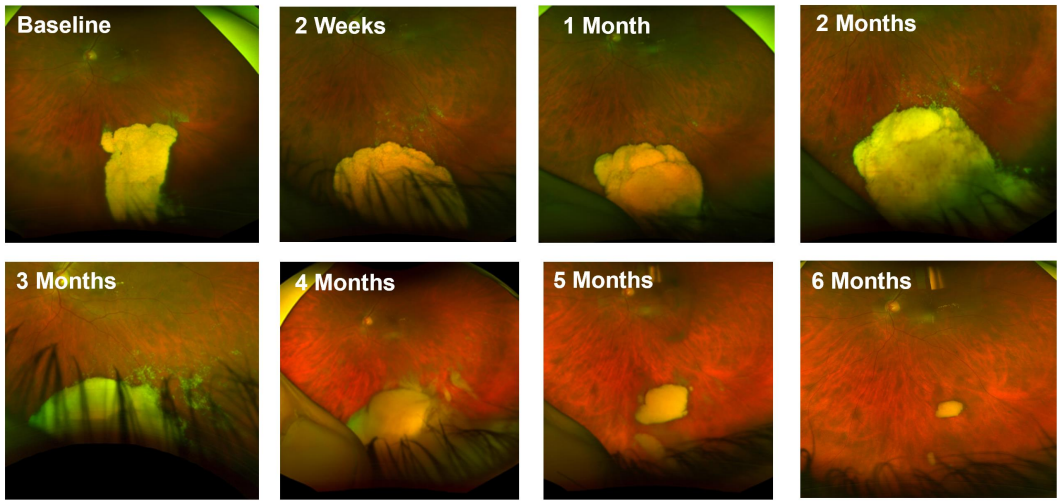
Phase 2 clinical trials

Phase 2a trial of GB-102 in ME secondary to DME or RVO. In September 2019, we initiated a Phase 2a clinical trial of GB-102 in 21 patients with ME secondary to DME and RVO. This trial was designed to be a six-month, single injection, multicenter, open-label, parallel arm trial with a primary endpoint of safety and tolerability of two dose levels of GB-102 (1 and 2 mg).

Six centers in the United States enrolled 21 patients (n=10 DME; n=5 BRVO; n=6 CRVO) who had received at least three prior injections of anti-VEGF and shown at least some response within the last 24 months. In addition to the primary safety and tolerability endpoints noted above, secondary endpoints of the ME study were pharmacodynamics measures including mean change from baseline in BCVA (ETDRS), mean change from baseline in CST (SD-OCT), and time to rescue treatment. As the focus of the ME trial was safety, disease control was not a requirement at enrollment, and patient eligibility was not verified by independent third parties. On average, at enrollment, patients required eight injections per year to control their disease. Eligible patients received GB-102 (1 or 2 mg) at day 1 and were followed monthly.

There were no drug related non-ocular AEs in the trial. The 1 mg dose met its primary endpoint of safety and tolerability with seven out of ten patients demonstrating no adverse events. One patient had only vitreous floaters and one patient had vitreous floaters, medication present in the vitreous, and reduction in vision. The other AEs occurred in a single patient with medication present in the anterior chamber. The 2 mg dose was associated with medication present in the anterior chamber of five out of 11 patients. The majority of AEs occurred in these patients. Two SAEs were reported in a single patient (severe vision loss due to presence of medication in the anterior chamber and corneal edema as a result of wash-out of the anterior chamber). On the basis of an interim analysis performed at month 3 in the ME trial, it was determined that the 1 mg dose was well-tolerated. We believe that the number of microparticles injected

in the 2 mg dose (approximately 2 million) were too many to allow adequate aggregation. The graphic below, photographed using wide field color fundus photography, represents an example of progression of the GB-102 1 mg depot throughout the six-month observation period.



The table below summarizes the drug-related adverse events reported in the ME trial.

Drug-Related AE-Preferred Term	1 mg (N=10)	2 mg (N=11)
Ocular SAE/Dose limiting Toxicity	0	1
Visual acuity reduced	2	5
Vitreous floaters	2	3
Medication in AC	1	5
Medication residue present in vitreous	1	3
Ocular hyperemia	1	0
Eye pain	1	3
Vision blurred	2	1
Eye swelling	1	1
Visual impairment		2
Lacrimation increased		1
Pupils unequal		1
Posterior uveitis		1
Iritis/iridocyclitis/anterior uveitis		3
Conjunctival redness		1
IOP increased		2
Corneal edema		1

These results provided additional support for terminating further development of GB-102 2 mg dose.

Phase 2b trial

We initiated the Phase 2b clinical trial of GB-102 in patients with wet AMD (ALTISSIMO trial) in September 2019 and reported topline data from the 12-month treatment phase in March 2021 (the Core Study). ALTISSIMO was a 12-month, multicenter, prospective, double-masked, randomized (3:3:2), 3-parallel arm trial comparing two doses of GB-102 (1 and 2 mg) administered every six months to aflibercept administered every two months in patients with anti-VEGF-responsive wet AMD. GB-102 subjects were injected on the first day of the study (D1, or Baseline) and at their six-month visit (M6, or Month 6) and were followed for a total of 12 months. Eligible subjects were offered monthly monitoring visits for an additional six months during the Extension Study. The results of the Extension Study were communicated in September 2021.

Similar to the population in the ADAGIO trial, key eligibility criteria included patients with wet AMD diagnosed less than 18 months prior to enrollment, who had received at least three prior injections of any anti-VEGF and demonstrated response to anti-VEGF treatment, defined as physician-reported reduction in macular thickness. In addition, those patients received an anti-VEGF injection within 21 days of screening. Eligible patients received either GB-102 (1 or 2 mg) or aflibercept at day one and were followed monthly for 12 consecutive months during the Core Study. Monthly assessments included adverse events, BCVA, CST, complete ophthalmic examination, wide-field fundus photography and plasma blood samples to detect systemic levels of sunitinib.

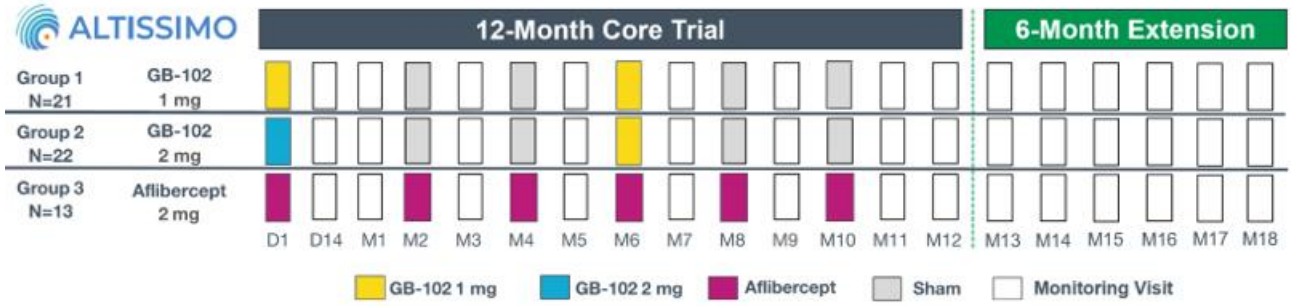
Patients were eligible for additional anti-VEGF supportive therapy (aflibercept) if they met the following prespecified criteria:

- Decrease in BCVA (any of the following criteria):
  - ≥ 5 ETDRS letter decrease compared with the average of last 2 visit BCVA ETDRS letter scores, and/or,
  - ≥ 10 ETDRS letter decrease compared with best on-study BCVA ETDRS letter score.
- Increase in CST (any of the following criteria):
  - ≥ 75 µm compared with the average of the last 2 visit CST measurements (µm), and/or,
  - ≥ 100 µm compared with the lowest on-study CST measurement (µm).

We initially designed the ALTISSIMO trial to enroll 160 patients and initiated the trial in September 2019. In December 2019, we voluntarily paused enrollment as a precautionary measure following the report of a single patient experiencing SAEs with the 2 mg dose in the Phase 2a trial of GB-102 in ME patients, as noted in the table above. Interim safety analyses of the macular edema trial demonstrated that five out of 11 patients in the 2 mg dose had medication in the anterior chamber as compared to one patient in the 1 mg dose. We then performed an ad-hoc interim safety analysis of ALTISSIMO in February 2020. In order to preserve data integrity, trial personnel including investigators, patients, study technicians and reading center remained masked at all times. No drug related SAEs were reported in ALTISSIMO. Presence of medication in the anterior chamber was reported in four patients in the GB-102 2 mg dose group and one patient in the 1 mg dose group.

Based on the number of patients in the 2 mg dose group who had medication in the anterior chamber in our ME and the ALTISSIMO trials, we decided to terminate the development of the GB-102 2 mg dose in all of our clinical trial programs. In addition, we capped enrollment in the ALTISSIMO trial at 56 patients as we had sufficient patients to explore repeat dosing with the GB-102 1 mg dose. We amended the protocol of the ALTISSIMO trial to ensure the GB-102 1 mg dose was used for re-dosing of all patients on GB-102 at month six, regardless of their original dose assignment. Finally, following discussions with the FDA, we shifted the primary endpoint—median time to first additional anti-VEGF supportive therapy—from month 10 to month 12. On the basis of a safety analysis of the ME trial and interim safety data in the ALTISSIMO trial, we terminated the development of the GB-102 2 mg dose in all of our clinical trial programs and amended the protocol of the ALTISSIMO trial, so that patients who had received a first dose of GB-102 2mg would be re-dosed with GB-102 1mg at their M6 visit.

The revised ALTISSIMO trial design is provided in the figure below:



A total of 56 patients were randomized with 21 patients receiving GB-102 1 mg/1 mg (Group 1), 22 patients receiving GB-102 2 mg/1 mg (Group 2), and 13 patients receiving aflibercept bimonthly as per label (Group 3). D1, or Day 1, indicates the first visit for each patient at which the patient was dosed with the drug for the study arm to which they were randomized; a safety monitoring visit occurred approximately two weeks (D14) following each patient's first injection, after which all study visits were monthly (M1, M2 and so on).

In December 2020, a total of 50 out of the 56 patients that enrolled (89.3%) completed the study through M12, and 6 patients (10.7%) discontinued prematurely due to reasons unrelated to the study medication. 28 patients continued into the Extension Study (11 patients in Group 1; 11 patients in Group 2 and 6 patients in Group 3).

The main safety endpoint was the occurrence of ocular and non-ocular AEs and SAEs. A higher proportion of patients in the GB-102 groups reported drug-related AEs in the study eye compared to patients in the aflibercept group. In the GB-102 groups, the majority of drug-related AEs in the study eye were mild or moderate in severity. AEs in the study eye that were considered by investigators to be related to study drug were reported in 17 patients (77.3%) in Group 2, 9 patients (42.9%) in Group 1 and no patients in Group 3.

The majority of patients in Group 1 (those receiving GB-102 1mg/1mg, the intended dose for future clinical trials) had no drug related AEs. Out of the 9 patients with drug-related AEs, four patients had vitreous floaters which were transient in nature, mostly noted after the first dose and were only associated with blurring of vision in one patient. Two patients had the majority of the AEs, both related to dispersion of particles and concurrent inflammation.

The amount of time between treatment and the need for subsequent treatment is known as duration. Of the 21 patients in Group 1, 48% (10 patients) achieved duration of 6 months or more and experienced an average 58% reduction in the annualized frequency of injections required to manage their disease, as compared to their treatments prior to entering the trial. Of the Group 1 patients who enrolled in the Extension Study, 55% of those patients (6 of 11) did not receive rescue treatment until Month 18 representing an average 73% reduction in the annualized frequency of injections required to manage their disease, as compared to their treatments prior to entering the trial.

CST was controlled by both GB-102 (1 mg/1 mg) and GB-102 (2 mg/1 mg) within about 50 μm of aflibercept. The mean BCVA trended lower as compared to aflibercept in both GB-102 groups. The decrease in BCVA was mainly driven by 4 subjects in Group 1. These subjects had a combination of high anti-VEGF need prior to enrollment, particle dispersion during the study, or AEs unrelated to the drug. It is likely that patients who require frequent high dose anti-VEGF injections to control their disease are not the best candidates to receive extended-release formulations such as GB-102 1mg.

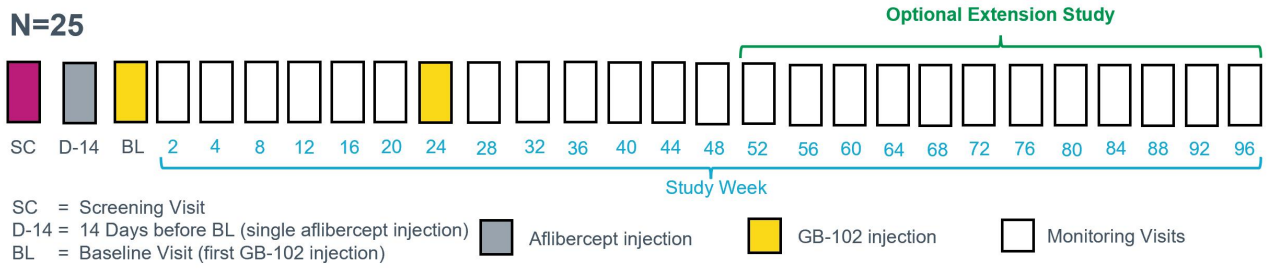
We believe that reduction in particle dispersion will likely lead to a better safety and efficacy profile in a future clinical trial. We have developed a reformulation of the diluent used in GB-102 1 mg to increase the speed at which the microparticles aggregate immediately following their injection into the eye. We have conducted preclinical studies of this reformulated diluent in anticipation of submitting an IND amendment in the second half of 2022. We have not modified the composition or manufacturing methods of the microparticles from those used in ALTISSIMO.

Our future development plans

Pending positive feedback from the FDA on our amended IND application, we expect that an additional Phase 2 study to evaluate the safety, efficacy and durability of GB-102 1mg, with the reformulated diluent, in non-naïve wet AMD patients could substantially mitigate the risk of proceeding to Phase 3 studies. We believe that the optimal design of this Phase 2 trial requires it to be open label

with only one study arm, and the visual acuity evaluator must be masked. Eligibility criteria will benefit from the lessons learned in ALTISSIMO, and will, among other things, require that patients participating in the study to have been diagnosed with wet AMD within 12 months of screening, treated at least three times with an anti-VEGF within six months of screening, and must have demonstrated good response to such treatments.

The design of the Phase 2 trial is provided in the figure below (numbers in blue indicate weeks from first injection with GB-102):



We expect that this study design will be sufficient to determine whether particle dispersion, which appeared to be most prevalent within three months following each injection of GB-102 1mg in ALTISSIMO, has been satisfactorily resolved by the new formulation.

GB-102: Potential for 6-month or longer duration in DR

Based on the results of the ALTISSIMO trial, GB-102 has demonstrated the potential to maintain therapeutic drug levels in the retinal tissue for up to 12 months from a single intravitreal injection. We believe that GB-102's potential for at least 6-month durability and reduction in frequency of injections could significantly improve the standard of care for DR patients.

The results of an additional Phase 2 study of GB-102 with the reformulated diluent in wet AMD will inform the timing and design of the clinical development program to explore the future development of GB-102 for DR.

GB-401

Disease overview

Glaucoma is an optic neuropathy that is characterized by the progressive degeneration of the optic nerve, leading to visual impairment, and is a leading cause of irreversible vision loss worldwide. POAG is the most common type of glaucoma.

Though the specific mechanism of neuronal damage in POAG has not been fully identified, progressive visual field loss is associated with increased IOP. Chronically elevated IOP can lead to neuronal degeneration and retinal ganglion cell death with resulting disruption of the visual pathway. Increased IOP is caused by the over-production of the clear fluid in the eye behind the cornea, or aqueous humor, and/or decreased drainage of the aqueous humor from the eye. Currently approved topical eye drops can lower IOP by either decreasing aqueous humor production and/or enhancing aqueous humor drainage when used as directed by a physician. These medications must be administered up to four times per day, and it is estimated that approximately 30% of patients often require more than one medication.

In the healthy eye, the ciliary body produces fluid that circulates through the pupil and drains in the corner, or the angle, of the eye where the cornea and iris meet. In POAG, pressure in the eye can increase if there is increased fluid production and/or decreased drainage in the angle leading to elevated IOP. Chronically elevated IOP can lead to neuronal degeneration and retinal ganglion cell death with resulting disruption of the visual pathway.

Market overview

Glaucoma is a leading cause of irreversible vision loss affecting approximately 76 million people worldwide in 2020, including approximately 2.7 million people in the United States. The global POAG therapeutics market is estimated to reach approximately $3.8 billion in 2026, of which the United States represents approximately $2.9 billion.

Various drug classes for glaucoma therapy include prostaglandin analogs, or PGAs, beta-blockers, alpha-adrenergic agonists, carbonic anhydrase inhibitors, rho-kinase inhibitors, combination drugs and others. PGAs are preferred as first-line therapy for glaucoma due to their effectiveness in reducing IOP, once-daily dosing and reduced side effects as compared to other therapies. The PGA segment accounted for a market share of approximately 40% in the United States in 2019 and is expected to remain dominant until meaningfully

superior agents are developed and approved. The second most prescribed class of eye drops is beta-blockers, however, these have a less favorable systemic side effect profile, including decreased heart rate, slowed breathing rate and decreased blood pressure.

A number of procedures have been developed to treat patients whose disease has significantly progressed. These include laser or surgical treatments reserved for patients for whom other measures have failed.

Unmet need

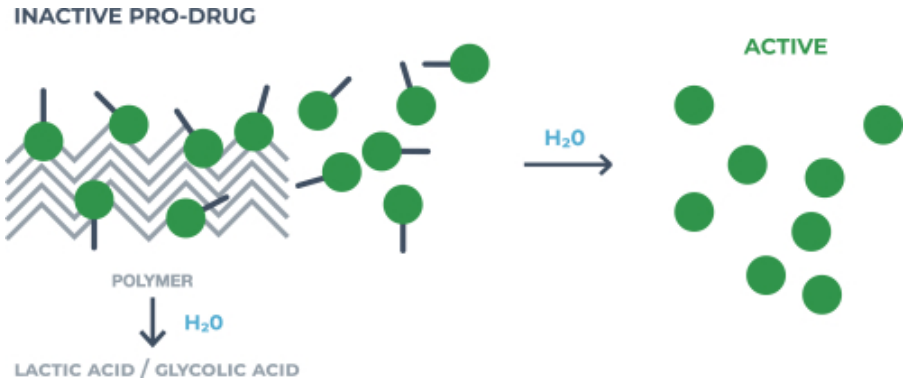
Importance of greater compliance in glaucoma is considered a large unmet need. It is estimated that approximately 50% of patients stop taking their glaucoma medications within the first six months of treatment initiation due to various reasons, including forgetfulness, lack of disease awareness and/or cost. Poor adherence to glaucoma medication regimens has been documented in numerous independent studies, particularly in patients on two or more prescription eye drops. Additionally, studies show that more than 30% of patients often require more than one medication.

Furthermore, because glaucoma progresses slowly and causes few symptoms, patients often do not adhere to their medication regimens as prescribed until the disease has progressed to the point of significant vision loss. As a result, despite the availability of medication to treat glaucoma, progressive visual loss and blindness still often occur. According to a 2015 analysis published in the Translational Vision Science & Technology Journal, 15% to 20% of glaucoma patients progress to blindness within 15 to 20 years of diagnosis.

Our goal is to provide sustained reduction of elevated IOP associated with POAG to increase compliance for patients and improve the medical management of glaucoma. For patients, our goal is to eliminate the need for daily eye drops required to manage elevated IOP. For physicians, our goal is to design a long-acting IOP-lowering treatment that can be administered in the office through intravitreal injections, ensuring patient compliance for up to six months.

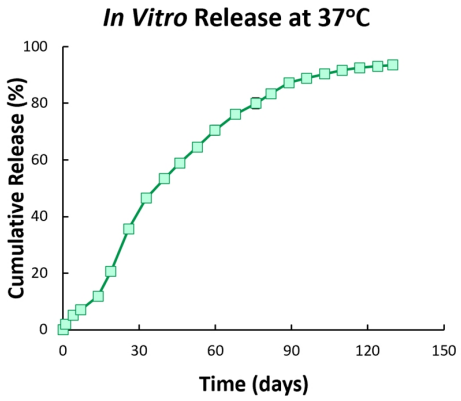
Our solution

GB-401 has the potential to reduce elevated IOP for up to six months. GB-401 contains a proprietary new chemical entity, or NCE, prodrug of a beta-adrenergic receptor inhibitor, or beta-blocker, formulated with our biodegradable polymer implant technology for controlled release and is designed to be administered intravitreally once every six months. Upon exposure to water under physiological conditions, the prodrug is released from the implant and is converted into the active beta-blocker by hydrolysis. The polymer biodegrades into normal metabolic by-products of lactic and glycolic acid and is naturally cleared from the eye.

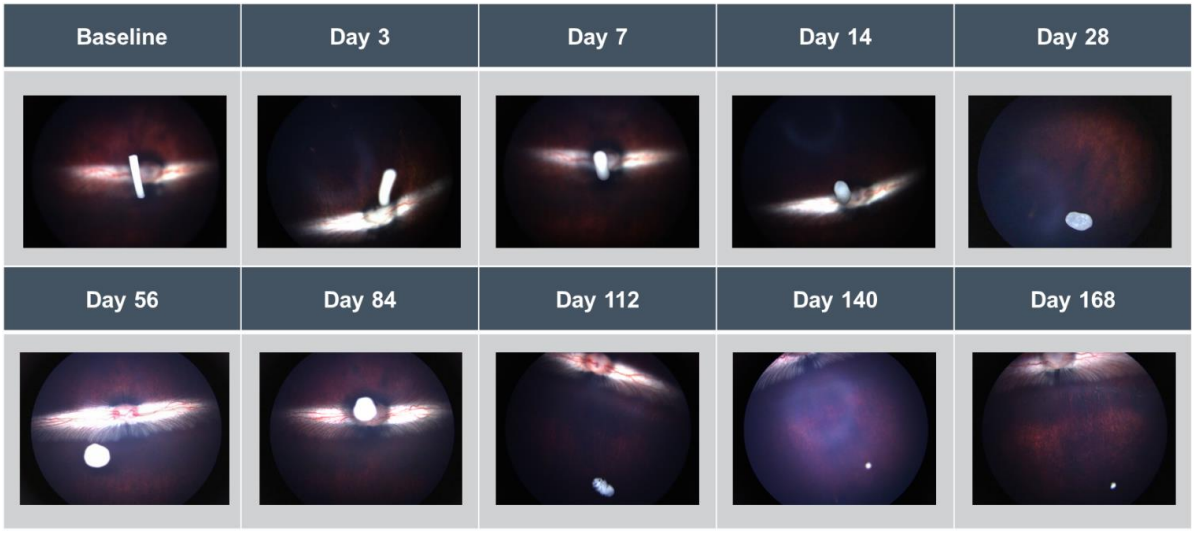


Our proprietary implant formulation of GB-401 is designed to provide controlled drug release within the eye that minimizes the risk for systemic exposure of the beta-blocker, a class of drugs known to have significant risks of cardiac side effects when administered topically, such as with eye drops. The figure below illustrates sustained *in vitro* drug release from the GB-401 implant for approximately 120 days at 37° C. We have successfully completed preclinical studies to evaluate the potential pharmacokinetics of GB-401. There is,

however, a lack of validated animal models for reliably predicting long-term pharmacokinetics and pharmacodynamics in humans in the treatment of glaucoma using beta-blockers, so preclinical results may not be predictive of human clinical results.



In a preclinical study in rabbits, the biodegradability of GB-401 implant was visually assessed over a period 24 weeks, or 168 days. Similar to prior experiences with GB-102 microparticles, which demonstrated a durability of six months for approximately half of the patients studied in clinical trials while appearing to be nearly biodegraded within approximately four months in rabbits, the GB-401 implants also appeared to be substantially biodegraded in rabbit eyes within four months post injection. The images below are representative color fundus photographs from different animals at different timepoints.



Beta-blockers have been used as the comparative control for the approval of topical agents for IOP reduction, including PGAs, carbonic anhydrase inhibitors, rho-kinase inhibitors and alpha-adrenergic receptor agonists. Beta-blocker eye drops must be administered once or twice daily and often produce systemic exposure which can lead to decreases in heart rate, blood pressure and respiratory function. Though prostaglandins are the leading class of agents used to reduce IOP, evidence suggests that continuous exposure may lead to loss of IOP reduction effects that may be due to receptor fatigue from continuous stimulation, as well as poor compliance due to topical side effects.

We believe that GB-401 has the potential to provide sustained reduction in IOP for up to six months, thus eliminating the need for frequent patient-instilled eye drops and potentially improving patient compliance in this vision-threatening disease. GB-401 could also improve tolerability by reducing ocular hyperemia (red eyes due to irritation) and sunken eye (reduction in peri-orbital fat), which are common side effects for PGAs and rho-kinase inhibitors, while eliminating systemic drug exposure. Therefore, we believe our proprietary beta-blocker technology represents a validated but differentiated pharmacological approach.

We have also developed a proprietary custom applicator that is designed to enable convenient and safe injection of the GB-401 implant in the vitreous.

Our future development plans

We may pursue clinical development for GB-401 under the 505(b)(2) regulatory pathway, which would obviate the need to conduct certain preclinical toxicology and safety studies. If we decide to use the 505(b)(2) pathway, we would rely in part on the FDA's prior findings for the previously approved active pharmaceutical ingredient, or API, as well as relevant publications, and to complete a repeat-dose GLP toxicology study with GB-401, to support the filing of an IND for GB-401 and any future 505(b)(2) new drug application, or NDA. At the time of NDA submission, we expect to provide the FDA with all required nonclinical elements in the NDA either directly through original studies, published literature, and the FDA's prior findings as reflected in the approved labeling for the previously approved API which contains the same API as GB-401. We plan to initiate a first-in-human, multicenter, open-label, sequential escalating dose-cohorts Phase 1/2a clinical trial evaluating the safety, tolerability and pharmacodynamic effects of a single intravitreal injection of GB-401 in patients with POAG in the first half of 2023. The primary endpoint will be the occurrence of ocular and non-ocular adverse events. Secondary endpoints will include pharmacodynamic evaluation of IOP. If we pursue the 505(b)(2) pathway, we would expect to rely upon this Phase 1/2a clinical trial, as well as two Phase 3 trials, which we currently envision as multi-center, randomized, double-blind trials with dosing once every 6 months in patients with POAG or ocular hypertension, with approximately 350 to 600 participants per trial. The final Phase 3 trial designs and sample sizes will be determined based upon our ongoing discussions with the FDA and the results of the Phase 1/2a trial.

Commercialization

We currently have no sales, marketing or commercial product distribution capabilities. We intend to secure a partner to fund and complete Phase 3 development of GB-102 and, if approved, commercialize it in the territories in which GB-102 would be licensed out.

If GB-401 receives marketing approval, we plan to commercialize it in the United States with our own specialty sales force, which we would expect to range from 50 to 125 sales representatives. We will also explore a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties in markets outside the United States.

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, generic drug 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.

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 organizations compete with us for 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 GB-102, if approved, are likely to be its efficacy, safety, method and frequency of administration, on-mechanism durability of therapeutic effect, convenience, price, level of generic competition and availability of coverage and reimbursement from government and other third-party payors. The method of administration of GB-102, 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 efficacy, safety and durability of the other method of administration.

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness among people who are 50 years of age or older in the industrialized world. Current anti-vascular endothelial growth factor (VEGF) treatments have proven to be safe and effective in restoring vision, but they require frequent injections to maintain the visual acuity gain (every 4 weeks with ranibizumab, every 4 to 8 weeks with aflibercept, and every 8 to 12 weeks with brolucizumab). This frequency of injection puts an enormous burden on the patients, their caregivers, physicians, and the healthcare system overall. As a result, many patients do not receive frequent injections, which leads to suboptimal visual acuity. An annual survey conducted for retinal specialists worldwide by the American Society of

Retinal Specialists (ASRS) reported that in wet AMD therapeutics, the greatest unmet needs is for “long-lasting therapies”, further reinforcing the need for durable intervention.

The current standard of care for wet AMD is monotherapy administration of anti-VEGF drugs, principally Avastin (bevacizumab), Lucentis (ranibizumab), and Eylea (aflibercept), which are well-established therapies and are widely accepted by physicians, patients and third-party payors. Beovu was approved in 2019 and demonstrated superior durability to the current standard of care but, due to rare but blinding complication of vascular occlusion, is being used as the 2nd line therapy

Recently, faricimab, a bispecific antibody against VEGF and Angiopoietin-2(Ang-2), was approved for the treatment of wet AMD and DME in the U.S. and is marketed under the trade name VABYSMO. Faricimab has the potential to prolong the existing treatment intervals with its demonstrated disease control of up to 16 weeks (VABYSMO Prescribing Information). The recent approval of the Port Delivery System (PDS) with ranibizumab, marketed under the trade name SUSVIMO, allows delivery of a steady dose of ranibizumab for 6 months or longer can further extend the injection intervals. In clinical trials of SUSVIMO, 98.4% of patients did not require supplemental intravitreal treatment for at least 24 weeks, however, SUSVIMO requires surgical intervention that may impose additional burden overall and is associated with AEs from the surgical procedure, including a boxed warning for endophthalmitis (SUSVIMO Prescribing Information 2021). Therefore, sustained, predictable disease control with infrequent injection remains an unmet need.

Kodiak Sciences is also developing KSI-301 and is in the phase 2b/3 trials for treatment of wet AMD, DME and RVO, but has recently announced that the first Phase 2b/3 trial of KSI-301 in wet AMD failed to meet its primary endpoint. REGENEXBIO is also developing a suprachoroidal or subretinal gene therapy that delivers anti-VEGF and is currently in phase 3 treatments for wet AMD, and Regeneron Pharmaceuticals is currently in a phase 3 trial of a higher dose of aflibercept, the active ingredient in Eylea. Results from the Regeneron Pharmaceutical trials are expected in 2022. Physicians, patients, and third-party payors may not accept the addition of GB-102 to their current treatment regimens for a variety of potential reasons, including:

- if they do not wish to incur the additional cost, if any, of GB-102;
- if they perceive the addition of GB-102 to be of limited benefit to patients compared to existing treatment options;
- if sufficient coverage and reimbursement are not available; and
- if they do not perceive GB-102 to have a favorable risk-benefit profile.

We are developing GB-102 as an alternative to existing anti-VEGF drugs, including Avastin, Lucentis, Eylea, Beovu, VABYSMO, and SUSVIMO. Accordingly, GB-102 would directly compete with these therapies. While we believe GB-102 will compete favorably with existing anti-VEGF drugs, future approved standalone or combination therapies for wet AMD and for DR with demonstrated improved efficacy over GB-102 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 twice-yearly intravitreal injection;
- a method of administration that effectively avoids intravitreal injection; and
- significant cost savings or reimbursement advantages compared to GB-102 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. An anti-VEGF gene therapy product might substantially reduce the number and frequency of intravitreal injections when treating wet AMD and DR, making GB-102 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.

We expect that product candidates currently in clinical development, or that could enter clinical development in the near future, could represent competition, if approved. These product candidates may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. Because there are a variety of means to treat wet AMD and DR, our patents and other proprietary protections for GB-102 will not prevent development or commercialization of product candidates that are different from GB-102.

Manufacturing

We have neither large-scale manufacturing facilities nor personnel, other than personnel who manage our contract manufacturing organization, or CMO, relationships. We currently rely, and expect to continue to rely, for the next few years, on third parties for the manufacture of certain components of our product candidates undergoing preclinical testing and clinical testing. We are establishing low-volume good manufacturing practice, or GMP, manufacturing capability to support our Ph 1/2a clinical trial of GB-401 and the next Phase 2 clinical trial of GB-102. We have contracted with a single contract manufacturing and development organization to design, develop, and manufacture a proprietary applicator for our GB-401 implant.

Our drug candidates include small molecules and are manufactured in synthetic processes from base materials. We purchase our drug substances from reliable sources and we believe that our microparticle and implant manufacturing processes are amenable to scale-up. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities. We anticipate that these arrangements will be sufficient for the manufacture of our product candidates until such time that we decide that we should establish our own large-scale manufacturing facility and it becomes operational.

Until we believe it is prudent to establish our own large-scale manufacturing facility, we will continue to rely on CMOs for parts of the drug manufacturing process, such as filling and labelling of our products for commercial sale and the manufacture of implant applicators. While we believe that having control over the whole manufacturing process would allow us to reduce cycle times, increase the robustness and consistency of the process and reduce cost of goods for commercial production, we also believe that investing in a dedicated manufacturing facility at this time would not be an efficient use of our capital.

Intellectual property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our therapeutic products for ocular diseases, which include our novel microparticle aggregation and implant technologies, to deliver known active agents such as sunitinib as well as our novel prodrugs such as the one in GB-401. We also seek to protect our proprietary methods of treatment using our delivery technologies for ocular disease, alone and in combination with other therapeutic agents. In addition, we seek protection on processes for the production of our aggregating microparticles and implants, and dosing regimens and formulations for the ocular administration of our products. Our success also depends on our ability to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary rights.

Our policy is to seek to protect our proprietary position by filing, purchasing, or exclusively in-licensing U.S. and foreign patent applications covering our proprietary technologies, active pharmaceutical ingredients, inventions, and improvements that are important to the development and implementation of our business. In addition, we currently plan to seek patent term adjustments, restorations and/or patent term extensions where applicable in the United States, Europe and other jurisdictions. We also rely on trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. Additionally, we expect to benefit, where appropriate, from statutory frameworks in the United States, Europe and other countries that provide a period of regulatory data exclusivity to compensate for the time required for regulatory approval of our drug products.

We are the sole owner of eleven patent families covering our products, active pharmaceutical ingredients, and proprietary aggregating microparticle technology, which include composition of matter, methods of use and processes of manufacture, as described in more detail below. Our owned patent estate as of December 31, 2021, on a worldwide basis, includes over 60 granted or pending patent applications with nine granted U.S. patents, one allowed U.S. patent application, eleven pending U.S. non-provisional applications, one pending international patent application filed under the Patent Cooperation Treaty and more than 40 pending patent applications that have entered the national phase of prosecution in countries outside the United States.

We have exclusively licensed five patent families from Johns Hopkins University, or JHU, described below, and have granted an exclusive sublicense to Kala Pharmaceuticals, Inc., or Kala, solely in the area of delivery through a mucosal barrier for the five families licensed from JHU only. Our patent estate exclusively licensed from JHU as of December 31, 2021, on a worldwide basis, includes 43 granted or pending patent applications with ten granted U.S. patents, four pending U.S. non-provisional applications and 30 pending or granted patents that have entered the national phase of prosecution in countries outside the United States.

We have acquired two patent families and licensed one patent family from a private company for the treatment of disorders of the ear and eye, including retinitis pigmentosa, Stargardt’s Disease, and Leber’s congenital amaurosis. The two patent families that we acquired have also been licensed back to the private company for their use in non-overlapping therapeutic areas. As of December 31, 2021, this acquired patent estate includes two pending U.S. non-provisional applications and five pending patent applications that have entered the national phase of prosecution in countries outside the United States.

We continually assess and refine our intellectual property strategies as we develop new technologies and product candidates. We plan to file additional patent applications based on our intellectual property strategies where appropriate, including where we seek to adapt to competition or to improve business opportunities. Further, we plan to file patent applications, as we consider appropriate under the circumstances, to protect new technologies that we develop. Our patent filing strategy generally includes seeking patent protection

in the United States, the European Union and China (which may include Macau and Hong Kong) and may in addition seek protection in countries where we believe such protection is likely to be useful, including one or more of Argentina, Australia, Brazil, Canada, countries of the Gulf Cooperation Council, India, Israel, Japan, Mexico, Russia and Taiwan.

The exclusivity terms of our patents depend upon the laws of the countries in which they are obtained. In the countries in which we currently file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. The term of a U.S. patent may be extended to compensate for the time required to obtain regulatory approval to sell a drug, referred to as a patent term extension, or by delays encountered during patent prosecution that are caused by the PTO, referred to as patent term adjustment. For example, the Hatch-Waxman Act permits a patent term extension for FDA-approved new chemical entity drugs of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review and diligence during the review process. Patent term extensions in the United States cannot extend the term of a patent beyond a total of 14 years from the date of product approval, and only one patent covering an approved drug or its method of use may be extended. A similar kind of patent extension, referred to as a Supplementary Protection Certificate, is available in Europe. Legal frameworks are also available in certain other jurisdictions to extend the term of a patent. We currently intend to seek patent term extensions on any of our issued patents in any jurisdiction where we have a qualifying patent and the extension is available; however, there is no guarantee that the applicable regulatory authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. Further, even if our patent is extended, the patent, including the extended portion of the patent, may be held invalid or unenforceable by a court of final jurisdiction in the United States or a foreign country.

Current issued patents and patent applications covering the composition of matter for GB-102 expires on dates ranging from 2031 to 2039, if the applications are issued and held valid by a court of final jurisdiction if challenged. Current issued patents and patent applications covering our clinical candidate GB-401 will also expire on dates ranging from 2031 to 2041, if the applications are issued and held valid if challenged. Our pending applications on additional methods of use of our clinical candidates, should they issue, will expire in 2039. We plan to file additional applications on aspects of our innovations that may have patent terms that extend beyond these dates. However, any of our patents, including patents that we may rely on to protect our market for approved products, may be held invalid or unenforceable by a court of final jurisdiction. Alternatively, we may decide that it is in our interest to settle a litigation in a manner that affects the term or enforceability of our patent. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish our ability to protect our inventions and enforce our intellectual property rights. Accordingly, we cannot predict the breadth or enforceability of claims that have been or may be granted on our patents or on third-party patents. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to obtain and maintain our proprietary position for our microparticle and implant technologies and novel prodrugs will depend on our success in enforcing the claims that have been granted or may grant. We do not know whether any of the pending patent applications that we have filed or may file or license from third parties will result in the issuance of any additional patents. The issued patents that we own or may receive in the future may be challenged, invalidated or circumvented, and the rights granted under any issued patents may not provide us with sufficient protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may be able to independently develop and commercialize drugs with similar mechanisms of action and/or duplicate our methods of treatments or strategies without infringing our patents. Because of the extensive time required for clinical development and regulatory review of a drug we may develop, it is possible that, before any of our drugs can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent.

GB-102 patent coverage

Patents solely owned by us

We own a first patent family that generally describes our proprietary surface modifying microparticle technology that allows the microparticles to remain separate prior to *in vivo* administration and then aggregate *in vivo* into at least one microparticle of at least 500 microns that provides controlled drug delivery. Alternatively, our microparticles can be formed into an implant that is used in the eye. This family consists of one issued U.S. Patent (US 10,441,548) and two pending U.S. applications (US 2020/0000734 and US 2020/0000735) covering the GB-102 aggregating microparticle composition-of-matter and their pharmaceutical compositions. Several pending corresponding patent applications cover methods of use of these aggregated microparticles and their processes of manufacture. This patent family is now also in the national stage of prosecution in Australia, Canada, China, Eurasia, Europe, Hong Kong, and Japan. The expected year of expiration for these composition-of-matter patents, where issued, valid and enforceable, is 2036, without regard to any extensions, adjustments or restorations of term that may be available under national law.

We also own a second patent family that cover additional microparticle formulations and methods of manufacture, including for example suspensions of GB-102 and lyophilized solid GB-102 that have been treated to remove adhered air or gas. It consists of one issued U.S. Patent (US 11,160,870), two U.S. applications, and is currently in the national phase of prosecution in Australia, Canada,

China, Europe, Hong Kong, Japan, and Russia. The expected year of expiration for this patent family, if issued, valid and enforceable, is 2038, without regard to any extensions, adjustments or restorations of term that may be available under U.S. or other national laws.

We own a third patent family that discloses coordinated control of a number of processing factors that result in a significantly harder or more durable aggregated microparticle, and which may be used in the process of manufacture of our GB-102 product. This family includes one U.S application (US 2021/0275456), and foreign applications in Taiwan, Argentina, Japan, Australia, Canada, China, Europe, and Russia. The expected year of expiration for this patent family, if issued, valid and enforceable, is 2039, without regard to any extensions, adjustments or restorations of term that may be available under U.S. or other national laws.

In addition, we own a fourth patent family that discloses various processes for the manufacture of our aggregating microparticles that can be used to manufacture GB-102. The family comprises one U.S. application (US 2021/085607). This patent family is now also in the national stage of prosecution in Australia, Canada, China, Europe, Japan, and Russia. The expected year of expiration for this patent family, if issued, valid and enforceable, is 2039, without regard to any extensions, adjustments or restorations of term that may be available under U.S. or other national laws.

Patent Filings Exclusively Licensed from JHU

We have exclusively licensed from JHU a first patent family that claims microparticles with a hydrophobic polymeric core (such as PLGA or polylactic acid (PLA) or a combination of both PLGA and PLA) and a hydrophilic coating (such as PLGA permanently linked to polyethylene glycol) to reduce inflammation for intraocular injections and their methods of use. This patent family includes four U.S. Patents (US 8,889,193; US 9,566,242; US 9,937,130; and US 10,369,107). This patent family also currently includes one pending U.S. application, , as well as a corresponding patent application in Europe and a granted patent in Canada. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2031, without regard to any extensions, adjustments or restorations of term that may be available under national law.

We have also exclusively licensed from JHU a second patent family, which covers sunitinib-encapsulated polymeric microparticles, including GB-102, and their use as therapeutic compositions to treat disorders of the eye. This patent family currently includes two U.S. pending applications, US 2017/0273901 and US 2019/0275001 and is also pending in Australia, Canada, China, Europe, Hong Kong, Japan, and Russia. The application has been allowed in Australia, Canada, Japan, and Russia. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2035, without regard to any extensions, adjustments or restorations of term that may be available under national law.

A third patent family exclusively licensed from JHU discloses method for reducing neuronal damage in the eye that includes administration of a sustained release formulation of dual leucine kinase inhibitor in a polymeric particle, and wherein the dual leucine kinase inhibitor may be sunitinib. This family consists of two issued U.S. Patents, US 10,525,034 and US 11,013,719, one pending U.S. application, US 2021/0251959, and corresponding applications in Europe, China, Japan and Hong Kong. The application has been allowed in Japan. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2035, without regard to any extensions, adjustments or restorations of term that may be available under national law.

GB-401 patent coverage

We own a fifth patent family that describes the composition of matter of a range of proprietary prodrugs, one of which is a prodrug of a beta-adrenergic receptor inhibitor that is in GB-401. This patent family provides the basis for compound (new chemical entity), pharmaceutical compositions and methods of use of these prodrugs. The family includes one pending U.S. patent application, US 2020/0031783, and corresponding applications in Australia, Canada, China, Europe, Hong Kong, Japan, and Russia. The expected year of expiration for these composition-of-matter patents, where issued, valid and enforceable, is 2038, without regard to any extensions, adjustments or restorations of term that may be available under national law.

We own a sixth patent family that consists of an international application (WO 2021/237096) that describes microparticles and implants with high-drug loadings of GB-401, which we intend to file in the United States and other selected foreign countries on or before the deadline to do so. The expected year of expiration for this patent family, if issued, valid and enforceable, is 2041, without regard to any extensions, adjustments or restorations of terms that may be available under U.S. or other national laws.

The four patent families that we solely own described above covering GB-102 also cover aggregating microparticles that encapsulate GB-401, pharmaceutical compositions of these aggregating microparticles, and methods of use. Therefore, we have six patent families that cover GB-401 as a compound and in an aggregating microparticle, and their uses and manufacture.

In addition, the first patent family exclusively licensed from JHU described above that describes polymeric microparticles has claims that cover GB-401, pharmaceutical compositions of these microparticles, and methods of use.

Patent filings that cover additional novel prodrugs, compositions, uses and manufacture

Patent filings solely owned by us

We also own several patent families that cover additional novel prodrugs, pharmaceutical compositions and methods of use in the area of ocular therapy. We may or may not develop these inventions to commercial products, and we have the possibility to license undeveloped technologies to other entities where advantageous to us.

The seventh patent family covers prodrug derivatives of ethacrynic acid, timolol, brinzolamide and pharmaceutical compositions, and methods of use for ocular disorders, including the lowering of intraocular pressure. The patent family includes one U.S. pending application (US 2020/0308162) and corresponding applications in Australia, Canada, China, Europe, Japan and Russia. The expected year of expiration for these composition-of-matter patents, where issued, valid and enforceable, is 2038, without regard to any extensions, adjustments or restorations of term that may be available under national law.

The eighth patent family covers novel prodrugs of loop diuretics, pharmaceutical compositions, and methods of use for ocular disorders, including the lowering of intraocular pressure. This family includes one U.S. application (US 2021-0040111). The expected year of expiration for this composition-of-matter patent, where issued, valid and enforceable, is 2039, without regard to any extensions, adjustments or restorations of term that may be available under national law.

Our ninth patent family includes one U. S. application (US 2021/0214374) and one patent application filed in Taiwan that covers additional novel prodrugs of sunitinib, brinzolamide, and dorzolamide, pharmaceutical compositions, and methods of use for ocular disorders. The expected year of expiration for these composition-of-matter patents, where issued, valid and enforceable, is 2039, without regard to any extensions, adjustments or restorations of term that may be available under national law.

Patent filings exclusively licensed from JHU

We have exclusively licensed a fourth patent family from JHU that covers hydrophobic-hydrophilic copolymers of HIF-1 inhibitors, pharmaceutical compositions, and method of use for ocular therapeutics. This patent family includes two granted U.S. Patents (US 8,962,577 and US 9,950,072) and corresponding applications in Australia, Canada, China, Eurasia, Europe, Hong Kong and Japan. These applications have granted in Australia, Canada, China, Eurasia, Hong Kong, and Japan. The expected year of expiration for these composition-of-matter patents, where issued, valid and enforceable, is 2033, without regard to any extensions, adjustments or restorations of term that may be available under national law.

We have in addition exclusively licensed a fifth patent family from JHU that covers hydrophobic-hydrophilic copolymers of non-HIF active agents for ocular therapy, pharmaceutical compositions, and method of use. The family includes two granted U.S. Patents (US 10,159,743 and US 10,933,144) and one pending U.S. application (US 2021/0177979) as well as corresponding granted patents in Australia, Canada, China, Eurasia, Europe, Hong Kong and two in Japan. The expected year of expiration for these composition-of-matter patents, where issued, valid and enforceable, is 2033, without regard to any extensions, adjustments or restorations of term that may be available under national law.

Acquired patent families

We have acquired two patent families from a private company. These patent families cover new cyclic monophosphate (cGMP) compounds for the treatment of ocular disorders. The first family is currently pending in the United States, Europe, Canada, and Japan. The second family is currently pending in the United States, Europe, and Japan. The expected year of expiration for these patent applications, where issued, valid and enforceable, is 2037, without regard to any extensions, adjustments or restorations of term that may be available under national law.

License agreements

Johns Hopkins University

In June 2011, we entered into an Exclusive License Agreement with JHU, which has been amended from time to time, which we refer to as the JHU Agreement. Pursuant to the JHU Agreement, JHU granted us an exclusive, worldwide, sublicensable license to three patent families to research, develop, make, use and sell products and provide services in any field, and a non-exclusive license to use specified know-how and materials with a provision that JHU will not grant a license to know how and materials to any other commercial entity. The JHU first patent family describes microparticles with a hydrophobic polymeric core (such as PLGA or PLA or a combination of both PLGA and PLA) and a hydrophilic coating (such as PLGA permanently linked to polyethylene glycol) to reduce inflammation for intraocular injections and their methods of use, which technology is incorporated into our GB-102 product candidate. The JHU licensed fourth and fifth patent families cover potential future technologies. See “Intellectual Property” above for additional description of the JHU patent families.

In September 2015, the JHU Agreement was amended to include the JHU second patent family which covers sunitinib-encapsulated polymeric microparticles, including GB-102, and their use as therapeutic compositions to treat disorders of the eye. Under the terms of the amended JHU Agreement, we paid a one-time, non-refundable upfront fee, with a remaining amount to be paid upon the occurrence of certain events. We also agreed to pay an additional one-time, non-refundable fee of $100,000 on the occurrence of the first commercial sale of a product falling under the claims of a patent in the second patent family.

In April 2016, the JHU Agreement was further amended to include a third patent family which discloses a method for reducing neuronal damage in the eye that includes administration of a sustained release formulation of a dual leucine kinase inhibitor in a polymeric particle, and wherein the dual leucine kinase inhibitor may be sunitinib, and thus is relevant to GB-102. Under the terms of the amended JHU Agreement, we paid a one-time, non-refundable upfront fee, and a milestone payment for the grant of the first patent. We also agreed to use our best efforts to develop a licensed product under the third patent family and enter into a Phase I clinical trial on or before April 2019, and to have cumulatively spent several million dollars on research and development within six years of execution of the amendment.

Upon execution of the JHU Agreement in 2011, we paid JHU an upfront license fee in the low tens of thousands of dollars and issued to JHU a low single digit percentage of our equity interests as of such date. We have also reimbursed JHU for the prosecution and maintenance costs incurred by JHU for the licensed patent rights prior to our entering into the JHU Agreement, and we are responsible for all of the ongoing costs relating to the prosecution and maintenance of the JHU patent rights licensed to us. We also agreed to pay minimum annual royalties in the tens of thousands of dollars per year until the first commercial sale of a licensed product or service.

The JHU Agreement further requires single digit running royalties on our annual net sales, which may be reduced by 50% of any payments we make to third parties for freedom to operate, up to a maximum credit of 50% of the running royalty rate otherwise due to JHU. Royalties must be paid on products that fall within a patent claim of an issued and unexpired patent or a pending patent application that has not been finally rejected or is pending for less than seven years. We also must pay developmental milestones for achieving certain clinical progression events, ranging from tens of thousands to hundreds of thousand dollars per event, which in the aggregate, total less than $2 million per product. Under the JHU Agreement, prior to the Kala Agreement renegotiation described below, we were responsible for paying each developmental milestone payment for the first three products to achieve such milestone, and milestones for the second and third products are reduced by 50%. We further agreed to pay a percentage of any sublicense consideration we receive. Once commercial, we expect ongoing royalties on sales to be in the low single digits.

The JHU Agreement will remain effective until (i) the later of the expiration date of the last-to-expire patents covered under the JHU Agreement or 20 years from the effective date; (ii) the termination by either party upon the bankruptcy or uncured breach of the other party or (iii) if we terminate the JHU Agreement, with a 90-day notification period. We may terminate the entire agreement or on a patent by patent basis if desired, subject to the 90-day notification period.

Kala Pharmaceuticals

A dispute arose between us, JHU and Kala, over rights licensed to us and Kala by JHU. In October 2014, we entered into a Settlement and License Agreement, or the Kala Agreement, with Kala and JHU, which settled all pending disputes and amended our and Kala's existing license agreements with JHU and created new rights and obligations among the parties.

Under the Kala Agreement, each of Kala and us provided the other with a royalty-free, exclusive sublicense with respect to certain intellectual property rights granted by JHU in limited fields of use. Specifically, we provided Kala with an exclusive sublicense for the use of a particle with specific characteristics for delivery of a biologically active material through mucus, mucin or a mucosal barrier (provided that such delivery does not involve administration via injection to the eye), or the Kala Field of Use, and Kala provided us with an exclusive sublicense to the use of a particle with specific characteristics for delivery of a biologically active material to the eye via injection (excluding such use of any particle comprising or consisting of loteprednol etabonate). Kala also agreed not to use a particle with those specific characteristics that include sunitinib in the Kala Field of Use under the license from us or JHU. Neither we nor Kala owe JHU any payments under its existing JHU agreement with respect to the sublicenses granted to the other. Both we and Kala hold rights to sublicense our respective rights in connection with a future collaboration arrangement and subject to any such sublicensee being bound by the applicable terms of the Kala Agreement.

Under the Kala Agreement, JHU agreed to a number of financial concessions to both us and Kala. The payments under the existing JHU agreements were modified by reducing all milestones and minimum annual royalties by 25%, including the development milestone payments due for the first licensed product; the development milestone payments due for the first license product were each extended by one year; development milestone payments for the second and third licensed products were eliminated; and the commercial milestone payments for the first commercial sale of a licensed product were reduced by 50% in the United States. New sales-based milestones were added for the second and third licensed products. Upon the second licensed product under the JHU Agreement reaching a certain level of sales or receiving sublicense royalty income, we are required to pay $100,000 plus the amounts of the eliminated development

milestones and reduced first commercial sale milestone. For the third licensed product, on reaching the same level of sales or receiving sublicense royalty income, we are required to pay $150,000 plus the amounts of the eliminated development milestones and reduced first commercial sale milestone. In addition, we, Kala and JHU released each other from any liability or claims known to Kala and us as of the Kala Agreement and arising out of the actions leading to, and related to the subject of, the Kala Agreement.

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

AffaMed Therapeutics

In July 2019, we entered into a letter agreement with AffaMed Project Limited, or AffaMed, in connection with their purchase of our Series C preferred stock, which we refer to as the AffaMed Letter. Under the AffaMed Letter, we granted AffaMed a right of first negotiation, or the Option, to enter into a license agreement to exclusively develop, register and commercialize GB-102 solely in the territories of China, Hong Kong, Taiwan, Macau and South Korea. The Option expired on July 31, 2021 and we have no further obligation to AffaMed to license rights to GB-102, and we no longer have any limits on our ability to develop, register and commercialize GB-102 in China, Hong Kong, Taiwan, Macau and South Korea.

Recent transactions

In December 2021, we entered into a cross-licensing agreement with a private company pursuant to which we acquired exclusive rights to several small molecules for use in the fields of ophthalmology and otology and by which we granted back exclusive rights to certain small molecules for use outside the fields of ophthalmology and otology. Per the terms of the agreement, we are required to work diligently to develop one or more products, make milestone payments upon the achievement of certain clinical and regulatory milestones, and pay royalties upon commercial sales of products that we develop incorporating these molecules.

In March 2022, we acquired a private company in the United States with certain gene therapy technology and preclinical data. The company was purchased for cash, and no further payments are required until FDA approval of a product based upon the acquired assets and the sale or utilization of any priority review voucher that may be granted in connection with such approval.

Government regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

FDA approval process

In the United States, pharmaceutical products are subject to extensive regulation by FDA under the Federal Food, Drug, and Cosmetic Act, or FDCA, and other federal and state statutes and regulations. The failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

Pharmaceutical product development for a new product or certain changes to an approved product in the U.S. typically involves preclinical laboratory and animal tests, the submission to FDA of an IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including good laboratory practices. The results of preclinical testing are submitted to FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is

submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans.

If FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to FDA as part of the IND.

FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence of effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, dosage tolerance and optimum dosage, and to identify common adverse effects and safety risks. If a drug demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases, FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial may be sufficient in rare instances, including (1) where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome, and confirmation of the result in a second trial would be practically or ethically impossible or (2) when in conjunction with other confirmatory evidence.

The manufacturer of an investigational drug in a Phase 2 or 3 clinical trial for a serious or life-threatening disease is required to disclose, such as by posting on its website, its policy on evaluating and responding to requests for expanded access to such investigational drug.

After completion of the required clinical testing, an NDA is prepared and submitted to FDA. FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls. The cost of preparing and submitting an NDA is substantial. Furthermore, under the Prescription Drug User Fee Act, or PDUFA, the submission of most NDAs is additionally subject to a substantial application user fee, and the applicant under an approved NDA is also subject to an annual program fee for each prescription product. These fees are typically increased annually.

FDA has 60 days from its receipt of an NDA to determine whether the application will be filed based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is filed, FDA begins an in-depth review. Under PDUFA, FDA has agreed to certain performance goals in the review of NDAs to encourage timeliness. NDAs for most standard review drug products are reviewed within twelve months from submission of NDAs for new molecular entities, or NMEs, and within ten months from submission of NDAs for non-NMEs. Priority review can be applied to drugs that FDA determines offer major advances in treatment or provide a treatment where no adequate therapy exists. NDAs for most priority review drug products are reviewed within eight months from submission of NDAs for NMEs and within six months from submission of NDAs for non-NMEs. The review process for both standard and priority review may be extended by FDA for three additional months to consider certain late-submitted information or information intended to clarify information already provided in the submission.

FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an outside 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. FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA, FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, FDA will inspect the facility or the facilities at which the drug is manufactured. FDA will not approve the product unless compliance

with current good manufacturing practices is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for FDA to reconsider the application. The applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. If, or when, those deficiencies have been addressed to FDA's satisfaction in a resubmission of the NDA, FDA will issue an approval letter. FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. Changes to some of the conditions established in an approved application, including changes in indications, labeling or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Disclosure of clinical trial information

Sponsors of clinical trials of FDA regulated products, including drugs, are required to register and disclose certain clinical trial information in the ClinicalTrials.gov database. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pediatric information

Under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. FDA may grant full or partial waivers, or deferrals, for submission of data. With certain exceptions, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month extension of any exclusivity—patent or nonpatent—for a drug if certain conditions are met. Conditions for exclusivity include FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, FDA making a written request for pediatric studies, and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

Post-approval requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements, including, among other things, record-keeping requirements, providing the FDA with updated safety information, product sampling and distribution requirements, and promotion and advertising requirements. For instance, FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed or promoted only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports are required following FDA approval of an NDA. FDA also may require post-marketing testing, known as Phase 4 testing, REMS and surveillance to monitor the effects of an approved product, or FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging and labeling procedures must continue to conform to current good manufacturing practices after approval. Drug

manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies. Registration with FDA subjects entities to periodic unannounced inspections by FDA, during which the Agency inspects manufacturing facilities to assess compliance with current good manufacturing practices. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality-control to maintain compliance with current good manufacturing practices. Regulatory authorities may withdraw product approvals, request product recalls or take other administrative or judicial enforcement actions if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

The Hatch-Waxman Amendments

Orange Book listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be referenced by potential generic competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug pursuant to each state's laws on drug substitution.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carve out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. A recent opinion from the United States Court of Appeals for the Federal Circuit, however, held that a generic manufacturer launching a product with a patented method-of-use carve out may, nonetheless, still be liable for patent infringement by inducement based on certain information in the label and external information such as press releases and product catalogues. *GlaxoSmithKline LLC v. Teva Pharms. USA, Inc.*, 7 F.4th 1320 (Fed. Cir. 2021) *reh'g denied, en banc, Glaxosmithkline LLC v. Teva Pharms. USA, Inc.*, 2022 U.S. App. LEXIS 3812 (Fed. Cir., Feb. 11, 2022).

If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Exclusivity

Upon NDA approval of a new chemical entity, or NCE, which is a drug that contains no active moiety that has been approved by FDA in any other NDA, that drug receives five years of marketing exclusivity during which FDA may not receive any ANDA seeking approval of a generic version of that drug. An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period. Certain changes to a drug, such as the addition of a new indication to the package insert, can be the subject of a three-year period of exclusivity if the application contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to approval of the application. FDA cannot approve an ANDA for a generic drug that includes the change during the period of exclusivity.

Patent term extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension. The allowable patent term extension is calculated as half of the drug's testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval up to a maximum of five years). The time can be shortened if FDA determines that the applicant did not pursue development or approval with due diligence. The total patent term after the extension may not exceed 14 years, and only one patent can be extended. For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the United States Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Hatch-Waxman patent certification and the 30-month stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent or a decision in the infringement case that is favorable to the ANDA applicant.

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

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application enables the applicant in certain circumstances to rely, in part, on the FDA's prior findings in approving a similar product or published literature in support of its application. A Section 505(b)(2) NDA may provide an alternate path to FDA approval for a new or improved formulation, a new route of administration or a new use of a previously approved product.

Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the

applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted." If the Section 505(b)(2) applicant can establish that reliance on the FDA's prior findings of safety and/or effectiveness is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all, or some, of the indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

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

Other U.S. healthcare laws and compliance requirements

In the United States, pharmaceutical company activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare & Medicaid Services, or CMS, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice, or DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, sales, marketing and scientific/educational grant programs may have to comply with the anti-fraud and abuse provisions of the Social Security Act, the federal false claims laws, the privacy and security provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws, each as amended.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering, recommending or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and/or formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, or ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law 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 federal False Claims Act (discussed below).

The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Federal false claims laws, including the federal civil False Claims Act, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for

money or property presented to the U.S. government. In addition, manufacturers can be held liable under the civil False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus generally non-reimbursable, uses and purportedly concealing price concessions in the pricing information submitted to the government for government priced reporting purposes.

HIPAA created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the 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.

Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Data privacy and security regulations by both the federal government and the states in which business is conducted may also be applicable. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes requirements on certain types of people and entities relating to the privacy, security and transmission of individually identifiable health information. HIPAA requires covered entities to limit the use and transmission of individually identifiable health information. HIPAA requires covered entities to limit the use and disclosure of protected health information to specifically authorized situations and requires covered entities to implement security measures to protect health information that they maintain in electronic form. Among other things, HITECH made HIPAA's security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. The reported information is made publicly available on a searchable website. Failure to submit required information may result in civil monetary penalties.

Commercial distribution of products requires compliance with state laws that require the registration of manufacturers and wholesale distributors of drug products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. Sales and marketing activities are also potentially subject to federal and state consumer protection and unfair competition laws.

Violation of any of the federal and state healthcare laws described above or any other governmental regulations may result in penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, refusal to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings.

Pharmaceutical insurance coverage and health care reform

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare reforms that have been adopted, and that may be adopted in the future, could result in further reductions in coverage and levels of reimbursement for pharmaceutical products, increases in rebates payable under U.S. government rebate programs and additional downward pressure on pharmaceutical product prices. On September 9, 2021, the Biden administration published a wide-ranging list of policy proposals, most of which would need to be carried out by Congress, to reduce drug prices and drug payment. The Department of Health and Human Services, or HHS, plan includes, among other reform measures, proposals to lower prescription drug prices, including by allowing Medicare to negotiate prices and disincentivizing price increases, and to support market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase price transparency. Many similar proposals, including the plans to give Medicare Part D authority to negotiate drug prices, require drug manufacturers to pay rebates on drugs whose prices increase greater than the rate of inflation, and cap out-of-pocket costs, have already been included in policy statements and legislation currently being considered by Congress. It is unclear to what extent these and other statutory, regulatory, and administrative initiatives will be enacted and implemented.

In March 2010, the United States Congress enacted the ACA, which, among other things, include changes to the coverage and payment for drug products under government health care programs.

There have been executive, legislative and judicial efforts to modify, repeal, replace, or otherwise invalidate all, or certain aspects, of the ACA. For example, the Tax Cuts and Jobs Act of 2017 included, among other things, a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." In June 2021, the U.S. Supreme Court held that plaintiffs did not have standing to challenge constitutionality of the individual mandate. It is unclear whether there may be other efforts to challenge, repeal or replace the ACA. Further, prior to the Supreme Court ruling, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and closed on August 15, 2021. The executive order also instructed 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. We are continuing to monitor any changes to the ACA that, in turn, may potentially impact our business in the future. We cannot predict the ultimate content, timing or effect of any healthcare reform legislation or other healthcare measures on our business.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted to reduce healthcare expenditures, including aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional Congressional action is taken. The Medicare reductions phase back in starting with a 1% reduction in effect from April 1, 2022 to June 30, 2022 before increasing to the full 2% reduction. Moreover, the American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Recently there has 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, reduce the costs of drugs under Medicare, and reform government program reimbursement methodologies for drug products. By way of example, in December 2020, CMS issued a final rule implementing significant manufacturer price reporting changes under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. On September 9, 2021, the Biden Administration published a wide-ranging list of policy proposals, most of which would need to be carried out by Congress, to reduce drug prices and drug payment. The HHS plan includes, among other reform measures, proposals to (1) give Medicare authority to directly negotiate drug prices with manufacturers, (2) authorize HHS to negotiate Medicaid supplemental rebates on behalf of states, (3) allow employer-based, ACA marketplace and commercial health insurance plans to access Medicare negotiated drug prices, (4) place a cap on out-of-pocket costs for Medicare Part D beneficiaries and redistribute a higher proportion of drug costs to Part D and manufacturers, (5) mandate purchase of the least costly-alternative and to institute value-based or outcomes-based pricing arrangements, (6) disincentivize drug price increases, (8) facilitate approval and prescription of biosimilar and generic drugs, (9) increase drug pricing transparency, (10) prohibit certain types of rebates to pharmacy benefit managers, and (11) develop drug pricing models by tying price to outcomes. Many similar proposals, including the plans to give Medicare authority to negotiate drug prices and cap out-of-pocket costs, have already been included in policy statements and legislation currently being considered by Congress. It is unclear to what extent new statutory, regulatory, and administrative initiatives will be enacted and implemented. Additional state and federal healthcare reform measures will likely be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for such product candidates or additional pricing pressures.

Finally, in the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings.

Employees and Human Capital Resources

As of December 31, 2021, we had 27 full time employees, all in the United States, 7 of whom have an M.D. or Ph.D. None of our employees are represented by a labor union or covered by collective bargaining agreements, and we believe our relationship with our employees is good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive and cash-based performance bonus plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

Properties and facilities

Our principal executive office is located Redwood City, California, and consists of 2,560 square feet of office space under a lease which expires in August 2022. We use this facility for operations and administrative purposes. We also have a facility located in Baltimore, Maryland, which consists of 15,649 square feet of office and laboratory space under a lease which expires in June 2023. We

use the Maryland facility for our internal research and development activities. We believe that our facilities are adequate to meet our needs for the foreseeable future.

Legal proceedings

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm, and other factors.

Corporate Information

We were incorporated in Delaware in May 2011 and our principal executive office is located in Redwood City, California. Our website is www.graybug.vision. We are subject to the informational requirements of the Securities and Exchange Act of 1934, as amended, or the Exchange Act, and file or furnish reports, including our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Exchange Act, proxy statements and other information with the SEC. We make copies of these reports and other information available free of charge through our website as soon as reasonably practicable after we file or furnish them with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC at www.sec.gov. The information contained on the websites referenced in this Annual Report is not incorporated by reference into this filing, and the website addresses are provided only as inactive textual references.

Item 1A. Risk Factors.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information contained in this Annual Report on Form 10-K, including our financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding to invest in our common stock. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that affect us. We cannot assure you that any of the events discussed below will not occur. If any of the following risks actually occur, our business, prospects, operating results and financial condition could suffer materially. Additionally, to the extent the ongoing COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risks incorporated by reference or set forth below. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.

Summary of Risk Factors

An investment in our common stock involves various risks, and prospective investors are urged to carefully consider the matters discussed in the section titled "Risk Factors" prior to making an investment in our common stock. These risks include, but are not limited to, the following:

- We are a clinical-stage biopharmaceutical company with no products approved. We have incurred significant losses since inception, and we expect to incur continued and increasing losses over the next several years and may never achieve or maintain profitability.
- We will need substantial additional funding to support our operations and pursue our growth strategy. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- Our approach to the treatment of retinal diseases is unproven, and we do not know whether we will be able to successfully develop any products.
- We are seeking a partner to fund, in whole or in part, further clinical trials of GB-102 for wet AMD. Without such a partnership, further development of GB-102 for wet AMD is uncertain.
- We depend heavily on the success of our wet AMD product candidates, in particular GB-102. Clinical trials of our product candidates may not be successful. If we are unable to successfully complete clinical development of, and obtain marketing approvals for, our product candidates, or experience significant delays in doing so, or if after obtaining marketing approvals, we fail to commercialize these product candidates, our business will be materially harmed.
- We have not yet successfully initiated or completed any Phase 3 clinical trials nor commercialized any pharmaceutical products, which may make it difficult to evaluate our future prospects.
- If clinical trials of GB-102 or any other product candidate that we develop fail to demonstrate safety and efficacy to the satisfaction of the FDA, the EMA or other regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be delayed or unable to complete, the development and commercialization of such product candidate.
- If serious adverse or unacceptable side effects are identified during the development of GB-102 or any other product candidates that we may develop, we may need to abandon or limit our development of such product candidates.
- The ongoing COVID-19 pandemic may, directly or indirectly, adversely affect our business, results of operations and financial condition.
- We may not be successful in our efforts to develop product candidates based on our proprietary technology other than GB-102 or expand the use of our proprietary technology for treating additional eye diseases and conditions.
- Sunitinib, the active ingredient of GB-102, has a boxed warning regarding hepatotoxicity for its use in oncology indications.
- Our business and operations would suffer in the event of computer system failures or security breaches.

- We could potentially contract with third parties for the production of our product candidates. This could increase the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- The manufacture of our product development candidates requires outsourced, custom manufacturing and we may encounter difficulties in production, particularly with respect to formulation, process development or scaling up of our manufacturing capabilities. If we, or our contract manufacturing organizations, or CMOs, encounter such difficulties, our ability to provide supply of our product candidates for preclinical studies, clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.
- We have no experience manufacturing any of our product candidates at a commercial scale. We, or our CMOs, may be unable to successfully scale up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.
- Our products may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, and the market opportunity for these products may be smaller than we estimate.
- We may enter into collaborations with third parties for the development and commercialization of GB-102 or other product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.
- If our patent position does not adequately protect our product candidates, others could compete against us more directly, which would harm our business.
- Patents filed by our licensor, Johns Hopkins University, may have been discovered through government funded programs and thus may be subject to federal regulations such as “march-in” rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.
- If we infringe or are alleged to infringe intellectual property rights of third parties, our business could be harmed.
- We may be required, or choose, to suspend, repeat or terminate our clinical trials if they are not conducted in accordance with regulatory requirements, the results are negative or inconclusive, the trials are not well-designed, or research participants experience adverse safety outcomes.
- If we are not able to obtain required regulatory approvals, we will not be able to commercialize our product candidates and our ability to generate significant revenue will be materially impaired. The regulatory approval process is expensive, time-consuming and uncertain. As a result, we cannot predict when or if we, or any collaborators we may have in the future, will obtain regulatory approval to commercialize our product candidates.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- We expect to expand our development, regulatory and manufacturing capabilities and potentially implement sales, marketing and distribution capabilities and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. If we are unable to establish and maintain our own adequate sales, marketing and distribution capabilities, we may not be successful in commercializing our other product candidates if and when they are approved.
- The market price of our stock has been and may continue to be volatile, and you could lose all or part of your investment.
- Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.
- We are an “emerging growth company” and a “smaller reporting company” and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.

Risks Related to Our Financial Position and Need For Additional Capital

We are a clinical-stage biopharmaceutical company no products approved. We have incurred significant losses since inception, and we expect to incur continued and increasing losses over the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $35.8 million and $27.5 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021 and 2020, we had an accumulated deficit of $169.2 million and $133.4 million, respectively. To date, we have financed our operations primarily through private placements of convertible preferred stock and convertible promissory notes and the issuance of common stock upon our initial public offering, or IPO. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials and general and administrative costs to support such efforts. We expect to continue to incur significant expenses and operating losses for the foreseeable future. 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:

- pursue reformulation and other pre-clinical activities in anticipation of a partnership to continue the clinical development of our most advanced product candidate, GB-102;
- commence clinical trials of our product candidate GB-401;
- continue the research and development of other product candidates;
- seek to identify and develop, or enter into strategic partnerships or collaborations to develop, additional product candidates;
- seek marketing approvals for any of our product candidates that successfully complete clinical development;
- develop and expand our sales, marketing and distribution capabilities for any of our product candidates for which we obtain marketing approval;
- scale up our manufacturing processes and capabilities or, in the future, establish and operate a manufacturing facility, to support sales of our product candidates, our ongoing clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- expand our operational, financial and management systems and personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company; and
- increase our product liability and clinical trial insurance coverage as we expand our clinical trials and commercialization efforts.

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

- we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or any additional international regulatory agency to perform trials or studies in addition to those currently expected;
- there are any delays in receipt of regulatory clearances or approvals to begin our planned clinical programs; or
- there are any delays in enrollment of patients in or completing our clinical trials or the development of our product candidates.

We have no product sales. We do not expect sales of any product candidate for several years. For us to become profitable, we will need to succeed in developing and commercializing products. This will require us to be successful in a range of challenging activities, including:

- successfully completing clinical development of our product candidates, which may require establishing one or more strategic partnerships;
- obtaining marketing approval for these product candidates;
- manufacturing at commercial scale and selling and distributing those products for which we obtain marketing approval;
- achieving an adequate level of market acceptance of and obtaining and maintaining coverage and adequate reimbursement from third-party payors for our products, which may require establishing a strategic partnership; and
- protecting our rights to our intellectual property portfolio.

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

We will need substantial additional funding to support our operations and pursue our growth strategy. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we conduct pre-clinical studies or clinical trials for our wet AMD product candidates, preclinical studies and clinical trials for our other product candidates, and seek marketing approval for any such product candidate for which we obtain favorable clinical results. We also expect to devote significant financial resources to conducting research and development and potentially seeking regulatory approval for our other product candidates. In addition, we plan to devote substantial financial resources to our commercialization efforts, including product manufacturing, sales, marketing and distribution for any of our product candidates for which we obtain marketing approval. Accordingly, we will need to obtain substantial additional funding in connection with our continuing and planned operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

As of December 31, 2021, we had cash, cash equivalents and short-term investments of $63.7 million, which we believe is sufficient to fund our operations as currently planned beyond the next 12 months. Our future funding requirements will depend on many factors, including:

- the scope, progress, costs and outcome of the clinical trials of our product candidates, in particular GB-102;
- the scope, progress, costs and outcome of preclinical development and clinical trials of our product candidates;
- the costs, timing and outcome of regulatory review of our product candidates by the FDA, the EMA or other regulatory authorities;
- the costs of manufacturing, sales, marketing, distribution and other commercialization efforts with respect to any products for which we obtain marketing approval;
- subject to receipt of marketing approval, revenue received from product sales;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the extent to which we choose to establish collaboration, distribution or other marketing arrangements for our products and product candidates;
- the effect of competing technological and market developments;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the extent to which we acquire or invest in other businesses, products and technologies; and
- the impact of the COVID-19 pandemic.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete. We may never generate the necessary data or results required to obtain regulatory approval of products with the market potential sufficient to enable us to achieve profitability. We do not expect to generate sales of any commercial product for several years, if at all. Accordingly, we may need to obtain substantial additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

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

We are an early-stage company. Our operations to date have been limited to organizing and staffing our company, acquiring rights to intellectual property, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and clinical trials and manufacturing initial quantities of our products and product candidates. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

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

Risks Related to Product Development, Regulatory Approval and Commercialization

Our approach to the treatment of retinal diseases is unproven, and we do not know whether we will be able to successfully develop any products.

GB-102 is designed to deliver therapeutic drug levels to the retinal tissue for up to six months from a single intravitreal injection. There are currently no FDA-approved therapies that treat retinal diseases with a six-month dosing regimen. Our future success depends on the successful development of product candidates, including GB-102, based on this novel therapeutic approach. We have not yet demonstrated efficacy and safety for GB-102 or any other product candidates in a pivotal trial or obtained marketing approval of any product candidate. GB-102 may not demonstrate in patients any or all of the pharmacological benefits we believe it may possess. If we are unsuccessful in our development efforts, we may not be able to advance the development of GB-102 or any other product candidate, commercialize products, raise capital, expand our business or continue our operations.

We will require a partner to fund, in whole or in part, further clinical trials of GB-102 for wet AMD. Without such a partnership, further clinical development of GB-102 for wet AMD is uncertain.

Although we plan to continue to prioritize investing in preclinical development of GB-102 for wet AMD, we do not have sufficient cash resources to complete additional clinical trials for both GB-102 and GB-401 at this time. We intend to pursue a partnership in which we license the commercial rights to GB-102 in one or more territories in exchange for funding of further clinical trials. Such partnerships generally require substantial amounts of time to secure, and often involve economic returns for the licensor that are significantly reduced from that attainable by developing and commercializing the product without a partner. Moreover, while we are actively seeking such a partnership, there can be no guarantee that we will secure one in a timely fashion, or on reasonable economic terms, if at all. Failing to secure such a partnership could have a material adverse effect on our business.

We depend heavily on the success of our wet AMD product candidates, in particular GB-102. Clinical trials of our product candidates may not be successful. If we are unable to successfully complete clinical development of, and obtain marketing approvals for, our product candidates, or experience significant delays in doing so, or if after obtaining marketing approvals, we fail to commercialize these product candidates, our business will be materially harmed.

We have devoted a significant portion of our financial resources and business efforts to the development of our product candidates for diseases and conditions of the eye. In particular, we are investing substantial resources to complete the development of GB-102 for wet AMD. We cannot accurately predict when or if any of our retinal disease product candidates will prove effective or safe in humans or whether these product candidates will receive marketing approval. Our ability to generate product revenues sufficient to achieve profitability will depend heavily on our obtaining marketing approval for and commercializing GB-102.

The success of GB-102 and other product candidates will depend on many factors, including:

- successful completion of preclinical studies and clinical trials that demonstrate to the satisfaction of the FDA, the EMA or comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications;
- our ability to find a partner to fund the next clinical trial in wet AMD with GB-102;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;

- effectively competing with other therapies;
- maintaining a continued acceptable safety profile of our products following approval;
- obtaining and maintaining coverage and adequate reimbursement from third-party payors;
- applying for and receiving marketing approvals from applicable regulatory authorities for our product candidates;
- scaling up our manufacturing processes and capabilities to support additional or larger clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval;
- developing, validating and maintaining a commercially viable manufacturing process that is compliant with current good manufacturing practices;
- developing and expanding our sales, marketing and distribution capabilities and launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- minimizing and managing any delay or disruption to our ongoing or planned clinical trials, and any adverse impacts to the U.S. and global market for pharmaceutical products, including as a result of the ongoing COVID-19 pandemic;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity; and
- protecting our rights in our intellectual property portfolio.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

We have not yet initiated or completed any Phase 3 clinical trials nor commercialized any pharmaceutical products, which may make it difficult to evaluate our future prospects.

Our operations to date have been limited to financing and staffing our company, developing our technology and conducting preclinical research and Phase 1 and Phase 2 clinical trials for our product candidates. We have not yet demonstrated an ability to initiate or complete Phase 3 clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by clinical-stage biopharmaceutical companies such as ours. Any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will eventually need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

If clinical trials of GB-102 or any other product candidate that we develop fail to demonstrate safety and efficacy to the satisfaction of the FDA, the EMA or other regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be delayed or unable to complete, the development and commercialization of such product candidate.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, including GB-102, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing.

We designed our Phase 1/2a, Phase 2a and Phase 2b clinical trials of GB-102 to assess safety and preliminary efficacy and did not power the trials to measure any efficacy endpoints with statistical significance. We expect that our Phase 3 clinical trials for GB-102 for the treatment of wet AMD will be the first clinical trial for GB-102 to be powered with an appropriate number of patients to allow us to measure with statistical significance the non-inferiority of GB-102 compared to the standard of care. As a result, favorable results from our Phase 1/2a, Phase 2a, and potential future clinical trials may not necessarily predict a likelihood of achieving statistical significance on our primary efficacy endpoint in the Phase 3 clinical trials, which will be required for us to obtain marketing approval of GB-102. Historically, the FDA has required that Phase 3 clinical trials in wet AMD use some measure of patient visual performance as the primary endpoint to evaluate efficacy, most often Best Corrected Visual Acuity, or BCVA. Although it was not powered to statistically determine efficacy, our Phase 2b clinical trial of GB-102 showed that, on average across all time points, patients on the 1 mg dose of GB-102 were assessed to have a mean BCVA across all time points of approximately 9 letters lower than that observed in the trial control arm, in which patients received bi-monthly injections of Eylea. If such a difference were to be repeated in a Phase 3 clinical trial

of GB-102, it is unlikely that the FDA would approve the product based on a claim of non-inferiority to Eylea. Additionally, our clinical trials to date have only evaluated GB-102 against treatment with Eylea, and there may be current or future products that deliver better results in terms of safety and/or efficacy.

The success of our product candidates is dependent upon the drug-elution profile during the course of intended therapy. Our Phase 1/2a and our Phase 2a trials have been open label and have not been compared to any active treatments. The treatment phase of our Phase 2b trial with GB-102 in wet AMD included a control arm with Eylea, which is the current standard of care. Compared to Eylea, GB-102 1 mg demonstrated median durability of 5 months and improved safety profile. Compared to Eylea, we observed non-statistical similar control of Central Subfield Thickness, or CST, of the retina, and lower average BCVA across all time points. In March 2020, we terminated the development of the 2 mg dose of GB-102 in all of our clinical trial programs, including the arm of our Phase 2b trial, so the results of that arm have been disregarded. If we determine to make any future changes to the formulation, such changes could affect the outcome of any subsequent clinical trials. As a result of any of these therapeutic or formulation changes, the outcome of our potential future or Phase 3 clinical trials may differ from the outcome of our Phase 1/2a and Phase 2b clinical trials. If the BCVA results of clinical trials with any potential new therapeutic or product formulation, including therapies that do not involve intravitreal delivery, are similar to the results from the Phase 2b trial, we may not be able to obtain regulatory approvals or, even if approved, achieve market acceptance of our product candidates.

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later-stage clinical trials.

Successful results in preclinical or early clinical trials do not ensure that later-stage clinical trials will be successful. In January 2019, we completed our Phase 1/2a trial of GB-102 evaluating various doses of GB-102 in patients with wet AMD. Although the data indicated that GB-102 was well-tolerated and reduced the need for supportive anti-vascular endothelial growth factor, or anti-VEGF, treatments, these results may not be indicative of future clinical trials with different designs. For example, 88% of patients in our Phase 1/2a trial of GB-102 1 mg did not require additional supportive therapy for six months or longer, while only 48% of patients in our Phase 2b ALTISSIMO trial of GB-102 1 mg achieved six months without requiring additional supportive therapy. Moreover, as is common for early trials, in our Phase 1/2a trial, we looked at a number of efficacy measures without accounting for multiplicity. Accordingly, it is possible that positive results, including nominally statistically significant results, observed in our Phase 1/2a trial will not be replicated in our future trials with a different design or in other future trials.

Subsequently, we tested two doses of an optimized formulation of GB-102 in a Phase 2a clinical trial in patients with macular edema, or ME, secondary to either DME or branch/central retinal vein occlusion, or RVO, as well as in the completed Phase 2b clinical trial in wet AMD. In the Phase 2a trial, we observed that there were more incidences of medication present in the anterior chamber with the 2 mg dose of GB-102, which, in a single patient, resulted in two serious adverse events, or SAEs (severe vision loss due to presence of medication in anterior chamber and corneal edema as a result of wash-out of the anterior chamber). As a result, we paused enrollment in our Phase 2b wet AMD trial until an interim safety analysis of both trials could be performed. On the basis of the results of this safety analysis, we terminated the development of the 2 mg dose of GB-102 in all of our clinical trial programs and have disregarded the results, other than those related to safety, of the GB-102 2 mg arm of the ALTISSIMO Phase 2b trial.

Some of our clinical trials, including our Phase 1/2a clinical trial and our completed Phase 2b clinical trial of GB-102 for the treatment of wet AMD, had small patient populations, making it difficult to predict whether the favorable results from such trials will be repeatable in larger, more advanced clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

Even if the results of future Phase 3 clinical trials are positive, we may have to commit substantial time and additional resources to conducting further preclinical studies and clinical trials before obtaining FDA approval for any of our drug candidates.

If serious adverse or unacceptable side effects are identified during the development of GB-102 or any other product candidates that we may develop, we may need to abandon or limit our development of such product candidates.

If GB-102 or any of our other product candidates are associated with SAEs or other undesirable side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the SAEs, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

Out of 32 patients enrolled in our Phase 1/2a trial, no GB-102 related non-ocular adverse events, or AEs, and no SAEs or dose limiting toxicities were reported. All drug-related AEs were mild or moderate and transient and resolved by the end of the trial. The most common AE observed in more than one patient was vitreous floaters (n=5). Most vitreous floaters are caused by age-related changes that occur as the vitreous becomes more liquid.

Microscopic fibers in the vitreous tend to clump and can cast tiny shadows on the retina, commonly referred to as floaters. Intravitreal injections can increase the number of floaters, and any other particle that similarly casts a shadow may also be referred to as a floater. For nine patients enrolled in the higher dose cohorts, medication presence was observed in the anterior chamber. All nine of those patients completed the trial. Overall, the medication presence in the anterior chamber appeared to be self-limited and reversible, with no long-term consequences.

In our Phase 2a clinical trial, there were no drug-related, non-ocular AEs. The patients in the 1 mg dose experienced nine drug related AEs, and seven out of ten patients demonstrated no AEs. One patient had only vitreous floaters, medication present in the vitreous, and one patient had vitreous floaters coincident with a reduction in vision. The other AEs occurred in a single patient with medication present in the anterior chamber. The 2 mg dose was associated with medication present in the anterior chamber in five out of 11 patients. The majority of AEs occurred in one patient. Two SAEs were reported in a single patient (severe vision loss due to presence of medication in the anterior chamber and corneal edema as a result of wash-out of the anterior chamber).

Our Phase 2b clinical trial of GB-102 was designed to test two different doses: 1 mg and 2 mg. We conducted an interim safety analysis in the trial and found that the presence of medication in the anterior chamber was reported in four patients in the GB-102 2 mg dose group and one patient in the 1 mg dose group. On the basis of these data, we terminated the development of the 2 mg dose of GB-102 in all of our clinical trial programs. We believe that the number of microparticles injected in the 2 mg dose (approximately 2 million) were too numerous to allow adequate aggregation. All patients in the Phase 2b trial having received GB-102 at either the 1 mg or 2 mg doses for the first six-month period of the trial received the 1 mg dose as repeat therapy at month six.

In the 12-month treatment phase of our Phase 2b clinical trial, there were no drug-related, non-ocular AEs in the GB-102 1 mg arm, nor were there any drug-related SAEs nor dose-limiting toxicity. No treatment-emergent adverse events led to drug discontinuation and none of the adverse events required surgical intervention. Nine out of the 21 patients in the 1 mg dose experienced 23 events of drug related AEs. Five patients had vitreous floaters attributable to GB-102 1 mg and, in the majority of patients, these had no or minimal transient effect on visual acuity. Medication was detected in the anterior chamber, or AC, in three out of 21 patients. In one patient, the presence of particles in the AC was transient with no other associated adverse events. In two patients, the presence of GB-102 microparticles in the AC was associated with transient inflammation and there was an associated moderate BCVA loss in one of these patients. An additional three patients had intraocular inflammation that was mild to moderate, responded well to short courses of treatment with corticosteroids, and was not associated with any change in BCVA. One patient had dispersion of GB-102 microparticles in the vitreous cavity that were not characterized as floaters but was associated with a decrease in visual acuity.

In the six-month, post treatment observational phase of our Phase 2b clinical trial, no drug-related adverse events or vision-threatening inflammation were reported. One patient on GB-102 1 mg developed a cataract, which was evaluated to be unrelated to GB-102 treatment.

There are potential side effects that are related to intravitreal injection procedures. These side effects are shared by any treatment that uses intravitreal injection as a means of delivering medication. These can include conjunctival hemorrhage, punctate keratitis, eye pain, conjunctival hyperemia, intraocular pressure rise, intraocular inflammation, retinal detachment and endophthalmitis.

Finally, clinical trials by their nature utilize a sample of the potential patient population. However, with a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered when a significantly larger number of patients are exposed to the product. If safety problems occur or are identified after one of our products reaches the market, the FDA, the EMA or other regulatory authorities may require that we amend the labeling of our product, recall our product or even withdraw approval for our product.

The ongoing COVID-19 pandemic may, directly or indirectly, adversely affect our business, results of operations and financial condition.

Our business could be materially adversely affected, directly or indirectly, by the widespread outbreak of contagious disease, including the ongoing COVID-19 pandemic, which has spread to many of the countries in which we and our suppliers do business. National, state, and local governments in affected regions have implemented and may continue to implement safety precautions, including quarantines, border closures, increased border controls, travel restrictions, shelter in place orders and shutdowns, business closures, cancellations of public gatherings and other measures. Organizations, businesses and individuals are taking additional steps to avoid or reduce infection, including business and facility closures or suspensions, limitations on travel and remote working measures. These measures are disrupting normal business operations both in and outside of affected areas and have had significant negative impacts

on businesses and financial markets worldwide. As new variants of the coronavirus emerge, or if the rates of infections increase, these measures and associated disruptions could intensify in both scope and adverse impact on our business, results of operations and financial condition.

The COVID-19 pandemic has caused us to modify our business practices (including but not limited to curtailing or modifying employee travel, moving to full remote work for many employees, and cancelling physical participation in meetings, events and conferences) and we may take further actions as may be required by government authorities or that we determine are in the best interests of our employees, patients and business partners. The majority of our office-based employees have been working from home since March 2020, while we ensure essential staffing levels in our physical operations remain in place, including maintaining key personnel in our laboratories. Further, given that a greater number of our employees are working remotely than usual in response to the COVID-19 pandemic and related government actions, we could be exposed to greater risks related to cybersecurity and our information technologies systems.

Notwithstanding these measures, the COVID-19 pandemic could affect the health and availability of our workforce as well as those of the third parties we rely on taking similar measures. If members of our management and other key personnel in critical functions across our organization are unable to perform their duties or have limited availability due to the COVID-19 pandemic, we may not be able to execute on our business strategy and/or our operations may be negatively impacted. We may also experience limitations in employee resources, including because of sickness of employees or their families or the desire of employees to avoid contact with individuals or large groups of people. In addition, we have experienced and will continue to experience disruptions to our business operations resulting from quarantines, self-isolations and other restrictions on the ability of our employees to perform their jobs.

The COVID-19 pandemic has disrupted business operations. The extent and severity of the impact on our business and clinical trials will be determined largely by the extent of future disruptions in the supply chains for GB-102 and our future product candidates and delays in the conduct of current and future clinical trials. Further, our ability to conduct our future clinical trials may be adversely affected, directly or indirectly, by the COVID-19 pandemic, which has been known to cause disruptions in the ability to monitor patients in person due to clinics and hospitals closing sites or diverting the resources that are necessary to conduct clinical trials to care for COVID-19 patients. Further, our suppliers, vendors and manufacturing and clinical trial partners have been adversely affected by the COVID-19 pandemic, including by adversely impacting the ability of their employees to get to their places of work and maintain the continuity of their on-site operations. COVID-19 could potentially lead to the closure of our research lab and potentially delay IND-enabling activities, which could delay the start of clinical trials. In addition, the impact of the COVID-19 pandemic on the operations of the FDA and other health authorities may delay potential approvals of GB-102 and our future product candidates.

The COVID-19 pandemic has also impacted and may further impact the global economic and capital markets, including by negatively impacting capital markets, which may adversely affect our business, liquidity and access to capital. It is further possible that the COVID-19 pandemic will cause another economic slowdown of potentially extended duration.

While it is not possible at this time to estimate the entirety of the impact that the COVID-19 pandemic will have on our business, operations, employees, customers or suppliers, continued spread of COVID-19, measures taken by governments, actions taken to protect employees and the broad impact of the pandemic on all business activities may materially and adversely affect our business, results of operations and financial condition, and the nature and extent of such impact is highly uncertain and unpredictable.

If we experience any of a number of possible unforeseen events in connection with our clinical trials, potential marketing approval or commercialization of our product candidates could be delayed or prevented.

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

- clinical trials of our product candidates may not produce statistically significant, positive results, and we may decide, or regulators may require us, to conduct additional clinical trials or amend product development programs, or abandon product development programs entirely;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our contractors may fail to comply with regulatory requirements or meet their obligations to us in a timely manner, or at all;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may decide, or regulators or institutional review boards may require us, to suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate; and
- the supply or quality of our clinical trial material or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

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

- be delayed in obtaining or unable to obtain marketing approval for our product candidates;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate clinical trials for our wet AMD, DME, diabetic retinopathy, or DR, or glaucoma product candidates or our other product candidates that we may develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, the EMA or similar regulatory authorities outside the United States. Although there is a significant prevalence of disease in the areas of ophthalmology in which we are focused, we may nonetheless experience unanticipated difficulty with patient enrollment.

A variety of factors affect patient enrollment, including:

- the prevalence and severity of the ophthalmic disease or condition under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate under study;
- the perceived risks and benefits of switching patients from treatment with eye drops to intravitreal therapy, in the case of certain glaucoma patients;
- the efforts to facilitate timely enrollment in clinical trials;
- any delay or disruption to enrollment or attendance for injections, including as a result of the ongoing COVID-19 pandemic;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of experienced clinical trial sites for prospective patients;
- the conduct of clinical trials by competitors for product candidates that treat the same indications as our product candidates; and
- the lack of adequate compensation for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment

delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

We may not be successful in our efforts to develop product candidates based on our proprietary technology other than GB-102 or expand the use of our proprietary technology for treating additional eye diseases and conditions.

We are currently directing all of our development efforts towards applying our proprietary technology to product candidates that are designed to provide sustained delivery of therapeutic agents to the eye using active pharmaceutical ingredients that are currently used in FDA-approved drugs. We have a number of product candidates at various stages of development and are exploring the potential use of our proprietary technologies in other eye diseases and conditions. Our existing product candidates and any other potential product candidates that we identify may not be suitable for continued preclinical or clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize our product candidates that we develop based upon our technological approach, we will not be able to obtain substantial product revenues in future periods.

Sunitinib, the active ingredient of GB-102, has a boxed warning regarding hepatotoxicity for its use in oncology indications.

Sunitinib, which was originally developed for the treatment of renal cell carcinoma and gastrointestinal stromal tumors, has been shown to cause liver damage, or hepatotoxicity, in some patients. As a result, in 2010, the prescribing information for orally administered sunitinib for its use in treating renal cell carcinoma and gastrointestinal stromal tumors was revised to include a boxed warning regarding hepatotoxicity. A boxed warning is a warning put in the labeling of a drug product that is designed to call attention to serious or life-threatening risks.

There is no approved therapy for retinal diseases using sunitinib. We have not seen any evidence of hepatotoxicity in our preclinical studies or clinical trials. Moreover, preclinical toxicity studies and the results of our Phase 1/2a and Phase 2b clinical trials with GB-102 have not detected the presence of sunitinib in the systemic blood circulation at any time point. However, the boxed warning for orally administered sunitinib may make it more difficult for us to achieve widespread market acceptance or regulatory approval for our product candidates.

Moreover, there can be no assurance that comparable AEs and other side effects will not appear over the course of our trials, which could have a material adverse effect on our business and operating results.

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

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

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

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to conditions imposed by the FDA. For example, the clinical trial must be well-designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of the applicable product candidates.

Other risks inherent in conducting international clinical trials include:

- foreign regulatory requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple sets of foreign regulations;
- failure of enrolled patients to adhere to clinical protocols as a result of differences in healthcare services or cultural customs;
- foreign exchange fluctuations;
- diminished protection of intellectual property in some countries; and
- political and economic risks relevant to foreign countries.

Our business and operations would suffer in the event of computer system failures or security breaches.

In the ordinary course of our business, we collect, store and transmit confidential information, including intellectual property, proprietary business information, health information and personal information. Despite the implementation of security measures, our internal computer systems, and those of our contract research organizations, or CROs, and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, cyberattacks, natural disasters, fire, terrorism, war and telecommunication and electrical failures. Cyberattacks are increasing in their frequency, sophistication and intensity. Cyberattacks could include the deployment of harmful malware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Significant disruptions of our information technology systems or security breaches could adversely affect our business operations and/or result in the loss, misappropriation, and/or unauthorized access, use or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and personal information), and could result in financial, legal, business and reputational harm to us. If such disruptions were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Further, the COVID-19 pandemic has resulted in a significant number of our employees and partners working remotely, which increases the risk of a data breach or issues with data and cybersecurity. To the extent that any disruption or security breach results in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our future product candidates could be delayed. In addition, our remediation efforts may not be successful. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary information.

Moreover, if a computer security breach affects our systems or results in the unauthorized access, use or disclosure of personal information, our reputation could be materially damaged. In addition, such a breach may require notification to governmental agencies, the media and/or affected individuals pursuant to various federal, state and international privacy and security laws, if applicable, including HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. We would also be exposed to a risk of loss or litigation and potential liability under laws, regulations and contracts that protect the privacy and security of personal information. As described below in "*We are subject to stringent and changing privacy laws, regulations and standards as well as contractual obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could harm our reputation, subject us to significant fines and liability, or otherwise adversely affect our business or prospects*," the California Consumer Privacy Act, or CCPA, provides a private right of action for security breaches, which could lead to some form of remedy including regulatory scrutiny, fines, private right of action settlements, and other consequences. The financial exposure from the events referenced above could either not be insured against or not be fully covered through any insurance that we may maintain, and there can be no assurance that the limitations of liability in any of our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages as a result of the events referenced above. Any of the foregoing could have a material adverse effect on our business, reputation, results of operations, financial condition and prospects.

Risks Related to Manufacturing

We could potentially contract with third parties for the production of our product candidates. This could increase the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We currently rely on third parties for the production of GB-102 and our product candidates for preclinical testing and clinical trials, including supply of active pharmaceutical ingredient drug substance, sunitinib, as well as polymers used in the formulations, such as poly(lactic-co-glycolic acid), or PLGA, injection devices, and other raw materials and for sterilization of the finished product. We intend to build our own manufacturing capabilities for our drug formulations, but could also decide to keep contracting with third parties

if it is more advantageous. While we believe that our existing manufacturing partners have facilities that will be sufficient to meet our requirements for manufacturing GB-102 and any of our product candidates for which we obtain marketing approval, we may in the future need to rely on additional contract manufacturing organizations, or CMOs, for some aspects of the manufacture of our product candidates.

Reliance on third parties for aspects of the supply of our product candidates entails additional risks, including:

- lack of direct control over regulatory compliance and quality assurance;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the possible breach of an agreement by the third party; and
- the possible termination or nonrenewal of an agreement by the third party at a time that is costly or inconvenient for us.

We, or our third-party suppliers or CMOs, may not be able to comply with quality assurance standards, current good manufacturing practices regulations or similar regulatory requirements outside the United States. If we or our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA and comparable regulatory authorities in other jurisdictions, if the quality and accuracy of the manufacturing and quality control data is compromised due to failure to adhere to protocols or to regulatory requirements or if we or our CMOs fail to maintain a compliance status acceptable to the FDA or comparable regulatory authorities in other jurisdictions, we may not be able to secure and/or maintain regulatory approval for our product candidates. In addition, we or our CMOs must maintain adequate quality control, quality assurance and qualified personnel. If we or our CMOs cannot maintain a compliance status acceptable to the FDA or a comparable regulatory authority in another jurisdiction, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

Any failure to achieve and maintain compliance with these laws, regulations and standards could subject us to the risk that we may have to suspend the manufacturing of our product candidates and that obtained approvals could be revoked, which would adversely affect our business and reputation. Our failure, or the failure of our suppliers or CMOs, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products and product candidates. The same risks, however, would also apply to any internal manufacturing facilities, should we in the future decide to build internal manufacturing capacity.

Our potential future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any products that receive regulatory approval on a timely and competitive basis.

The manufacture of our product development candidates requires outsourced, custom manufacturing and we may encounter difficulties in production, particularly with respect to formulation, process development or scaling up of our manufacturing capabilities. If we, or our CMOs, encounter such difficulties, our ability to provide supply of our product candidates for preclinical studies, clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

As product candidates are developed, 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. For example, due to adverse events related to presence of medication in the anterior chamber observed in some patients in the Phase 1/2a trial for GB-102, changes were made to the manufacturing process for GB-102. 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 preclinical studies or future clinical trials.

For our recently completed Phase 2b trial, GB-102 was manufactured by Lubrizol Life Science Health. We will need to obtain future supplies of GB-102 from our own manufacturing or from third-party manufacturers that we have engaged, or expect to engage. Although we are working to develop commercially viable manufacturing processes, doing so is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, cost overruns, potential problems with process scale up, formulation or formulation changes, process reproducibility, stability issues, lot consistency and timely availability of reagents or raw materials. Any of these challenges could delay completion of preclinical studies or clinical trials, require bridging studies or trials, or the repetition of one or more studies or trials, increase development costs, delay approval of our product candidates, impair commercialization efforts, increase our cost of goods and have an adverse effect on our business, financial condition, results of operations and growth prospects.

We have no experience manufacturing any of our product candidates at a commercial scale. We, or our CMOs, may be unable to successfully scale up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.

In order to conduct clinical trials of, and commercialize, our product candidates, we will need to manufacture them in large quantities. We may, in the future, establish and operate our own manufacturing facility, which will require significant amounts of additional capital and adequate personnel infrastructure. We, or any 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 we, or any 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 that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

Changes in methods of product candidate manufacturing, including changes introduced by building our own manufacturing capabilities, may result in additional costs or delay.

We currently rely on third parties for the production of GB-102 and our product candidates for preclinical testing and clinical trials, including supply of active pharmaceutical ingredient drug substance, sunitinib, as well as polymers used in the formulations, such as PLGA, injection devices, other raw materials, and for the sterilization of the finished product. We intend to build our own manufacturing capabilities, and it is common that various aspects of the development program, such as manufacturing methods, may be altered in an effort to optimize yield, manufacturing batch size, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. 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 conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates and generate revenue.

Our current operations are in two locations, and we or the third parties upon whom we depend, may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our current operations are located in Baltimore, Maryland and Redwood City, California, and our planned clinical trials will be conducted at a limited number of other sites. Any unplanned event, such as earthquake, flood, fire, explosion, extreme weather condition, medical epidemic or pandemic, including COVID-19, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our CMOs, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. Earthquakes or other natural disasters could further disrupt our operations and have a material and adverse effect on our business, financial condition, operating results and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research or manufacturing facilities or the manufacturing facilities of our CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. In addition, the long-term effects of climate change on a general economic conditions and the pharmaceutical industry in particular are unclear, and may heighten or intensify existing risk of natural disasters. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our CMOs, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption could have a material and adverse effect on our business, financial condition, operating results and prospects.

Risks Related to Commercialization

Our products may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, and the market opportunity for these products may be smaller than we estimate.

GB-102 or any of our product candidates that receives marketing approval may fail to gain market acceptance by physicians, patients, third-party payors and others in the medical community. We have not received marketing approval and have not commercially launched GB-102 or any of our product candidates and cannot yet accurately predict whether it or they will gain market acceptance and become commercially successful.

The degree of market acceptance of GB-102 or any product candidate for which we obtain marketing approval will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- our ability to offer our products for sale at competitive prices, particularly in light of the lower cost of alternative treatments;
- the clinical indications for which the product is approved;
- the convenience and ease of administration compared to alternative treatments, including the retention of any of our products as preferred treatment by patients and doctors;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of our marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

For example, even though we believe that GB-102 will have a longer duration of effect compared to approved treatments for wet AMD, it is possible that the market acceptance of GB-102, if it is approved for marketing, could be less than anticipated.

Our assessment of the potential market opportunity for GB-102 and our other product candidates is based on industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data. If the actual market for GB-102 or any of our product candidates is smaller than we expect, our product revenue may be limited, and it may be more difficult for us to achieve or maintain profitability.

If we are unable to secure a partner that can establish and maintain adequate sales, marketing and distribution capabilities, we may not be successful in commercializing any of our product candidates if and when they are approved. If we are unable to establish and maintain our own adequate sales, marketing and distribution capabilities, we may not be successful in commercializing our other product candidates if and when they are approved.

We have no experience in the sales, marketing and distribution of drug and device products, or in building a commercial team to do so. Furthermore, we lack sufficient capital resources to complete development of GB-102 without a partner, and we will be dependent on such partner, should we secure one, for the successful sales, marketing and distribution of GB-102. To achieve commercial success for any other product candidate for which we obtain marketing approval, we will need to establish and maintain adequate sales, marketing and distribution capabilities, either ourselves or through collaborations or other arrangements with third parties. If product candidates other than GB-102 are approved for marketing, we plan on commercializing them through our own specialty sales force. Alternatively, we may rely on a network of independent distributors across the United States to sell such products. We expect that a direct sales force will be required to effectively market and sell these products. We cannot be certain when, if ever, we will recognize revenue from commercialization of our product candidates in any international market. If we decide to commercialize our potential products outside of the United States, we expect to utilize a variety of collaboration, distribution and other marketing arrangements with one or more third parties. These may include independent distributors, pharmaceutical companies or our own direct sales organization.

There are risks involved with both establishing our own sales, marketing, and distribution capabilities and with entering into arrangements with third parties to perform these services. We may not be successful in entering into arrangements with third parties to sell, market and distribute our products or may be unable to do so on terms that are most beneficial to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to market, sell and distribute our products effectively. Our product revenues and our profitability, if any, under third-party collaboration, distribution or other marketing arrangements may also be lower than if we were to sell, market and distribute a product ourselves. On the other hand, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of any product candidate for which we recruit a sales force and establish marketing 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 sales and marketing personnel.

Other factors that may inhibit our efforts to commercialize products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to use or prescribe our products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we do not establish sales, marketing, and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing, or commercializing products before or more successfully than we do.

The development and commercialization of new drug and device products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to our product candidates that we may seek to develop or commercialize. 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.

The current standard of care for wet AMD is monotherapy administration of anti-VEGF drugs, principally Eylea, Avastin and Lucentis, which are well-established therapies and are widely accepted by physicians, patients and third-party payors, as well as the Port Delivery System with ranibizumab, or PDS, and Beovu, the two most recently approved anti-VEGF drugs. There are also several product candidates in late-stage clinical development for wet AMD, including those being developed by F. Hoffmann-La Roche AG, Kodiak Sciences Inc., Samsung Bioepis, Clearside Biomedical, Inc., Regeneron Pharmaceuticals, Inc., REGENXBIO, Inc., Chengdu Kanghong Pharmaceutical Group Co., Ltd, Outlook Therapeutics, Inc., and Opthea Limited. Physicians, patients and third-party payors may not accept the addition of GB-102 to their current treatment regimens for a variety of potential reasons, including:

- if they do not wish to incur the additional cost, if any, of GB-102;
- if they perceive the addition of GB-102 to be of limited benefit to patients compared to existing treatment options;
- if sufficient coverage and reimbursement are not available; and
- if they do not perceive GB-102 to have a favorable risk-benefit profile.

We are developing GB-102 as an alternative to existing anti-VEGF drugs, including Eylea, Avastin, Lucentis, Beovu, and PDS. Accordingly, if approved, GB-102 would directly compete with these therapies. While we believe GB-102 will compete favorably with existing anti-VEGF drugs, future approved standalone or combination therapies for wet AMD with demonstrated improved efficacy over GB-102 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 twice-yearly intravitreal injection;
- a method of administration that effectively avoids intravitreal injection; and
- significant cost savings or reimbursement advantages compared to GB-102 and other anti-VEGF therapies.

We also expect that product candidates currently in clinical development, or that could enter clinical development in the near future, could represent additional competition, if approved. These product candidates may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. Because there are a variety of means to treat wet AMD, our patents and other proprietary protections for GB-102 will not prevent development or commercialization of product candidates that are different from GB-102.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than our products. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, certain of these products may be available on a biosimilar basis, and our product candidates may not demonstrate sufficient additional clinical benefits to

physicians, patients or payors to justify a higher price compared to generic products. In many cases, insurers or other third-party payors, particularly Medicare, seek to encourage the use of biosimilar products.

If the development of GB-102 is delayed due to the time required to secure partner funding, or if such a partner requires additional clinical trials before commencing Phase 3 trials, the commercial launch of GB-102 could be delayed by several years. Such a delay could afford our competitors significant advantages in market adoption, penetration and reimbursement, and the future pricing of our products could be driven down substantially by a larger number of mature competitors. Any or all of these factors could significantly reduce the potential future revenue generated by GB-102 and adversely impact our stock price.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Any product candidate for which we obtain marketing approval may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

Our ability to commercialize our product candidates that we may develop successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers, managed care plans and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug and device companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for GB-102 or any other product that we commercialize and, even if they are available, the level of reimbursement may not be satisfactory.

Inadequate reimbursement may adversely affect the demand for, or the price of, GB-102 or any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize GB-102 or any other product candidates for which we obtain marketing approval.

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

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

limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Any product candidate for which we obtain marketing approval in the United States or in other countries may not be considered medically reasonable and necessary for a specific indication, may not be considered cost-effective by third-party payors, coverage and an adequate level of reimbursement may not be available and reimbursement policies of third-party payors may adversely affect our ability to sell our product candidates profitably.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we develop.

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

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

We currently hold $10 million in product liability insurance coverage, with a per incident limit of $250,000, which may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage as we conduct additional or larger clinical trials and should we eventually realize sales of any product candidate for which we obtain marketing approval.

Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Dependence on Third Parties

We intend to enter into collaborations with third parties in which they may complete or fund the clinical development, secure regulatory approval, and conduct the commercialization of GB-102, and may also do so for our other product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may utilize a variety of types of collaboration arrangements with third parties to develop or commercialize GB-102 and any of our other product candidates. We also may enter into arrangements with third parties to perform these services in the United States if we do not establish our own sales, marketing and distribution capabilities in the United States for our product candidates or if we determine that such arrangements are otherwise beneficial. We also may seek collaborators for development and commercialization of other product candidates. Our likely collaborators for any sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangement. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

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

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our product candidates that receive marketing approval or may elect not to continue or renew development or commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would divert management attention and resources and be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If any collaborations that we enter into do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed and we may need additional resources to develop our product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K also apply to the activities of our collaborators.

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

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

For some of our product candidates, we may decide to collaborate with pharmaceutical, biotechnology and medical device companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the product candidate, the costs and complexities of manufacturing and delivering a product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development

programs, delay 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 fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform.

We have relied, and may continue to rely, on third parties for certain aspects of our clinical development, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We have relied and may continue to rely on third parties, such as CROs to conduct clinical trials of GB-102 and other product candidates. If we deem necessary, we may engage CROs, clinical data management organizations, medical institutions and clinical investigators to conduct or assist in our clinical trials or other clinical development work. If we are unable to enter into an agreement with a service provider when required, our product development activities would be delayed.

Our reliance on third parties for development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We are also required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If we engage third parties and they do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

Risks Related to Our Intellectual Property

If our patent position does not adequately protect our product candidates, others could compete against us more directly, which would harm our business.

We own and exclusively license a number of U.S. issued patents, pending U.S. provisional and non-provisional patent applications, as well as pending Patent Cooperating Treaty applications and associated foreign patents and patent applications. Our success depends in large part on our ability to obtain and maintain patent protection both in the United States and in other countries for our product candidates. Our ability to protect our product candidates from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the scope of claims made under these patents, our ability to maintain, obtain and enforce patents is uncertain and involves complex legal and factual questions. Accordingly, rights under any issued patents may not provide us with sufficient protection for our product candidates or provide sufficient protection to afford us a commercial advantage against competitive products or processes. We cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us.

The patent prosecution process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may choose not to seek patent protection for certain innovations and may choose not to pursue patent protection in certain jurisdictions. Under the laws of certain jurisdictions, patents or other intellectual property rights may be unavailable or limited in scope. It is also possible that we will fail to identify patentable aspects of our research and development before it is too late to obtain patent protection.

We currently solely own or exclusively license patents and patent applications that encompass our current product candidates. We do not control the prosecution of the exclusively licensed patents and patent applications from Johns Hopkins University, or JHU, although we have input into the prosecution. In the future, we may choose to license additional patents or patent applications from third parties that we conclude are useful or necessary for our business goals. We may not have the right to control the preparation, filing, prosecution or maintenance of such additional licensed patent applications. Therefore, if we do license additional patents or patent applications in the future, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Patent applications in the United States are maintained in confidence for up to 18 months after their filing. In some cases, however, patent applications remain confidential in the U.S. Patent and Trademark Office, or PTO, for the entire time prior to issuance as a U.S. patent. Similarly, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Consequently, we cannot be certain that we or our licensors were the first to invent, or the first to file patent applications on, our product candidates or

their intended uses. Furthermore, we may not have identified all U.S. and foreign patents or published applications that affect our business either by blocking our ability to commercialize our products or by covering similar technologies that affect our product market or patentability, or all prior art that could be considered relevant to our patent claims.

The claims of any patents which have already issued or may issue in the future and are owned by or licensed to us, may not confer on us significant commercial protection against competing products. Additionally, our patents may be challenged by third parties, resulting in the patent being deemed invalid, cancelled, unenforceable or narrowed in scope, or the third party may circumvent any such issued patents.

Our patents may be challenged, for example, in a U.S. federal court or alternatively challenged in an adversarial proceeding at the Patent Trial and Appeals Board, or PTAB, at the PTO, using an *inter partes* Review or Post Grant Review process. The cost of these procedures is often substantial, and it is possible that our efforts would be unsuccessful resulting in a loss of our U.S. patent position. Further, even if a U.S. federal court or PTAB rules that a patent owned by us is valid and enforceable, if the other venue takes a contrary position, the patent can be considered invalid and not enforceable.

Therefore, a party seeking to invalidate a patent owned by or licensed to us in the United States has the procedural advantage of two alternative venues. To date, the PTAB has cancelled over 60% of the patent claims it has reviewed and is considered to be a forum of choice for infringers for patent cancellation.

Also, our pending patent applications may not issue, and we may not receive any additional patents. Our patents might not contain claims that are sufficiently broad to prevent others from utilizing our technologies. For instance, GB-102 uses our proprietary aggregating microparticle technologies to deliver sunitinib for ocular treatment. If a competitor develops a product that uses a different particle or non-particle technology to deliver sunitinib to the eye, it may be able to compete with us without infringing our owned or licensed patents, as the patents on sunitinib expired in August 2021. GB-401 includes our proprietary beta-adrenergic blocking agent prodrug molecule in our proprietary sustained release formulation technology. If a competitor develops a product that uses a different prodrug of the same beta-blocker, or the beta-blocker itself, or uses a delivery system that is different from our proprietary sustained release formulation technologies, then it may be able to compete with our GB-401 product without infringing our owned or licensed patent claims. Consequently, our competitors may independently develop competing products that do not infringe our patents or other intellectual property. To the extent a competitor can develop similar products using a different delivery system, microparticle or molecule, our patents may not prevent them from directly competing with us.

The Leahy-Smith America Invents Act, or America Invents Act, was signed into law in September 2011, and many of the substantive changes became effective in March 2013. The America Invents Act revised U.S. patent law in part by changing the standard for patent approval from a “first to invent” standard to a “first to file” standard and developing a post-grant review system. This legislation changes U.S. patent law in a way that may weaken our ability to obtain patent protection in the United States for those applications filed after March 2013. For example, if we were the first to invent a new product or its use, but another party is the first to file a patent application on this invention, under the new law the other party may be entitled to the patent rights on the invention.

The America Invents Act created for the first time new procedures to challenge issued patents in the United States, including post-grant review and *inter partes* review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent with a priority date of March 16, 2013 or later, a petition for post-grant review can be filed by a third party in a nine-month window from issuance of the patent. A petition for *inter partes* review can be filed immediately following the issuance of a patent if the patent was filed prior to March 16, 2013. A petition for *inter partes* review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with a priority date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of challenge, whereas *inter partes* review proceedings can only be brought to raise a challenge based on published prior art. These adversarial actions at the PTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts and use a lower burden of proof than used in litigation in U.S. federal courts. The PTO issued a Final Rule on November 11, 2018, announcing that it will now use the same claim construction currently used in the U.S. federal courts to interpret patent claims, which is the plain and ordinary meaning of words used. If any of our patents are challenged by a third party in such a PTO proceeding, there is no guarantee that we or our licensors will be successful in defending the patent, which would result in a loss of the challenged patent right to us.

The U.S. Supreme Court has issued opinions in patent cases in the last few years that many consider may weaken patent protection in the United States, either by narrowing the scope of patent protection available in certain circumstances, holding that certain kinds of innovations are not patentable or generally otherwise making it easier to invalidate patents in court. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the PTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

The laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as in the United States and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed. For example, we could become a party to foreign opposition proceedings, such as at the European Patent Office, or patent litigation and other proceedings in a foreign court. If so, uncertainties resulting from the initiation and continuation of such proceedings could have a material adverse effect on our ability to compete in the marketplace. The cost of foreign adversarial proceedings can also be substantial, and in many foreign jurisdictions, the losing party must pay the attorney fees of the winning party.

Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization of our product candidates, thereby reducing or eliminating any advantages of the patent. To the extent our product candidates based on that technology are not commercialized significantly ahead of the date of any applicable patent, or to the extent we have no other patent protection on such product candidates, those product candidates would not be protected by patents, and we would then rely solely on other forms of exclusivity, such as regulatory exclusivity provided by the Federal Food, Drug, and Cosmetic Act, or FDCA, or trade secret protection.

Patents filed by our licensor, Johns Hopkins University, may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and may limit our ability to contract with non-U.S. manufacturers.

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

If we infringe or are alleged to infringe intellectual property rights of third parties, our business could be harmed.

Our research, development or commercialization activities, including any product candidates or products resulting from these activities, may infringe or be claimed to infringe patents or other proprietary rights owned by third parties and to which we do not hold licenses or other rights. We may not be aware of third-party patents that a third party might assert against us. For example, there may be third-party applications that have been filed but not published that, if issued, could be asserted against us. If a patent infringement suit were brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. Further, if we are found to have infringed a third-party patent, we could be obligated to pay royalties and/or other payments to the third party for the sale of our product, which may be substantial, or we could be enjoined from selling our product. We could also incur substantial litigation costs.

Litigation regarding patents, intellectual property and other proprietary rights may be expensive and time-consuming. If we are involved in such litigation, it could cause delays in bringing product candidates to market and harm our ability to operate.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Although we are not currently aware of any litigation or other proceedings or third-party claims of patent infringement against us related to our product candidates, the pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may obtain patents in the future and allege that the use of our technologies infringes these patent claims or that we are employing their proprietary technology without authorization. Likewise, third parties may challenge or infringe upon our existing or future patents. Proceedings involving our patents or patent applications or those of others could result in adverse decisions regarding:

- the patentability of our inventions relating to our product candidates; and/or
- the enforceability, validity or scope of protection offered by our patents relating to our product candidates.

Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may:

- incur substantial monetary damages;
- encounter significant delays in bringing our product candidates to market; and/or
- be precluded from participating in the manufacture, use or sale of our product candidates or methods of treatment requiring licenses.

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. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

Because our current clinical candidates incorporate small molecules, after commercialization they will be subject in the United States to the patent litigation process of the Hatch-Waxman Amendments, which allows a generic company to submit an Abbreviated New Drug Application, or ANDA, to the FDA to obtain approval to sell our drug using bioequivalence data only. Under the Hatch-Waxman Amendments, we will have the opportunity to list all of our patents that cover our drug product or its method of use in the FDA's compendium of "Approved Drug Products with Therapeutic Equivalence Evaluation," sometimes referred to as the FDA's Orange Book. Currently, in the United States, the FDA may grant three years of exclusivity to a new formulation, for which our GB-102 product would qualify, and other changes to a drug, such as the addition of a new indication to the package insert, if the application contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to the approval of the application. The FDA also may grant five years of exclusivity for new chemical entities, or NCEs, for which GB-401 would qualify. An NCE is a drug that contains no active moiety that has been approved by the FDA in any other NDA. A generic company can submit an ANDA to the FDA immediately after FDA approval of our GB-102 product and four years after approval of GB-401. The submission of an ANDA by a generic company is considered a technical act of patent infringement. The generic company can certify that it will wait until the natural expiration date of our listed patents to sell a generic version of our product or can certify that one or more of our listed patents are invalid, unenforceable or not infringed. If the latter, we will have 45 days to bring a patent infringement lawsuit against the generic company. This will initiate a challenge to one or more of our Orange Book listed patents based on arguments from the generic company that either our patent is invalid, unenforceable or not infringed. Under the Hatch-Waxman Amendments, if a lawsuit is brought, the FDA is prevented from issuing a final approval on the generic drug until 30 months after the end of the data exclusivity period, or a final decision of a court holding that our asserted patent claims are invalid, unenforceable or not infringed. If we do not properly list our relevant patents in the Orange Book, or timely file a lawsuit in response to a certification from a generic company under an ANDA, or if we do not prevail in the resulting patent litigation, we can lose our proprietary market, which can rapidly become generic. Further, even if we do correctly list our relevant patents in the Orange Book, bring a lawsuit in a timely manner and prevail in that lawsuit, it may be at a very significant cost to us of attorneys' fees and employee time and distraction over a long period. Further, it is common for more than one generic company to try to sell an innovator drug at the same time, and so we may be faced with the cost and distraction of multiple lawsuits. We may also determine it is necessary to settle the lawsuit in a manner that allows the generic company to enter our market prior to the expiration of our patent or otherwise in a manner that adversely affects the strength, validity, or enforceability of our patent.

A number of pharmaceutical companies have been the subject of intense review by the U.S. Federal Trade Commission or a corresponding agency in another country based on how they have conducted or settled drug patent litigation, and certain reviews

have led to an allegation of an anti-trust violation, sometimes resulting in a fine or loss of rights. We cannot be sure that we would not also be subject to such a review or that the result of the review would be favorable to us, which could result in a fine or penalty.

The U.S. Federal Trade Commission, or FTC, has brought a number of lawsuits in federal court in the past few years to challenge Hatch-Waxman ANDA litigation settlements between innovator companies and generic companies as anti-competitive. The FTC has taken an aggressive position that anything of value is a payment, whether money is paid or not. Under their approach, if an innovator as part of a patent settlement agrees not to launch or delay launch of an authorized generic during the 180-day period granted to the first generic company to challenge an Orange Book listed patent covering an innovator drug, or negotiates a delay in entry without payment, the FTC may consider it an unacceptable reverse payment. The biopharmaceutical industry has argued that such agreements are rational business decisions to dismiss risk and are immune from antitrust attack if the terms of the settlement are within the scope of the exclusionary potential of the patent. In 2013, the U.S. Supreme Court, in a five-to-three decision in FTC v. Actavis, Inc. rejected both the biopharmaceutical industry's and the FTC's arguments with regard to so-called reverse payments, and held that whether a "reverse payment" settlement involving the exchange of consideration for a delay in entry is subject to an anticompetitive analysis depends on five considerations: (a) the potential for genuine adverse effects on competition; (b) the justification of payment; (c) the patentee's ability to bring about anticompetitive harm; (d) whether the size of the payment is a workable surrogate for the patent's weakness; and (e) that antitrust liability for large unjustified payments does not prevent litigating parties from settling their lawsuits, for example, by allowing the generic to enter the market before the patent expires without the patentee's paying the generic. Furthermore, whether a reverse payment is justified depends upon its size, its scale in relation to the patentee's anticipated future litigation costs, its independence from other services for which it might represent payment, as was the case in Actavis, and the lack of any other convincing justification. The Court held that reverse payment settlements can potentially violate antitrust laws and are subject to the standard antitrust rule-of-reason analysis, with the burden of proving that an agreement is unlawful on the FTC and leaving to lower courts the structuring of such rule of reason analysis. If we are faced with drug patent litigation, including Hatch-Waxman litigation with a generic company, we could be faced with such an FTC challenge based on that activity, including how or whether we settle the case, and even if we strongly disagree with the FTC's position, we could face a significant expense or penalty.

We may not be able to enforce our intellectual property rights throughout the world.

Filing, prosecuting, and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. 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 may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, may not favor the enforcement of our patents and other intellectual property rights.

This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights in certain foreign countries. A number of foreign countries have stated that they are willing to issue compulsory licenses to patents held by innovator companies on approved drugs to allow the government or one or more third-party companies to sell the approved drug without the permission of the innovator patentee where the foreign government concludes it is in the public interest. India, for example, has used such a procedure to allow domestic companies to make and sell patented drugs without innovator approval. There is no guarantee that patents covering any of our drugs will not be subject to a compulsory license in a foreign country, or that we will have any influence over if or how such a compulsory license is granted. Further, Brazil allows its regulatory agency ANVISA to participate in deciding whether to grant a drug patent in Brazil, and patent grant decisions are made based on several factors, including whether the patent meets the requirements for a patent and whether such a patent is deemed in the country's interest. In addition, several other countries have created laws that make it more difficult to enforce drug patents than patents on other kinds of technologies. Further, under the treaty on the Trade-Related Aspects of Intellectual Property, or TRIPS, as interpreted by the Doha Declaration, countries in which drugs are manufactured are required to allow exportation of the drug to a developing country that lacks adequate manufacturing capability. Therefore, our drug markets in the United States or foreign countries may be affected by the influence of current public policy on patent issuance, enforcement or involuntary licensing in the healthcare area.

In addition, in November 2015, members of the World Trade Organization, or WTO, which administers TRIPS, voted to extend the exemption against enforcing pharmaceutical drug patents in least developed countries until 2033. We currently have no patent applications filed in least developed countries, and our current intent is not to file in these countries in the future, at least in part due to this WTO pharmaceutical patent exemption.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the PTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

We rely on our ability to stop others from competing by enforcing our patents; however, some jurisdictions may require us to grant licenses to third parties. Such compulsory licenses could be extended to include some of our product candidates, which may limit our potential revenue opportunities.

Many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties, in certain circumstances. For example, compulsory licensing, or the threat of compulsory licensing, of life-saving products and expensive products is becoming increasingly popular in developing countries, either through direct legislation or international initiatives. Compulsory licenses could be extended to include some of our product candidates, if they receive marketing approval, which may limit our potential revenue opportunities. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. Competitors may also 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, if our ability to enforce our patents to stop infringing activities is inadequate. 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. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in major markets for our products where such patent rights exist, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may be limited to monetary relief and may be unable to enjoin infringement if a government is the infringer, which could materially diminish the value of the patent.

If we fail to comply with our obligations under the license agreement with JHU, we could lose license rights that are necessary for developing and commercializing one or more of our product candidates.

Our exclusive license with JHU for technology relating to our lead product candidates imposes various development, commercialization, royalty payment, diligence and other obligations on us. Specifically, we are required to:

- pay JHU a minimum royalty fee and potential milestone payments;
- pay JHU low single-digit royalties on all net sales of products and a share of any sublicensing revenues;
- use commercially reasonable efforts to bring products to market;
- provide royalty reports to JHU; and
- indemnify JHU against certain claims and maintain insurance coverage.

If we breach any of these obligations, JHU may have the right to terminate the license, which would result in our being unable to develop, manufacture and sell products that are covered by the licensed technology, or in a competitor’s gaining access to the licensed technology.

The rights we rely upon to protect our unpatented trade secrets may be inadequate.

We rely on unpatented trade secrets, know-how and technology, which are difficult to protect, especially in the pharmaceutical industry, where much of the information about a product must be made public during the regulatory approval process. We seek to protect trade secrets, in part, by entering into confidentiality agreements with employees, consultants and others. These parties may breach or terminate these agreements or may refuse to enter into such agreements with us, and we may not have adequate remedies for such breaches. Furthermore, these agreements may not provide meaningful protection for our trade secrets or other proprietary information or result in the effective assignment to us of intellectual property and may not provide an adequate remedy in the event of unauthorized use or disclosure of confidential information or other breaches of the agreements. Despite our efforts to protect our trade secrets, we or our collaboration partners, board members, employees, consultants, contractors or scientific and other advisors may unintentionally or willfully disclose our proprietary information to competitors.

If we fail to maintain trade secret protection, our competitive position may be adversely affected. Competitors may also independently discover our trade secrets. Enforcement of claims that a third party has illegally obtained and is using trade secrets is expensive, time consuming and uncertain. If our competitors independently develop equivalent knowledge, methods and know-how, we would not be able to assert our trade secrets against them and our business could be harmed.

Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information and may not adequately protect our intellectual property.

We rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. To protect our proprietary technology and processes, we also rely in part on confidentiality and intellectual property assignment agreements with our current and potential corporate partners, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information nor result in the effective assignment to us of intellectual property and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information or other breaches of the agreements. In addition, others may independently discover our trade secrets and proprietary information, and in such case, we could not assert any trade secret rights against such party. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. Costly and time-consuming litigation could be necessary to seek to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

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

We may be required, or choose, to suspend, repeat or terminate our clinical trials if they are not conducted in accordance with regulatory requirements, the results are negative or inconclusive, the trials are not well-designed, or research participants experience adverse safety outcomes.

Regulatory agencies, institutional review boards, or IRBs, or data safety monitoring boards may at any time recommend the temporary or permanent discontinuation of our clinical trials or request that we cease using investigators in the clinical trials if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, or that they present an unacceptable safety risk to participants. Clinical trials must be conducted in accordance with GCPs and other applicable foreign regulatory authority guidelines. Clinical trials are subject to oversight by the FDA, foreign regulatory authorities and IRBs at the trial sites where the clinical trials are conducted. In addition, clinical trials must be conducted with product candidates produced in accordance with applicable current good manufacturing practices. Clinical trials may be placed on a full or partial clinical hold by the FDA, foreign regulatory authorities, or us for various reasons, including, but not limited to: deficiencies in the conduct of the clinical trials, including failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols; deficiencies in the clinical trial operations or trial sites; deficiencies in the trial designs necessary to demonstrate efficacy; fatalities or other AEs arising during a clinical trial due to medical problems that may or may not be related to clinical trial treatments; the product candidates may not appear to be more effective than current therapies; or the quality or stability of the product candidates may fall below acceptable standards.

Although we have never been asked by a regulatory agency, IRB or data safety monitoring board to temporarily or permanently discontinue a clinical trial, if we elect or are forced to suspend or terminate a clinical trial of any of our current or future product candidates, the commercial prospects for that product may be harmed and our ability to generate product revenue from that product may be delayed or eliminated. Furthermore, any of these events could prevent us or our partners from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our product candidates and impair our ability to generate revenue from the commercialization of these products either by us or by our collaboration partners. In our Phase 2a trial of GB-102 for the treatment of ME secondary to DME or RVO, 16 of the 21 patients had at least one drug-related AE, with the majority of them in the 2 mg dosing arm. In addition, one patient in the 2 mg dosing arm experienced two ocular SAEs. As a result, we decided to pause enrollment of new patients in our Phase 2b wet AMD trial until we could collect more data on the Phase 2a trial. We subsequently conducted an interim safety analysis which led to the selection of the 1 mg dose for GB-102. We then amended the Phase

2b protocol such that all patients having originally received the 2 mg dose of GB-102 received the 1 mg dose as their repeat therapy at their six-month visit. In the treatment phase of our Phase 2b trial, nine of 21 patients in the 1 mg arm had at least one drug-related AE, and 17 of 22 patients in the 2 mg arm who were all subsequently re-dosed with 1 mg had at least one drug-related AE.

In our future clinical trials, any SAEs could result in the FDA delaying such clinical trials or denying or delaying clearance or approval of a product. Even though an AE may not be the result of the failure of one of our drug candidates, the FDA or an IRB could delay or halt a clinical trial for an indefinite period of time while an AE is reviewed, and likely would do so in the event of multiple such events. Any delay or termination of our current or future clinical trials as a result of the risks summarized above, including delays in obtaining or maintaining required approvals from IRBs, delays in patient enrollment, the failure of patients to continue to participate in a clinical trial, and delays or termination of clinical trials as a result of protocol modifications or AEs during the trials, may cause an increase in costs and delays in the submission of any New Drug Applications, or NDAs, to the FDA, delay the approval and commercialization of our products or result in the failure of the clinical trial, which could adversely affect our business, operating results and prospects. Lengthy delays in the completion of clinical trials of our products would adversely affect our business and prospects and could cause us to cease operations.

If preliminary data demonstrate that any of our product candidates has an unfavorable safety profile and is unlikely to receive regulatory approval or be successfully commercialized, we may voluntarily suspend or terminate future development of such product candidate. Any one or a combination of these events could prevent us from obtaining regulatory approval and achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing the product candidate, which in turn could delay or prevent us from generating significant revenues from the sale of the product.

If we are not able to obtain required regulatory approvals, we will not be able to commercialize our product candidates and our ability to generate significant revenue will be materially impaired. The regulatory approval process is expensive, time-consuming and uncertain. As a result, we cannot predict when or if we, or any collaborators we may have in the future, will obtain regulatory approval to commercialize our product candidates.

The activities associated with the development of our product candidates, including design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside the United States. Failure to obtain regulatory approval for a product candidate will prevent us from commercializing a product candidate. We have not submitted for regulatory approval to market GB-102 or any other product candidate.

The process of obtaining regulatory approvals, both in the United States and abroad, is expensive and may take many years, especially if additional clinical trials are required, if approval is obtained at all. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and purity. The FDA's and other regulatory agencies' decision to grant us regulatory approval will depend on our ability to demonstrate with substantial clinical evidence through adequate well-controlled clinical trials, that the product candidates are effective, as measured statistically by comparing the overall improvement in actively-treated patients against improvement in the control group. However, there is a possibility that our data may fail to demonstrate statistically significant non-inferiority versus the active control. Alternatively, there is a possibility that our data may be statistically significant, but that the actual clinical benefit of the product candidates may not be considered to be clinically significant, clinically relevant or clinically meaningful. We cannot predict whether the regulatory agencies will find that our clinical trial results provide compelling data. Even if we believe that the data from our trials will support regulatory approval in the United States or in Europe, we cannot predict whether the agencies will agree with our analyses and approve our applications.

Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA, the EMA or other regulatory authorities may determine that our product candidates are not safe or effective, are only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining regulatory approval or prevent or limit commercial use. In addition, while we have had general discussions with the FDA concerning the design of some of our clinical trials, we have not discussed with the FDA the specifics of the regulatory pathways for our product candidates. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Approval of our product candidates may be delayed or refused for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications;

- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical programs or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- potential delays in enrollment, site visits, evaluations, dosing of patients participating in the clinical trial as hospitals prioritize the treatment of COVID-19 patients or patients decide to not enroll in the trial as a result of the COVID-19 pandemic;
- government regulations that may be imposed in response to the COVID-19 pandemic may restrict the movement of our global supply chain, divert hospital resources that are necessary to administer our product candidates;
- the facilities or conduct of the third-party manufacturers with which we contract may not be adequate to support approval of our product candidates; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Even if our product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

The regulatory process can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. If we experience delays in obtaining approval, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

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

In order to market and sell our product candidates in the European Union and many other jurisdictions, we or our third-party collaborators must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be sold in that country. We or our collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in other countries. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. The United Kingdom and European Union entered into the Trade and Cooperation Agreement, effective January 1, 2021, which sought to resolve some of the outstanding issues related to Brexit, including free trade and an overarching governance structure for business conducted between the jurisdictions. Under the Trade and Cooperation Agreement, there was a transition period in which the U.K. was not designated as a "third country" and, as a result, personal data could flow from the EU to the U.K. without any adequacy mechanisms (e.g., Standard Contractual Clauses, etc.). The Trade and Cooperation Agreement went into full force on May 1, 2021, and the transition period with regard to personal data automatically terminated on June 26, 2021. On June 28, 2021, the European Commission adopted two definitive adequacy decisions addressing the transfers of personal data to the United Kingdom under the General Data Protection Regulation, or GDPR, and the Law Enforcement Directive.

Because this Trade and Cooperation Agreement is still new, it is unclear how it may affect the regulatory framework for our products. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products

and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

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

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

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to current good manufacturing practices applicable to drug manufacturers or quality assurance standards applicable to medical device manufacturers, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, any CMOs we may engage in the future, our future collaborators and their CMOs will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to physicians, recordkeeping and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a risk evaluation and mitigation strategy.

If any of our product candidates receives regulatory approval and we or others later identify undesirable side effects caused by the product, our ability to market and derive revenue from the products could be compromised.

In the event any of our product candidates receive regulatory approval and we or others identify undesirable side effects, AEs or other problems caused by one of our products, any of the following adverse outcomes could occur, which could result in the loss of significant revenue to us and materially and adversely affect our operating results and business:

- regulatory authorities may withdraw or modify their approval of the product and require us to take the product off the market or seize the product;
- we may need to recall the product or change the way the product is administered to patients;
- we may need to conduct additional preclinical studies or clinical trials or change the labeling of the product;
- additional restrictions may be imposed on the marketing and promotion of the particular product or the manufacturing processes for the product or any component thereof;
- we may not be able to secure or maintain adequate coverage and reimbursement for our products from government (including U.S. federal health care programs) and private payors;
- regulatory authorities may require the addition of labeling statements, such as a boxed warning, or equivalent, or contraindications or limitations on the indications for use;
- regulatory authorities may require us to implement a Risk Evaluation and Mitigation Strategy, or REMS, plan, or to conduct post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product;
- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we may be exposed to potential lawsuits and associated legal expenses, including costs of resolving claims;
- the product may become less competitive and sales may decrease; and
- our reputation may suffer both among clinicians and patients.

Any of these events could have a material and adverse effect on our operations and business. The commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

If our product candidates receive regulatory approval, we will also be subject to ongoing FDA obligations and continued regulatory review, such as continued safety reporting requirements, and we may also be subject to additional FDA post-marketing obligations or new regulations, all of which may result in significant expense and limit our ability to commercialize our drugs.

Any regulatory approvals that we receive for our product candidates will require surveillance to monitor the safety and efficacy of the product candidate and may require us to conduct post-approval clinical studies. The FDA has significant post-market authority, including the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate safety risks related to the use of a product or to require withdrawal of the product from the market. The manufacturing facilities used to manufacture our product candidates will also be subject to periodic review and inspection by the FDA and other regulatory agencies, including for continued compliance with current good manufacturing practices requirements. The discovery of any new or previously unknown problems with our third-party manufacturers, manufacturing processes or facilities may result in restrictions on the product, manufacturer or facility, including withdrawal of the product from the market. Any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products. If we promote our product candidates in a manner inconsistent with FDA-approved labeling or otherwise not in compliance with FDA regulations, we may be subject to enforcement action.

In addition, if the FDA or a foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, AE reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practices and GCPs, for any clinical trials that we conduct post-approval.

Moreover, if we obtain regulatory approval for our product candidates, we will only be permitted to market our products for the indication approved by the FDA or foreign regulatory authority, and such approval may involve limitations on the indicated uses or promotional claims we may make for our products, or otherwise not permit labeling that sufficiently differentiates our product candidates from competitive products with comparable therapeutic profiles. For example, we will not be able to claim that our products have fewer side effects, or improve compliance or efficacy as compared to other drugs unless we can demonstrate those attributes to the FDA or foreign regulatory authority in comparative clinical trials.

If we or our CMOs or service providers fail to comply with applicable continuing regulatory requirements in the United States or foreign jurisdictions in which we seek to market our products, we or they may be subject to, among other things, fines, warning or untitled letters, holds on clinical trials, delay of approval or refusal by the FDA or similar foreign regulatory bodies to approve pending applications or supplements to approved applications, suspension or withdrawal of regulatory approval, product recalls and seizures, administrative detention of products, refusal to permit the import or export of products, operating restrictions, injunction, civil penalties and criminal prosecution.

The FDA's and foreign regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any regulatory approval that we may have obtained, and we may not achieve or sustain profitability.

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

Violations of the FDCA relating to the promotion or manufacturing of drug products may lead to investigations by the FDA, the Department of Justice and state Attorneys General alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws. In addition, later discovery of previously unknown AEs or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;

- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of our products;
- product seizure or detention; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, or with requirements related to the development of products for the pediatric population, can also result in significant financial penalties.

If the FDA does not conclude that the product candidates for which we may use the Section 505(b)(2) regulatory approval pathway satisfy the requirements for the use of such pathway, or if the requirements for such product candidates under Section 505(b)(2) are not as we expect, the approval pathway for any such product candidates will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may not be successful.

We may seek FDA approval through the Section 505(b)(2) regulatory pathway for GB-401. The Hatch-Waxman Amendments added Section 505(b)(2) to the FDCA. Section 505(b)(2) permits the submission of an NDA where at least some of the information required for approval comes from studies that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Section 505(b)(2), if applicable to us under the FDCA, would allow an NDA to rely in part on data in the public domain or the FDA's prior conclusions regarding the safety and effectiveness of approved drug products, which could expedite the development program for our product candidates by potentially decreasing the amount of preclinical or clinical data that we would need to generate in order to obtain FDA approval. For GB-102, we are seeking to rely on the FDA's prior conclusions regarding the safety and effectiveness of sunitinib, which has previously been approved for the treatment of gastrointestinal stromal tumors, advanced renal cell carcinoma, and a certain type of pancreatic cancer. For GB-401, we intend to rely in part on the FDA's prior findings for the previously approved active pharmaceutical ingredient, or API, as well as relevant publications, and to conduct additional good laboratory practice, or GLP, toxicology studies with GB-401, to support the GB-401 IND and any future 505(b)(2) NDA.

If we cannot pursue the Section 505(b)(2) regulatory pathway, we may need to conduct additional clinical trials, provide additional data and information, and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for these product candidates, and complications and risks associated with these product candidates, would likely substantially increase.

Moreover, our inability to pursue the Section 505(b)(2) regulatory pathway would likely result in new competitive products reaching the market more quickly than GB-102 or GB-401, which would likely adversely impact our competitive position and prospects. Even if we can pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that GB-102 or GB-401 will receive the requisite approvals for commercialization.

In addition, notwithstanding the approval of products by the FDA under Section 505(b)(2), certain pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's current interpretation of Section 505(b)(2) is successfully challenged, the FDA may change its 505(b)(2) policies and practices, which could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b)(2). In addition, the pharmaceutical industry is highly competitive, and Section 505(b)(2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs that are referenced in a Section 505(b)(2) NDA. These requirements may give rise to patent litigation and mandatory delays in approval of our NDAs for up to 30 months or longer depending on the outcome of any litigation. It is not uncommon for the owner of the NDA of an approved product to file a citizen petition with the FDA seeking to delay approval of, or impose additional approval requirements for, pending competing products. If successful, such petitions could significantly delay, or even prevent, the approval of a new product. However, even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. In addition, even if we are able to utilize the Section 505(b)(2) regulatory pathway, there is no guarantee this would ultimately lead to earlier approval.

Moreover, even if our product candidates are approved under Section 505(b)(2), the approval may be subject to limitations on the indicated uses for which the products may be marketed or to other conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

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

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation, affordability, and use of any product candidates for which we obtain regulatory approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain regulatory approval. In addition, we may be subject to transparency laws and patient privacy regulation by U.S. federal and state governments and by governments in foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which impose criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by HITECH, and their respective implementing regulations, which imposes obligations, including mandatory contractual terms, on covered healthcare providers, health plans and healthcare clearinghouses, as well as their business associates, with respect to safeguarding the privacy, security and transmission of protected health information; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government funded healthcare programs. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

Recently enacted and future legislation, including healthcare legislative reform measures, may adversely affect or limit our ability to commercialize our products, including the prices that we can obtain for any products that are approved in the United States or foreign jurisdictions, and may negatively impact our business and results of operations.

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

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products. Cost reduction initiatives and other provisions of this legislation could limit coverage of and reduce the price that we receive for any FDA approved products. While the MMA applies only to product benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA or other healthcare reform measures may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA. Among the provisions of the ACA of importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any of our product candidates and that are approved for sale, are increased manufacturer rebate liability under the Medicaid Drug Rebate Program, imposition of a significant annual fee on companies that manufacture or import branded prescription drug products and the requirement for manufacturers to provide a discount off the negotiated price of prescriptions filled by beneficiaries in the Medicare Part D coverage gap, referred to as the “donut hole,” which is now 70% of the negotiated price.

There have been executive, legislative and judicial efforts to modify, repeal, or otherwise invalidate all, or certain aspects of, the ACA. By way of example, the Tax Cuts and Jobs Act of 2017, or the Tax Reform Act, included, among other things, a provision repealing the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate.” On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the “individual mandate” was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and closed on August 15, 2021. The executive order also instructed 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 possible that the ACA will be subject to judicial or Congressional challenges in the future. It is uncertain how any such challenges and the healthcare 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 to reduce healthcare expenditures. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional Congressional action is taken. The Medicare reductions phase back in starting with a 1% reduction in effect from April 1, 2022 to June 30, 2022 before increasing to the full 2% reduction. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations.

Further, there has 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. By way of example, in December 2020, CMS issued a final rule implementing significant manufacturer price reporting changes under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. On September 9, 2021, the Biden Administration published a wide-ranging list of policy proposals, most of which would need to be carried out by Congress, to reduce drug prices and drug payment. The HHS plan includes, among other reform measures, proposals to (1) give Medicare authority to directly negotiate drug prices with manufacturers, (2) authorize HHS to negotiate Medicaid supplemental rebates on behalf of states, (3) allow employer-based, ACA marketplace and commercial health insurance plans to access Medicare negotiated drug prices, (4) place a cap on out-of-pocket costs for Medicare Part D beneficiaries and redistribute a higher proportion of drug costs to Part D and

manufacturers, (5) mandate purchase of the least costly-alternative and to institute value-based or outcomes-based pricing arrangements, (6) disincentivize drug price increases, (8) facilitate approval and prescription of biosimilar and generic drugs, (9) increase drug pricing transparency, (10) prohibit certain types of rebates to pharmacy benefit managers, and (11) develop drug pricing models by tying price to outcomes. Many similar proposals, including the plans to give Medicare authority to negotiate drug prices and cap out-of-pocket costs, have already been included in policy statements and legislation currently being considered by Congress. It is unclear to what extent new statutory, regulatory, and administrative initiatives will be enacted and implemented and to what extent these or any future legislation or regulations by the Biden administration will have on our business, including our ability to generate revenue and achieve profitability.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of regulatory approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

We expect that additional state and federal healthcare reform measures will be adopted in the future, particularly in light of the new presidential administration. Such reform measures may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our therapeutics.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing or selling certain products outside of the United States and such foreign operations would require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

We are subject to stringent and changing privacy laws, regulations and standards as well as contractual obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could harm our reputation, subject us to significant fines and liability, or otherwise adversely affect our business or prospects.

We are, and may increasingly become, subject to various laws and regulations, as well as contractual obligations, relating to data privacy and security in the jurisdictions in which we operate. The regulatory environment related to data privacy and security is increasingly rigorous, with new and constantly changing requirements applicable to our business, and enforcement practices are likely to remain uncertain for the foreseeable future. These laws and regulations may be interpreted and applied differently over time and from

jurisdiction to jurisdiction, and it is possible that they will be interpreted and applied in ways that may have a material adverse effect on our business, financial condition, results of operations and prospects.

In the United States, in addition to HIPAA, various federal and state regulators have adopted, or are considering adopting, laws and regulations concerning personal information and data security. Certain state laws may be more stringent or broader in scope, or offer greater individual rights, with respect to personal information than federal, international or other state laws, and such laws may differ from each other, all of which may complicate compliance efforts. For example, the California Consumer Privacy Act, or CCPA, which increases privacy rights for California residents and imposes obligations on companies that process their personal information, came into effect on January 1, 2020, and became enforceable by the California Attorney General on July 1, 2020, along with related regulations which came into force on August 14, 2020. Additionally, although not effective until January 1, 2023, the California Privacy Rights Act, or the CPRA, which expands upon the CCPA, was passed in the recent election on November 3, 2020. Among other things, the CCPA requires covered companies to provide new disclosures to California consumers about their data collection, use and sharing practices and provide such consumers new data protection and privacy rights, including the ability to opt out of certain sales of personal information, right to request correction, access, and deletion of their personal information, the right to opt out of certain personal information sharing, and the right to receive detailed information about how their personal information is processed. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that result in the loss of personal information. This private right of action may increase the likelihood of, and risks associated with, data breach litigation. The CPRA significantly modifies the CCPA, including by expanding consumers' rights with respect to certain personal information and creating a new state agency to oversee implementation and enforcement efforts. The CCPA and CPRA may increase our compliance costs and potential liability, particularly in the event of a data breach, and could have a material adverse effect on our business, including how we use personal information, our financial condition, the results of our operations or prospects. State laws are changing rapidly and there is discussion in the U.S. of a new comprehensive federal data privacy law to which we would become subject if it is enacted.

Additionally, the CCPA has prompted a number of proposals for new federal and state-level privacy legislation, such as in Nevada, Virginia, New Hampshire, Illinois and Nebraska. Such new privacy laws add additional complexity, requirements, restrictions and potential legal risk, require additional investment in resources for compliance programs, and could impact business strategies and the availability of previously useful data.

Internationally, laws, regulations and standards in many jurisdictions apply broadly to the collection, use, retention, security, disclosure, transfer and other processing of personal information. For example, the General Data Protection Regulation, or GDPR, of the European Union, or EU, which became effective in May 2018, greatly increased the European Commission's jurisdictional reach of its laws and adds a broad array of requirements for handling personal information, including, for example, requirements to establish a legal basis for processing, higher standards for obtaining consent from individuals to process their personal information, more robust disclosures to individuals and a strengthened individual data rights regime, requirements to implement safeguards to protect the security and confidentiality of personal information that requires the adoption of administrative, physical and technical safeguards, shortened timelines for data breach notifications to appropriate data protection authorities or data subjects, limitations on retention and secondary use of information, increased requirements pertaining to health data and additional requirements that we impose certain contractual obligations on third-party processors in connection with the processing of the personal information. EU member states are tasked under the GDPR to enact, and have enacted, certain implementing legislation that adds to and/or further interprets the GDPR requirements and potentially extends our obligations and potential liability for failing to meet such obligations. The GDPR, together with national legislation, regulations and guidelines of the EU member states governing the processing of personal information, impose strict obligations and restrictions on the ability to collect, use, retain, protect, disclose, transfer and otherwise process personal information. In particular, the GDPR includes obligations and restrictions concerning the consent and rights of individuals to whom the personal information relates, the transfer of personal information out of the European Economic Area, security breach notifications and the security and confidentiality of personal information. The GDPR authorizes fines for certain violations of up to 4% of global annual revenue or €20 million, whichever is greater, and other administrative penalties. Additionally, the United Kingdom ("UK") implemented the Data Protection Act effective in May 2018 and statutorily amended in 2019, that substantially implements the GDPR and contains provisions, including UK-specific derogations, for how GDPR is applied in the UK. On May 1, 2021, the transition period of the Trade and Cooperation Agreement between the EU and the UK ended. Subsequently, the European Commission adopted a definitive adequacy decision addressing the transfers of personal data from the European Economic Area to the United Kingdom under the GDPR on June 28, 2021. As a result, we will have to continue to comply with the GDPR and also the Data Protection Act in the UK as well as the EU, with each regime having the ability to fine up to the greater of €20 million (£17 million) or 4% of global turnover. The costs of compliance with, and other burdens imposed by, such laws and regulations that are applicable to our business operations may limit the use and adoption of our services, reduce overall demand for them. Changes in these legislations may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment in resources for compliance programs, could impact strategies and availability of previously useful data, and could result in increased compliance costs and/or changes in business practices and policies.

Additionally, on July 16, 2020, the Court of Justice of the European Union, or the Court of Justice, invalidated the European Union-United States (EU-U.S.) Privacy Shield on the grounds that the EU-U.S. Privacy Shield failed to offer adequate protections to

EU personal information transferred to the United States. While the Court of Justice upheld the use of other data transfer mechanisms, such as the Standard Contractual Clauses, the decision has led to some uncertainty regarding the use of such mechanisms for data transfers to the United States, and the court made clear that reliance on Standard Contractual Clauses alone may not necessarily be sufficient in all circumstances. The use of Standard Contractual Clauses for the transfer of personal information specifically to the United States also remains under review by a number of European data protection supervisory authorities. For example, German and Irish supervisory authorities have indicated that the Standard Contractual Clauses alone provide inadequate protection for EU-U.S. data transfers. Use of the data transfer mechanisms must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals. The European Data Protection Board (the EDPB) issued additional guidance regarding the Court of Justice's decision on November 11, 2020 which imposes higher burdens on the use of data transfer mechanisms, such as the Standard Contractual Clauses, for cross-border data transfers.

To comply with this guidance, we may need to implement additional safeguards to further enhance the security of data transferred out of the EU, which could increase our compliance costs, expose us to further regulatory scrutiny and liability, and adversely affect our business. Further, in November 2020, the European Commission published new versions of the Standard Contractual Clauses. Other countries (e.g., Australia and Japan) have also adopted certain legal requirements for cross-border transfers of personal information. These obligations may be interpreted and applied in a manner that is inconsistent from one jurisdiction to another and may conflict with other requirements or our practices. While the Court of Justice of the European Union has upheld the adequacy of the Standard Contractual Clauses, it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. Some countries also are considering or have passed legislation requiring local storage and processing of data, or similar requirements, which could increase the cost and complexity of delivering our products and services. If we are required to implement additional measures to transfer data from the European Economic Area, this could increase our compliance costs, and could adversely affect our business, financial condition and results of operations.

All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, distract management or divert resources from other initiatives and projects, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Any failure or perceived failure by us to comply with any applicable federal, state or similar foreign laws and regulations relating to data privacy and security could result in damage to our reputation, as well as proceedings or litigation by governmental agencies or other third parties, including class action privacy litigation in certain jurisdictions, which would subject us to significant fines, sanctions, awards, injunctions, penalties or judgments. Any of the foregoing could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

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

Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

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

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

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on the research and development, clinical and business development expertise of Frederic Guerard, our chief executive officer, as well as other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time.

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

We expect to expand our development, regulatory and manufacturing capabilities and potentially implement sales, marketing, and distribution capabilities and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of product development, clinical, regulatory affairs, manufacturing, sales, marketing, finance and distribution, which growth we expect to begin before we receive regulatory approval from the FDA or other regulatory authorities, and we may never receive such regulatory approval for any of our product approvals. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational, and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and our limited experience in managing such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Ownership of Our Common Stock

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expense related to the ongoing development of our product candidates or future development programs;
- results of clinical trials, or the addition or termination of clinical trials or funding support by us, or existing or future collaborators or licensing partners;
- our execution of any additional collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under existing or future arrangements or the termination or modification of any such existing or future arrangements;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any of our product candidates receives regulatory approval, the terms of such approval and market acceptance and demand for such product candidates;
- regulatory developments affecting our product candidates or those of our competitors; and
- changes in general market and economic conditions.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our common stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

The market price of our stock has been and may continue to be volatile, and you could lose all or part of your investment.

The trading price of our common stock has been in the past, and may continue to be, highly volatile and subject to wide fluctuations in response to various factors, many of which we cannot control. The market price for our common stock may be influenced by many factors, including the other risks described in this section and elsewhere in this filing, and the following:

- results of preclinical studies and clinical trials of our product candidates, or those of our competitors or our existing or future collaborators;
- the impact of the COVID-19 pandemic on our employees, trials, collaboration partners, suppliers, our results of operations, liquidity and financial condition;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our product candidates;
- the success of competitive products or technologies;
- introductions and announcements of new products by us, our future commercialization partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to our products, clinical trials, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our efforts to secure a partner to fund further clinical development of GB-102;
- the success of our efforts to acquire or in-license additional technologies, products or product candidates;
- developments concerning any future collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- market conditions in the pharmaceutical and biotechnology sectors;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our product candidates and products;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- changes in the structure or policies of healthcare payment systems;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;
- trading volume of our common stock;
- sales of our common stock by us or our stockholders;
- the concentrated ownership of our common stock;
- changes in accounting principles;

- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters, pandemics and other calamities; and
- general economic, industry and market conditions.

In addition, the stock market in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme price and volume fluctuations that have been often unrelated or disproportionate to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our actual operating performance. Finally, recent market volatility in certain stocks has at times been driven by factors unrelated to the underlying businesses, or macro or industry fundamentals, of public companies, and it is impossible to predict how long these dynamics will last. The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

The future sale and issuance of equity or of debt securities that are convertible into equity will dilute our share capital.

We may choose to raise additional capital in the future, depending on market conditions, strategic considerations and operational requirements. To the extent that additional capital is raised through the sale and issuance of shares or other securities convertible into shares, our stockholders will be diluted. Future issuances of our common stock or other equity securities, or the perception that such sales may occur, could adversely affect the trading price of our common stock and impair our ability to raise capital through future offerings of shares or equity securities. No prediction can be made as to the effect, if any, that future sales of common stock or the availability of common stock for future sales will have on the trading price of our common stock.

Sales of a substantial number of shares of our common stock may cause the price of our common stock to decline.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly. We had a total of 21,357,773 shares of our common stock outstanding as of December 31, 2021. All shares of our common stock are freely tradable, generally without restrictions or further registration under the Securities Act of 1933, as amended, or the Securities Act, subject to certain exceptions for shares held by our "affiliates" as defined in Rule 144 under the Securities Act.

We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. However, future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options or warrants, or the perception that such sales may occur, could adversely affect the market price of our common stock.

We also expect that significant additional capital may be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not have any control over the analysts or the content and opinions included in their reports. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies and clinical trials and results of operations fail to meet the expectations of analysts, our stock price would likely decline. If one or more of such analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause a decline in our stock price or trading volume.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Based on the beneficial ownership of our common stock as of December 31, 2021, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned a significant percentage of our voting stock.

As a result, these stockholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, amendment of our organizational documents, any merger,

consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

We are an "emerging growth company" and a "smaller reporting company" and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (1) not being required to comply with the independent auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley Act, (2) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (3) exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not approved previously. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements and two years of selected financial data in our periodic reports.

We will remain an EGC until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the closing of our IPO, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a "large accelerated filer," which requires the market value of our common stock that is held by non-affiliates to exceed $700.0 million as of the prior June 30, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Even after we no longer qualify as an EGC, we may still qualify as a "smaller reporting company," or SRC, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the independent auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may be more volatile.

Under the JOBS Act, EGCs can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to take advantage of the benefits of this extended transition period. Our financial statements may therefore not be comparable to those of companies that comply with such new or revised accounting standards. Until the date that we are no longer an EGC, or we affirmatively and irrevocably opt out of the exemption provided by Section 7(a)(2)(B) of the Securities Act, upon issuance of a new or revised accounting standard that applies to our financial statements and that has a different effective date for public and private companies, we will disclose the date on which adoption is required for non-EGCs and the date on which we will adopt the recently issued accounting standard.

We are also currently an SRC, in part because the market value of our stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We are also currently considered an SRC because the market value of our stock held by non-affiliates is less than $250.0 million. We may continue to be a SRC if either (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million as of June 30th. If we are an SRC at the time we cease to be an EGC, we may continue to rely on exemptions from certain disclosure requirements that are available to SRCs. Specifically, as an SRC we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to EGCs, SRCs have reduced disclosure obligations regarding executive compensation.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Our restated certificate of incorporation and our restated bylaws contain provisions that could delay or prevent a change in control of our company. These provisions could also make it difficult for stockholders to elect directors who are not nominated by current members of our board of directors or take other corporate actions, including effecting changes in our management. These provisions:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;

- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- require super-majority voting to amend some provisions in our restated certificate of incorporation and restated bylaws;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan;
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting; and
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

In addition, our restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, or DGCL, our restated certificate of incorporation, or our restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine.

Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all claims brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Our restated bylaws provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, referred to as a Federal Forum Provision. Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law. While there can be no assurance that federal courts or state courts will follow the holding of the Delaware Supreme Court or determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court. While neither the exclusive forum provision nor the Federal Forum Provision applies to suits brought to enforce any duty or liability created by the Exchange Act of 1934, as amended, or Exchange Act, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all claims brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. Accordingly, actions by our stockholders to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder also must be brought in federal court. Our stockholders will not be deemed to have waived our compliance with the federal securities laws and the regulations promulgated thereunder.

Any person or entity purchasing or otherwise acquiring or holding any interest in any of our securities shall be deemed to have notice of and consented to our exclusive forum provisions, including the Federal Forum Provision. These provisions may limit a stockholder's ability to bring a claim in a judicial forum of their choosing for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers, and other employees.

In addition, Section 203 of the DGCL may discourage, delay or prevent a change in control of our company. Section 203 imposes certain restrictions on mergers, business combinations and other transactions between us and holders of 15% or more of our common stock.

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

As a public company, and particularly after we are no longer an emerging growth company or smaller reporting company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. Moreover, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock has been and may continue to be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties and facilities.

Our principal executive office is located in Redwood City, California, and consists of 2,560 square feet of office space under a lease which expires in August 2022. We use this facility for operations and administrative purposes. We also have a facility located in Baltimore, Maryland. The Maryland facility consists of 15,649 square feet of office and laboratory space under a lease which expires in June 2023. We use the Maryland facility for our internal research and development activities. We believe that our facilities are adequate to meet our needs for the foreseeable future.

Item 3. Legal Proceedings.

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm, and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our common stock is traded on The Nasdaq Global Market under the symbol "GRAY."

Holders of Record

As of March 4, 2022, there were 34 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table sets forth certain information, as of December 31, 2021, concerning securities authorized for issuance under all of our equity compensation plans: our 2015 Stock Incentive Plan, which terminated when we adopted our 2020 Equity Incentive Plan, or 2020 Plan, and our 2020 Employee Stock Purchase Plan, or ESPP.

Plan Category	(a) Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights (1)	(b) Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights (2)	(c) Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a) (3)
Equity compensation plans approved by security holders	4,747,098	$ 6.58	655,617[1]
Equity compensation plans not approved by security Holders			
Total	4,747,098	$ 6.58	655,617

(1) The amount shown in column (a) includes 3,777,398 outstanding options and 969,700 restricted stock units.

(2) The weighted average exercise price in column (b) includes options only as restricted stock units do not have exercise prices.

(3) The amount shown in column (c) represents 445,617 shares available for issuance under the 2020 Plan, which plan permits the grant of incentive and non-qualified stock options, stock appreciation rights, restricted stock, stock awards and restricted stock units; and 210,000 shares available for issuance under the ESPP. The 2020 Plan and ESPP each contain an "evergreen" provision, pursuant to which on January 1st of each year we automatically add 5% and 1% of our shares of common stock outstanding on the preceding December 31st to the shares reserved for issuance, respectively, provided that the Compensation Committee of our Board may authorize a lesser number in each case. As we have not yet implemented our ESPP, no increase in the shares available for issuance under the ESPP have been authorized by the Compensation Committee. In addition, pursuant to a "pour over" provision in our 2020 Plan, options that are cancelled, expired or terminated under the 2015 Stock Incentive Plan are added to the number of shares reserved for issuance under the 2020 Plan.

Performance Graph

As a "smaller reporting company" as defined by Rule 12b-2 of the Exchange Act, we are not required to provide this information.

Recent Sales of Unregistered Securities

None.

Use of Proceeds from our Initial Public Offering

On September 29, 2020, we completed our initial public offering, or IPO, and issued and sold 5,625,000 shares of our common stock at an initial offering price of $16.00 per share and on October 22, 2020, we issued and sold an additional 843,750 shares in connection with the full exercise of the underwriters' option to purchase additional shares. We received net proceeds from the IPO, including the full exercise of the option, of approximately $92.0 million, after deducting underwriting discounts and commissions of approximately $7.2 million and expenses of approximately $4.2 million. The offer and sale of all of the shares in the IPO were registered under the Securities Act pursuant to registration statements on Form S-1 (File Nos. 333-248611 and 333-249030), which were declared effective by the SEC on September 24, 2020.

There has been no material change in the planned use of proceeds from our IPO as described in the Prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b)(4) under the Securities Act on September 24, 2020.

Item 6. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our financial statements and related notes included elsewhere in this Annual Report. In addition to historical financial information, the following discussion contains forward-looking statements that involve risks and uncertainties. You should carefully read the sections entitled "Special Note Regarding Forward-Looking Statements" and "Risk Factors" to gain an understanding of the important factors that could cause our actual results to differ materially from those expressed or implied in any forward-looking statements.

Overview

We are a clinical-stage biopharmaceutical company focused on developing transformative medicines for the treatment of diseases of the eye, including the retina and optic nerve. Our novel proprietary technologies are designed to release drugs in ocular tissue at a controlled rate for up to 12 months in order to improve patient compliance, reduce healthcare burdens and, ultimately, deliver better clinical outcomes. Our lead product candidate, GB-102, is an intravitreal injection of a microparticle depot formulation of sunitinib, a potent inhibitor of neovascular growth and permeability, which are leading causes of retinal disease. We are developing GB-102 as a once-every-six month intravitreal injection for the treatment of wet age-related macular degeneration, or wet AMD. In our Phase 1/2a clinical trial, GB-102 administered as a single 1 mg dose was well-tolerated in wet AMD patients and demonstrated durable clinical evidence of disease control of at least six months in approximately 88% of patients in this cohort. GB-102 has also completed a dose-ranging, standard-of-care controlled and masked safety and efficacy Phase 2b clinical trial in patients with wet AMD. We reported topline data from this trial in March of 2021 and we reported further data from an observational six-month extension trial in September 2021. We are evaluating the possibility to develop GB-102 in diabetic retinopathy, or DR. We are also using our proprietary technologies to develop GB-401, an intravitreally injected implant formulation of a beta-adrenergic blocking agent prodrug with a target dosing regimen of once-every-six months or longer for the treatment of primary open-angle glaucoma, or POAG. We believe that our product candidates could significantly improve clinical outcomes versus the respective standards of care for several ocular diseases.

We were incorporated in May 2011 and our operations to date have been financed primarily by gross proceeds of approximately $134.0 million from the issuance of convertible promissory notes and convertible preferred stock, and $92.0 million in net proceeds from our initial public offering of our common stock, or IPO, after deducting underwriters' discounts and commissions of $7.2 million and offering costs of $4.2 million.

Since inception, we have had significant operating losses. Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures and, to a lesser extent, general and administrative expenditures. Our net loss was $35.8 million and $27.5 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $169.2 million and cash, cash equivalents and short-term investments of $63.7 million.

We expect to continue to incur net losses for the foreseeable future, and we expect our research and development expenses, general and administrative expenses, and capital expenditures to continue to increase. In particular, we expect our expenses to increase as we continue our development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products, as well as hire additional personnel, develop commercial infrastructure, pay fees to outside consultants, lawyers and accountants, and incur increased costs associated with being a public company, such as expenses related to services associated with maintaining compliance with Nasdaq listing rules and SEC reporting requirements, insurance and investor relations. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending upon the timing of our clinical trials and our expenditures on other research and development activities. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our accounts payable and accrued research and development and other current liabilities.

Recent Developments

Business Effects of the COVID-19 Pandemic

The current COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting our employees, communities and business operations, as well as the U.S. economy and financial markets. To date, our financial condition and operations have not been significantly impacted by the COVID-19 outbreak; however, the ongoing challenges associated with the pandemic, including the emergence of new variants of the coronavirus, such as the Delta and Omicron variants, and resurgences in the number and rates of infections, make it difficult to assess the full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations, liquidity and financial condition, all of which will depend on future developments, which are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets.

To date, our CROs, CMOs and other vendors have been able to continue to provide services and supply reagents, materials, and products and currently do not anticipate any disruption in services or interruptions in supply. Our CMOs continue to operate their manufacturing facilities at or near normal levels. While we currently do not anticipate any interruptions in our manufacturing process,

it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our third-party suppliers and contract manufacturing partners' ability to manufacture reagents, materials or products that we need to use in our research and clinical trial. However, we are continuing to assess the potential impact of the COVID-19 pandemic on our business and operations, including our expenses, our clinical trials, and our ability to hire and retain employees.

Given the persistent uncertainty of the evolving pandemic, we expect that COVID-19 precautions may directly or indirectly impact the timeline for some of our future clinical trial activities due to the inability of patients to come to their screening or monitoring visits, the closing of eye clinics, and/or diversion of resources that are necessary to conduct our future studies to care for COVID-19 patients.

The COVID-19 pandemic has caused us to modify our business practices including, but not limited to, curtailing or modifying employee travel, moving to partial remote work, and cancelling physical participation in meetings, events and conferences. We may take further actions as may be required by government authorities or that we determine are in the best interests of our employees, patients and business partners.

The majority of our office-based employees have been working from home since March 2020, while ensuring essential staffing levels in our operations remain in place, including maintaining key personnel in our laboratories.

For additional information on the various risks posed by the COVID-19 pandemic, please read Item 1A. Risk Factors.

Components of Operating Results

Research and Development Expenses

Our research and development expenses include:

- personnel costs, which include salaries, benefits and stock-based compensation;
- expenses incurred under agreements with consultants, third-party contract organizations that conduct research and development activities on our behalf;
- costs related to sponsored research service agreements;
- costs related to production of preclinical and clinical materials, including fees paid to contract manufacturers;
- laboratory and vendor expenses related to the execution of preclinical studies and planned clinical trials;
- milestones and royalty expense from our Johns Hopkins University Exclusive License Agreement;
- laboratory supplies and materials used for internal research and development activities;
- the acquisition cost of in-licensed and purchased intellectual property; and
- facilities and equipment costs.

Most of our research and development expenses have been related to the preclinical and clinical development of GB-102. We have not reported program costs since inception because we have not tracked or recorded our research and development expenses on a program-by-program basis historically. We use our personnel and infrastructure resources across the breadth of our research and development activities, which are directed toward identifying and developing product candidates.

We expense all research and development costs in the periods in which they are incurred. Costs for certain research and development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and third-party service providers.

We expect our research and development expenditures to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, including investments in manufacturing, as we advance our programs and conduct clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain.

Because of the numerous risks and uncertainties associated with product development, we cannot determine with certainty the duration and completion costs of the current or future preclinical studies and clinical trials or if, when, or to what extent we will generate revenues from the commercialization and sale of our product candidates. We may never succeed in achieving regulatory approval for

our product candidates. The duration, costs and timing of preclinical studies and clinical trials and development of our product candidates will depend on a variety of factors, including:

- securing partner-funding for GB-102 and the timely execution of resulting development plans;
- successful completion of preclinical studies and clinical trials to the satisfaction of the U.S. Food and Drug Administration, or FDA, European Medicines Agency, or EMA or other regulatory authorities;
- that our product candidates are safe and effective for any of their proposed indications;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- maintaining a continued acceptable safety and profile of our products following approval;
- obtaining and maintaining coverage and adequate reimbursement from third-party payors;
- applying for and receiving marketing approvals from applicable regulatory authorities for our product candidates;
- scaling up our manufacturing processes and capabilities to support additional or larger clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval;
- developing, validating and maintaining a commercially viable manufacturing process that is compliant with current good manufacturing practices;
- developing and expanding our sales, marketing and distribution capabilities and launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- minimizing and managing any delay or disruption to our ongoing or planned clinical trials, and any adverse impacts to the U.S. and global market for pharmaceutical products, as a result of the current COVID-19 pandemic;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting our rights in our intellectual property portfolio; and
- the impact of the COVID-19 pandemic and the corresponding responses of businesses and governments.

We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our preclinical studies and clinical trials. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. A change in the outcome of any of these factors could mean a significant change in the costs and timing associated with the development of our current and future preclinical and clinical product candidates. For example, if the FDA, or another regulatory authority, were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development, or if we experience significant delays in execution of or enrollment in any of our preclinical studies or clinical trials, we could be required to expend significant additional financial resources and time on the completion of preclinical and clinical development.

General and Administrative Expenses

Our general and administrative expenses consist primarily of personnel costs, costs related to maintenance and filing of intellectual property and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, benefits and stock-based compensation expense. We expect our general and administrative expenses to increase over the next several years to support our expanding headcount and operations, increased costs of operating as a public company, the development of a commercial infrastructure to support the potential commercialization of our product candidates, and the use of outside service providers such as insurers, consultants, lawyers, and accountants.

Interest Income

Our interest income principally reflects interest earned on our investments. Our investments include U.S. government-backed money-market funds, corporate debt securities, commercial paper and government bonds. We place cash in excess of immediate requirements into a custodial account and invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation.

Preferred Stock Tranche Obligation

We provided investors in our Series C preferred stock financing the option to buy additional shares of our Series C Preferred Stock upon our achievement of certain development milestones, or the Preferred Stock Tranche Obligation. The fair value of the Preferred

Stock Tranche Obligation was remeasured and adjusted to fair value each reporting period until its expiration using an option pricing valuation methodology. In September 2020, our board of directors and the Series C investors amended the Series C stock purchase agreement such that the option to purchase additional shares of our Series C preferred stock would no longer be exercisable and would expire upon the effectiveness of our IPO registration statement. As a result, the Preferred Stock Tranche Obligation expired on September 24, 2020.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following sets forth our results of operations (dollars in thousands):

	Year Ended December 31,		Change	
	2021	2020	Amount	%
Operating expenses:				
Research and development	$ 18,903	$ 20,962	$ (2,059)	(10)%
General and administrative	17,044	8,870	8,174	92%
Total operating expenses	35,947	29,832	6,115	20%
Loss from operations	(35,947)	(29,832)	(6,115)	(20)%
Interest income	126	143	(17)	(12)%
Change in fair value of preferred stock tranche obligation	—	2,158	(2,158)	(100)%
Net loss	$ (35,821)	$ (27,531)	$ (8,290)	(30)%

Research and Development Expenses

Research and development expenses comprised (dollars in thousands):

	Year Ended December 31,		Change	
	2021	2020	Amount	%
Personnel costs	$ 7,445	$ 6,485	$ 960	15%
CRO, CMO, nonclinical and other services	6,088	10,406	(4,318)	(41)%
Facility costs, travel and other	3,290	2,016	1,274	63%
Consulting	1,079	1,332	(253)	(19)%
Materials and supplies	1,001	723	278	38%
Total research and development expenses	$ 18,903	$ 20,962	$ (2,059)	(10)%

As of December 31, 2021 and 2020, we had 19 and 24 employees, respectively, engaged in research and development activities in our Baltimore, Maryland and Redwood City, California facilities.

Our research and development activities consist primarily of costs associated with the development of GB-102 for which we completed one U.S. Phase 2 clinical trial in patients with wet AMD during 2021, one U.S. Phase 2 clinical trial in patients with DME which was completed in 2020, and pre-clinical costs associated with the development of GB-401. Research and development expenses were $18.9 million in 2021 compared to $21.0 million in 2020. The decrease was primarily due to a reduction in clinical trial expenses due to the completion of the treatment phase of the GB-102 Phase 2b clinical trial in December 2020, offset in part by an increase in compensation costs. Based on our current plans to fund the advancement of GB-102 only through an additional open-label Phase 2a trial in wet AMD, the pre-clinical development of in-licensed and purchased pre-clinical programs, and our plans to commence a Phase 1 trial for GB-401 in glaucoma no earlier than the first half of 2023, we expect R&D expenses to increase in 2022 compared to 2021.

General and Administrative Expenses

General and administrative expenses to support our business activities comprised (dollars in thousands):

	Year Ended December 31,		Change	
	2021	2020	Amount	%
Personnel costs	$ 7,663	$ 3,283	$ 4,380	*
Facility costs, travel and other expenses	3,917	1,431	2,486	*
Professional services	3,034	3,031	3	0%
Write-off deposits on fixed assets purchase commitments	1,352	—	1,352	*
Patent filing and portfolio costs	1,078	1,125	(47)	(4)%
Total general and administrative expenses	$ 17,044	$ 8,870	$ 8,174	92%

* Percentage change is greater than 100%.

As of December 31, 2021 and 2020, we had eight and seven employees, respectively, engaged in general and administrative activities.

General and administrative expenses were $17.0 million in 2021 compared to $8.9 million in 2020. The increase was primarily due to a $2.8 million increase in stock-based compensation, a $1.8 million increase in the cost of directors and officers insurance as a result of becoming a public company and the $1.3 million write-off of deposits on fixed assets purchase commitments.

Interest Income

Interest income was $126,000 and $143,000 for the years ended December 31, 2021 and 2020, respectively. The decrease was primarily due to the decrease in short term investments.

Preferred Stock Tranche Obligation

The change in fair value of Preferred Stock Tranche Obligation for the year ended December 31, 2020 relates to the fair value adjustment that resulted in a $2.1 million gain in connection with our IPO. In September 2020, the Preferred Stock Tranche Obligation expired upon the effectiveness of the IPO registration statement, resulting in a corresponding elimination of the associated liability.

Liquidity and Capital Resources

Overview

To date, we have incurred losses and negative cash flows from operations. As of December 31, 2021, we had available cash, cash equivalents and short-term investments of $63.7 million and an accumulated deficit of $169.2 million. Prior to our IPO, our operations had been financed primarily by gross proceeds of approximately $134.0 million from the sale of convertible promissory notes and our convertible preferred stock. In connection with our IPO, we issued and sold an aggregate of 6,468,750 shares of common stock (inclusive of 843,750 shares of common stock issued and sold pursuant to the exercise of the underwriters' option to purchase additional shares) at a price of $16.00 per share for net proceeds of $92.0 million, after deducting underwriters' discounts and commissions and offering costs.

We have incurred significant net losses of $35.8 million and $27.5 million for the years ended December 31, 2021 and 2020, respectively. We expect to continue to incur significant operational expenses and net losses in the upcoming 12 months and beyond. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the stage and complexity of our R&D studies and related expenditures, the receipt of additional payments on the licensing of our technology, if any, and the receipt of payments under any current or future collaborations we may enter into.

We believe our cash, cash equivalents and short-term investments of $63.7 million at December 31, 2021 will fund our projected operations into the second half of 2023.

Commitments and Other Obligations

For a detailed description of our commitments and obligations, see Note 5 – Commitments and Contingencies, to the financial statements included in Item 8 of this Annual Report on Form 10-K.

Leases

We have lease arrangements for certain equipment and facilities, including, corporate, manufacturing and data center space. As of December 31, 2021, we had fixed lease payment obligations of $732,000, with $527,000 payable within 12 months.

License Agreements

We are party to agreements pursuant to which we have in-licensed and purchased various intellectual property rights. These agreements obligate us to make certain milestone payments related to achievement of specified events, as well as royalties in the low-single digits based on sales of certain products. None of these events had occurred as of December 31, 2021, and no royalties were due from the sales of licensed products.

Other Commitments

We enter into contracts in the normal course of business with CROs for clinical trials and CMOs for clinical supply manufacturing and with vendors for equipment, preclinical research studies, research supplies and other services and products for operating purposes. As of December 31, 2021, these commitments were approximately $0.8 million due within 3 to 15 months. These contracts generally provide for termination on notice of 60 to 90 days, and therefore we believe that our non-cancelable obligations under these agreements are not material.

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements as defined under SEC rules.

Funding Requirements

Any product candidates we may develop may never achieve commercialization and we anticipate that we will continue to incur losses for the foreseeable future. We expect that our research and development expenses, general and administrative expenses, and capital expenditures will continue to increase. As a result, until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research, manufacturing and development services, costs relating to the build-out of our headquarters, laboratories and manufacturing facility, license payments or milestone obligations that may arise, laboratory and related supplies, clinical costs, manufacturing costs, legal and other regulatory expenses and general overhead costs.

Based on our current operating plan, which no longer includes the cost of Phase 3 clinical trials for GB-102, we believe our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements in excess of 12 months from the issuance date of these financial statements. We base this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We base the sufficiency of our existing cash, cash equivalents and short-term investments to fund our operations on the current period re-forecast of our projected cash burn rate following our decision to only proceed with further Phase 3 clinical trials for GB-102 if fully or partially funded by a partner. While we believe that our current cash, cash equivalents and short-term investments are adequate to meet our needs for the next 12 months from issuance, we will seek to raise additional funds in order to further advance our research and development programs, operate our business and meet our obligations as they come due.

We will continue to require additional financing to advance our current product candidates through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. We will continue to seek funds through equity offerings, debt financings or other capital sources, potentially including collaborations, licenses and other similar arrangements. We may, however, be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise capital, we will need to delay, reduce or terminate planned activities to reduce costs.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of researching, developing and manufacturing our product candidates or any future product candidates, and conducting preclinical studies and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals or clearances for our product candidates or any future product candidates;

- the number and characteristics of any additional product candidates we develop or acquire;
- the cost of manufacturing our product candidates or any future product candidates and any products we successfully commercialize, including costs associated with building-out our manufacturing capabilities;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of any such agreements that we may enter into;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the timing, receipt and amount of sales of any future approved or cleared products, if any; and
- the impact of the COVID-19 pandemic and the corresponding responses of businesses and governments.

Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development activities. We currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital and operating expenditures associated with our current and anticipated product development programs.

Cash Flows

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	$ (31,500)	$ (32,064)
Investing activities	10,751	(42,560)
Financing activities	695	92,172
Net (decrease) increase in cash and cash equivalents	$ (20,054)	$ 17,548

Operating Activities

Cash used in operating activities of $31.5 million during the year ended December 31, 2021 was primarily attributable to our net loss of $35.8 million and an increase of $1.6 million in our working capital, partially offset by non-cash stock-based compensation expense of $5.4 million.

Cash used in operating activities of $32.1 million during the year ended December 31, 2020 was attributable to our net loss of $27.5 million and an increase of $4.6 million in our working capital.

Investing Activities

Cash provided by investing activities of $10.8 million during the year ended December 31, 2021 consisted of $105.8 million provided upon maturity of short-term investments, partially offset by $94.6 million of purchases of short-term investments and $0.5 million of purchases of property and equipment.

Cash used in investing activities of $42.6 million during the year ended December 31, 2020 consisted of $61.6 million of purchases of short-term investments and $1.0 million of purchases of property and equipment, partially offset by $20.0 million provided upon maturity of short-term investments.

Financing Activities

Cash provided by financing activities of $0.7 million for the year ended December 31, 2021 was related to proceeds received from the exercise of stock options.

Cash provided by financing activities of $92.2 million for the year ended December 31, 2020 consisted of $96.3 million of proceeds, net of the underwriters' discounts and commissions, from the issuance of common stock in connection with our IPO and $0.1 million received from the exercise of stock options, partially offset by $4.2 million related to the payments of offering costs.

Critical Accounting Policies and Significant Judgments and Estimates

Management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. Generally Accepted Accounting Principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions and any such differences may be material.

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.

Research and Development Expense and Accruals

We record research and development expenses to operations as incurred. Research and development expenses represent costs incurred by us for the discovery and development of our product candidates and the development of our technology and include: employee-related expenses, including salaries, benefits, travel and non-cash stock-based compensation expense; external research and development expenses incurred under arrangements with third parties, such as CROs, preclinical testing organizations, CMOs, academic and non-profit institutions and consultants; license fees; and other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

As part of the process of preparing financial statements, we are required to estimate and accrue expenses. We estimate costs of research and development activities conducted by service providers, which include the conduct of sponsored research, preclinical studies and contract manufacturing activities. Payments made prior to the receipt of goods or services to be used in research and development are deferred and recognized as expense in the period in which the related goods are received or services are rendered. If the costs have been prepaid, this expense reduces the prepaid expenses on the balance sheet, and if not yet invoiced, the costs are included in accrued liabilities on the balance sheet. We classify such prepaid assets as current or non-current assets based on our estimates of the timing of when the goods or services will be realized or consumed. These costs are a significant component of our research and development expenses.

We estimate these costs based on factors such as estimates of the work completed and budget provided and in accordance with agreements established with our collaboration partners and third-party service providers. We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from external CROs and other third-party service providers. Amounts ultimately incurred in relation to amounts accrued for these services at a reporting date may be substantially higher or lower than our estimates.

Our expenses related to clinical trials are based on estimates of patient enrollment and related expenses at clinical investigator sites as well as estimates for the services provided and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that may be used to conduct and manage clinical trials on our behalf. We generally accrue expenses related to clinical trials based on contracted amounts applied to the level of patient enrollment and activity. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis.

We have and may continue to enter into purchase and license agreements to access and utilize certain technologies. We evaluate if such agreements are an acquisition of an asset or a business. To date none of these agreements have been considered to be an acquisition of a business. For asset acquisitions, the upfront payments to acquire such assets, or licenses to such assets, as well as any future milestone payments made before product approval, will be immediately recognized as research and development expenses when due, provided there is no alternative future use of the rights in other research and development projects. These agreements may also include contingent consideration in the form of cash. We assess whether such contingent consideration meets the definition of a derivative.

Preferred Stock Tranche Obligation

Convertible preferred stock that includes features we have determined are not clearly and closely related to the equity host are bifurcated and accounted for separately as freestanding derivative assets or liabilities on the balance sheet at their estimated fair value.

We recognized a derivative liability as a result of certain investors' having rights to purchase from us, on the same terms as the Series C Preferred Stock Purchase Agreement executed in July 2019, additional shares of our Series C preferred stock in subsequent tranches based on the achievement of certain development milestones, or the Preferred Stock Tranche Obligation. At initial recognition, we recorded the liability for the Preferred Stock Tranche Obligation on the balance sheet at its estimated fair value. This liability was subject to remeasurement at each balance sheet date until the expiration of the Preferred Stock Tranche Obligation in September 2020, with changes in fair value recognized in our statements of operations.

The liability for the Preferred Stock Tranche Obligation was measured at fair value using an option pricing valuation methodology that included inputs not observable in the market and thus represents a Level 3 measurement. The option pricing valuation methodology utilized requires inputs based on certain subjective assumptions, including (a) expected stock price volatility, (b) calculation of an expected term, (c) a risk-free interest rate and (d) expected dividends. Significant judgment was used in determining these assumptions at initial recognition and at each subsequent reporting period.

Stock-based Compensation

We recognize compensation costs related to stock-based awards to employees and non-employees based on the estimated fair value of the awards on the date of grant. We estimate the grant date fair value, and the resulting stock-based compensation, using the Black-Scholes option-pricing model, or Black-Scholes. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards.

Black-Scholes requires the use of subjective assumptions to determine the fair value of stock-based awards including:

- Fair Value of Common Stock— see subsection entitled "Common Stock Valuations" below.
- Expected Term—The expected term represents the period that stock-based awards are expected to be outstanding. The expected term for option grants is determined using the simplified method. The simplified method deems the expected term to be the midpoint between the vesting date and the contractual life of the stock-based awards.
- Expected Volatility—Since we were a privately held company until September 2020, and do not yet have sufficient trading history for our common stock, the expected volatility is estimated based on the average volatility for comparable publicly traded biotechnology companies over a period equal to the expected term of the stock option grants. The comparable companies are chosen based on their similar size, stage in the life cycle or area of specialty. We will continue to apply this method until a sufficient amount of historical information over a period equal to the expected term of the stock-based awards becomes available.
- Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the option.
- Expected Dividend—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

We will continue to use judgment in evaluating the assumptions utilized for our stock-based compensation expense calculations on a prospective basis. In addition to the assumptions used in Black-Scholes, the amount of stock-based compensation expense we recognize in our financial statements includes stock option forfeitures as they occur. Such assumptions involve inherent uncertainties and the application of significant judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation could be materially different.

Common Stock Valuations

Historically, for all periods prior to our IPO, the fair value of the shares of common stock underlying our stock-based awards was estimated on each grant date by our board of directors. In the absence of a public trading market for our common stock, our board of directors exercised their judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including contemporaneous valuations, our stage of development, important developments in our operations, the prices at which we sold shares of our preferred stock, the rights, preferences and privileges of our preferred stock relative to those of our common stock, actual operating results and financial performance, the conditions in the biotechnology industry and the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of our common stock, among other factors.

In determining the fair value of our common stock, the methodologies used to estimate our enterprise value were performed using methodologies, approaches and assumptions consistent with the guidance outlined in the American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately Held Company Equity Securities Issued as Compensation*. The grant date fair value of our common stock was determined using valuation methodologies incorporating a number of assumptions including probability weighting of events, volatility, time to liquidation, a risk-free interest rate and an assumption for a discount for lack of

marketability (Level 3 inputs). The methodology to determine the fair value of our common stock included estimating the fair value of the enterprise using a hybrid-method market approach, which estimates the fair value of the company by including an estimation of the value of the business based on scenarios in a probability-weighted expected return method, or PWERM, framework. Under the hybrid-method market approach, the per share value calculated under the scenarios are weighted based on expected exit outcomes and the quality of the information specific to each allocation methodology to arrive at a final estimated fair value per share value of the common stock before a discount for lack of marketability is applied.

Following the closing of our IPO, our board of directors determines the fair market value of our common stock based on its closing price as reported on The Nasdaq Global Market on the date of grant.

Emerging Growth Company and Smaller Reporting Company Status

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We are also a "smaller reporting company," as defined by Rule 12b-2 of the Securities Exchange Act of 1934, because both the market value of our stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Recently Adopted Accounting Pronouncements

For a full discussion of recently adopted accounting pronouncements, see Note 2 to the financial statements included elsewhere in this Annual Report on Form 10-K for more information.

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

We are a smaller reporting company, as defined by Rule 12b-2 under the Securities and Exchange Act of 1934 and in Item 10(f)(1) of Regulation S-K, and are not required to provide the information under this item.

Item 8. Financial Statements and Supplementary Data.

GRAYBUG VISION, INC.
INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors of Graybug Vision, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Graybug Vision, Inc. (the Company) as of December 31, 2021 and 2020, the related statements of operations, comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2017.

Redwood City, California
March 10, 2022

GRAYBUG VISION, INC.
Balance Sheets
(In thousands, except share and per share amounts)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 13,364	$ 33,418
Short-term investments	50,306	61,615
Prepaid expenses and other current assets	3,408	4,207
Total current assets	67,078	99,240
Property and equipment, net	1,981	1,946
Prepaid expenses and other non-current assets	29	608
Total assets	$ 69,088	$ 101,794
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 527	$ 2,513
Accrued research and development	304	1,356
Other current liabilities	3,226	3,128
Total current liabilities	4,057	6,997
Deferred rent, long term portion	8	11
Total liabilities	4,065	7,008
Commitments and contingencies (Note 5)		
Stockholders' Equity:		
Preferred stock, $0.0001 par value; 10,000,000 authorized, no shares outstanding as of December 31, 2021 and 2020, respectively	—	—
Common stock, $0.0001 par value; 500,000,000 shares authorized, 21,357,773 and 20,979,265 shares issued and outstanding as of December 31, 2021 and 2020, respectively	2	2
Additional paid-in capital	234,225	228,155
Accumulated deficit	(169,188)	(133,367)
Accumulated other comprehensive loss	(16)	(4)
Total stockholders' equity	65,023	94,786
Total liabilities and stockholders' equity	$ 69,088	$ 101,794

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

GRAYBUG VISION, INC.
Statements of Operations
(In thousands, except share and per share amounts)

	Year Ended December 31,	
	2021	2020
Operating expenses:		
Research and development	$ 18,903	$ 20,962
General and administrative	17,044	8,870
Total operating expenses	35,947	29,832
Loss from operations	(35,947)	(29,832)
Interest income	126	143
Change in fair value of preferred stock tranche obligation	—	2,158
Net loss	(35,821)	(27,531)
Cumulative dividends on convertible preferred stock	—	(7,189)
Net loss attributable to common stockholders	$ (35,821)	$ (34,720)
Net loss per common share—basic and diluted	$ (1.69)	$ (5.25)
Weighted-average number of shares outstanding used in computing net loss per common share—basic and diluted	21,199,291	6,618,445

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

GRAYBUG VISION, INC.
Statements of Comprehensive Loss
(In thousands)

	Year Ended December 31,	
	2021	**2020**
Net loss	$ (35,821)	$ (27,531)
Unrealized loss on available-for-sale securities, net of tax	(12)	(7)
Comprehensive loss	$ (35,833)	$ (27,538)

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

GRAYBUG VISION, INC.
Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (loss)	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance—December 31, 2019	117,809,883	$ 131,363	1,371,467	$ —	$ 2,879	$ (105,836)	$ 3	$ (102,954)
Issuance of common stock upon the initial public offering, net			6,468,750	1	92,049	—	—	92,050
Conversion of convertible preferred stock into common stock upon the initial public offering	(117,809,883)	(131,363)	13,085,913	1	131,362	—	—	131,363
Stock issued on exercise of stock options	—	—	53,135	—	77	—	—	77
Stock-based compensation expense	—	—	—	—	1,788		—	1,788
Net loss	—	—	—	—	—	(27,531)		(27,531)
Unrealized loss on available-for-sale securities, net of tax	—	—	—	—	—	—	(7)	(7)
Balance—December 31, 2020	—	$ —	20,979,265	$ 2	$ 228,155	$ (133,367)	$ (4)	94,786
Stock issued on exercise of stock options	—	—	353,508	—	695	—	—	695
Issuance of common stock upon vesting of restricted stock units	—	—	25,000	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	5,375	—	—	5,375
Net loss	—	—	—	—	—	(35,821)	—	(35,821)
Unrealized loss on available-for-sale securities, net of tax	—	—	—	—	—	—	(12)	(12)
Balance—December 31, 2021	—	$ —	21,357,773	$ 2	$ 234,225	$ (169,188)	$ (16)	$ 65,023

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

GRAYBUG VISION, INC.
Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2021	2020
Operating activities:		
Net loss	$ (35,821)	$ (27,531)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	5,375	1,788
Depreciation	519	395
Change in fair value of preferred stock tranche obligation	—	(2,158)
Accretion of premium and discounts on short-term investments	58	1
Changes in operating assets and liabilities:		
Prepaid expenses and other current and non-current assets	1,378	(2,400)
Accounts payable	(2,052)	(1,462)
Accrued research and development	(1,052)	(977)
Other current and non-current liabilities	95	280
Net cash used in operating activities	(31,500)	(32,064)
Investing activities:		
Purchases of property and equipment	(488)	(1,023)
Purchases of investments	(94,570)	(61,637)
Maturity of investments	105,809	20,100
Net cash provided by (used in) investing activities	10,751	(42,560)
Financing activities:		
Proceeds from issuance of common stock upon initial public offering, net of underwriting discounts and commissions	—	96,255
Proceeds from exercise of stock options	695	77
Payment of offering costs	—	(4,160)
Net cash provided by financing activities	695	92,172
Net (decrease) increase in cash and cash equivalents	(20,054)	17,548
Cash and cash equivalents at beginning of period	33,418	15,870
Cash and cash equivalents at end of period	$ 13,364	$ 33,418
Supplemental disclosure of noncash items:		
Conversion of convertible preferred stock into common stock upon initial public offering	$ —	$ 131,363
Property and equipment purchases included in accounts payable	$ 115	$ 49

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

1. Organization

Graybug Vision, Inc., the Company or Graybug, is a clinical-stage biopharmaceutical company developing medicines for the treatment of diseases of the retina and optic nerve. The Company presently devotes substantially all of its resources to conducting research and development and raising capital. The Company was founded in May 2011 and maintains facilities in Redwood City, California and Baltimore, Maryland.

The Company is subject to risks common to clinical stage companies in the biopharmaceutical industry, including dependence on the clinical success of its product candidates, ability to obtain regulatory approvals of its product candidates, compliance with regulatory requirements, the need for substantial additional financing and protection of its proprietary technology.

Going Concern Considerations

The Company incurred losses from operations and had negative cash flows from operating activities for the years ended December 31, 2021, and 2020, and the Company's accumulated deficit at December 31, 2021 is $169.2 million. The Company's current operating plan indicates it will continue to incur losses from operations and generate negative cash flows from operating activities, given ongoing expenditures related to extensive research and development and the Company's lack of revenue-generating activities at this point in the Company's life cycle. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

In March 2021, the Company decided not to proceed with the significant investment required to initiate two Phase 3 clinical trials for GB-102 in late 2021. As a result, management continues to believe that the Company's current cash, cash equivalents and short-term investments are adequate to meet its cash needs for at least 12 months from the issuance date of this Form 10-K. The Company will seek to raise additional funds in order to further advance its research and development programs other than GB-102, operate its business, secure research and development collaborations, and meet its obligations as they come due. The Company is pursuing financing alternatives, similar to what the Company has previously executed, which include debt and equity financing. Such sources of capital may not, however, be available to the Company in the necessary time frame, in the amounts that the Company requires, on terms that are acceptable to the Company, or at all. If the Company is unable to raise the necessary funds when needed or reduce spending on currently planned activities, it may not be able to continue the development of its products or the Company could be required to delay, scale back, or eliminate some or all of its research and development programs and other operations, which may materially harm its business, financial position and results of operations.

COVID-19 Pandemic

The impact of the worldwide spread of a novel strain of coronavirus ("COVID-19") has been unprecedented and unpredictable, including the emergence of new variants of the coronavirus, such as the Delta and Omicron variants, and resurgences in number and rates of infections, but based on the Company's current assessment, the Company does not expect any material impact on its long-term strategic plans, operations, or its liquidity due to the worldwide spread of COVID-19. However, the Company is continuing to assess the effect on its operations by monitoring the spread of COVID-19 and the actions implemented to combat the virus and new variants thereof throughout the world and its assessment of the impact of COVID-19 may change.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America, or GAAP, and stated in U.S. dollars. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification, or ASC, and Accounting Standards Updates, or ASUs, of the Financial Accounting Standards Board, or FASB.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires the Company to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements and reported amounts of expenses during the reporting periods. Actual results could differ from those estimates. On an ongoing basis, the Company evaluates its estimates, including those related to accrued research and development expenses, contingent

milestone payments, other long-lived assets, stock-based compensation, and the valuation of deferred tax assets. The Company bases its estimates using historical experience, Company forecasts and future plans, current economic conditions, and information from third-party professionals that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities and recorded amounts of expenses that are not readily apparent from other sources, and adjusts those estimates and assumptions when facts and circumstances dictate.

The Company's results can also be affected by economic, political, legislative, regulatory and legal actions. Economic conditions, such as recessionary trends, inflation, interest, changes in regulatory laws and monetary exchange rates, and government fiscal policies, can have a significant effect on operations. While the Company maintains reserves for anticipated liabilities, the Company could be adversely affected by civil, criminal, regulatory or administrative actions, claims, or related proceedings.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities at the date of purchase of three months or less to be cash equivalents. Cash and cash equivalents are stated at fair value and may include money market funds, corporate debt securities and commercial paper. The Company's cash equivalents consist of money market fund investments, corporate debt securities, and commercial paper.

Investments

The Company invests its excess cash balances in marketable government agency bonds, corporate debt securities and commercial paper. The Company classifies its investments as available-for-sale, reports available-for-sale investments at their fair value at each balance sheet date, and includes any unrealized holding gains and losses (the adjustment to fair value) in accumulated other comprehensive loss, a component of stockholders' equity. Should there be any realized gains or losses, they will be determined using the specific-identification method and included as other income or expense in the statements of operations.

The Company periodically evaluates whether declines in fair values of its marketable securities below their book value are other-than-temporary. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss as well as the Company's ability and intent to hold the marketable security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the security or it is more likely than not it will be required to sell any marketable securities before recovery of its amortized cost basis. Impairment assessments are made at the individual security level each reporting period. When the fair value of an available-for-sale security is less than its cost at the balance sheet date, a determination is made as to whether the impairment is other-than-temporary and, if it is other-than-temporary, an impairment loss is recognized in the statements of operations, equal to the difference between the investment's amortized cost and fair value at such date. The Company did not record any impairment charges related to its marketable securities during the years ended December 31, 2021 and 2020.

The Company classifies its available-for-sale marketable securities as non-current if such instrument's underlying effective maturity date exceeds 12 months and for which the Company has the intent and ability to hold the investment for a period of greater than 12 months. The Company's marketable securities at December 31, 2021 and 2020 mature in less than 12 months and are included in short-term investments in the balance sheets.

Concentrations of Credit Risk and Off-balance Sheet Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist primarily of cash and cash equivalents and available-for-sale marketable securities. The Company's investment policy includes guidelines regarding the quality of the financial institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk. The Company may invest in money market funds, U.S. Treasury securities, corporate debt, U.S. government-related agency securities, commercial paper and certificates of deposit. At December 31, 2021 and 2020, the Company's cash and cash equivalents were held in financial institutions that management believes are creditworthy. These deposits may exceed federally insured limits. The Company has not experienced any losses historically in these accounts and believes it is not exposed to significant credit risk in its cash and cash equivalents. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts, or other hedging arrangements.

Property and Equipment

Property and equipment are stated at cost, subject to adjustments for impairments, less accumulated depreciation and amortization. Depreciation is calculated using the straight-line method over the useful lives of the assets as follows:

Asset	Estimated useful life
Manufacturing and laboratory equipment	Three to five years
Computer hardware	Three to five years
Office furniture and equipment	Three to five years

Leasehold improvements are amortized over the shorter of their useful lives or the related lease term. Maintenance and repairs that do not improve or extend the life of the respective asset are expensed to operations as incurred. Manufacturing and laboratory equipment received is classified as construction in progress until placed into service, at which time depreciation commences. Upon disposal of an asset, the related cost and accumulated depreciation are removed from the accounts and any resulting gain or loss is included in the results of operations.

Impairment of Long-lived Assets

The Company evaluates whether current facts or circumstances indicate that the carrying values of its long-lived assets may not be recoverable. If such facts or circumstances are determined to exist, an estimate of the sum of the undiscounted future cash flows of these assets is compared to the carrying value the assets to determine whether impairment exists. If the assets are determined to be impaired, the loss is measured based on the difference between the sum of the undiscounted future cash flows and the carrying value of the assets. No impairment losses were recorded during the years ended December 31, 2021 or 2020.

Research and Development Expenses

Research and development costs are expensed as incurred. The Company's research and development expenses consist primarily of costs incurred for the development of its product candidates and include expenses incurred under agreements with contract manufacturing organizations, or CMOs, contract research organizations, or CROs, investigative sites and consultants to conduct clinical trials and preclinical and non-clinical studies, costs to acquire, develop and manufacture supplies for clinical trials and other studies, salaries and related costs, including stock-based compensation, depreciation and other allocated facility-related and overhead expenses.

Accrued Research and Development Costs

The Company records accruals for estimated costs of preclinical and clinical studies and manufacturing development. The Company's clinical and manufacturing development activities are conducted by third-party service providers, including CROs and CMOs. The financial terms of these contracts are subject to negotiation, which vary by contract and may result in payments that do not match the periods over which materials or services are provided. The Company accrues the costs incurred under the agreements based on an estimate of actual work completed in accordance with the agreements. In the event the Company makes advance payments for goods or services that will be used or rendered for future research and development activities, the payments are deferred and capitalized as a prepaid expense and recognized as expense as the goods are received or the related services are rendered. Such payments are evaluated for current or non-current classification based on when they are expected to be realized. If the Company does not identify costs that have begun to be incurred or if the Company underestimates or overestimates the level of services performed or the costs of these services, actual expenses could differ from the Company's estimates. To date, the Company has not experienced significant changes in its estimates of preclinical studies, clinical trial and manufacturing accruals.

Patent Costs

Costs to secure and maintain patents covering the Company's technology and product candidates are expensed as incurred and are classified as general and administrative expenses in the statements of operations.

Convertible Preferred Stock

The Company classified convertible preferred stock outside of stockholders' equity (deficit) on its balance sheet as of December 31, 2019, as the requirements of triggering a deemed liquidation event were not within the Company's control. In the event of a deemed liquidation event, the proceeds from the event would have been distributed in accordance with liquidation preferences of such securities.

The Company would have adjusted the carrying value of the convertible preferred stock to their redemption values when it became probable a redemption event would occur. Prior to the completion of the IPO on September 24, 2020, all of the outstanding shares of convertible preferred stock automatically converted into 13,085,913 shares of common stock. Subsequent to the closing of the IPO on September 29, 2020, there were no shares of convertible preferred stock outstanding.

Preferred Stock Tranche Obligation

The Company's Series C convertible preferred stock included features the Company determined were not clearly and closely related to the equity host. These features were therefore bifurcated and accounted for separately as a freestanding derivative liability on the balance sheet at its estimated fair value. This derivative liability was a result of certain investors' rights to purchase from the Company, on the same terms as the Series C Preferred Stock Purchase Agreement executed in July 2019, additional shares of Series C convertible preferred stock in subsequent tranches based on the achievement of certain development milestones, or the Preferred Stock Tranche Obligation. At initial recognition, the Company recorded this derivative as a liability on the balance sheet at its estimated fair value. The derivative was subject to remeasurement at each balance sheet date until its expiration in September 2020, with changes in fair value recognized in change in fair value of Preferred Stock Tranche Obligation on the Company's statements of operations.

Stock-based Compensation

Stock-based compensation expense related to stock options and warrants granted to employees, directors and non-employees is recognized based on the grant-date estimated fair values of the awards using the Black-Scholes option pricing model, or Black-Scholes. The valuation of restricted stock units, or RSUs, is determined at the date of grant using the Company's closing stock price. The value is recognized as expense ratably over the requisite service period, which is generally the vesting term of the award. The Company adjusts the expense for actual forfeitures as they occur.

Income Taxes

The Company uses the liability method to account for income taxes. Under this method, deferred tax assets and liabilities are determined based on temporary differences between the financial statement carrying amounts of existing assets and liabilities and their tax bases. Deferred tax assets and liabilities are measured using enacted tax rates applied to taxable income in the years in which those temporary differences are expected to be recovered or settled. A valuation allowance is established when necessary to reduce deferred tax assets to the amount expected to be realized.

The Company assesses the likelihood of deferred tax assets being realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. For the Company, the ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible. Based on the Company's operations to date and the uncertainty as to the timing and amount of future taxable income, the Company has recorded a full valuation allowance in all periods and for all jurisdictions.

Financial statement effects of uncertain tax positions are recognized when it is more likely than not, based on the technical merits of the position, that it will be sustained upon examination. The Company evaluates uncertain tax positions on a regular basis. The evaluations are based on a number of factors, including changes in facts and circumstances, changes in tax law, correspondence with tax authorities during the course of an audit, and effective settlement of audit issues. Interest and penalties related to unrecognized tax benefits would be included within the income tax provision.

Net Loss Per Share

The Company calculates basic and diluted net loss per share attributable to common stockholders in conformity with the two-class method required for participating securities. While it was outstanding, the Company considered its convertible preferred stock to be participating securities as, in the event a dividend was paid on common stock, the holders of convertible preferred stock and unvested shares of common stock would have been entitled to receive dividends on a basis consistent with the common stockholders. The net loss attributable to common stockholders was not allocated to the convertible preferred stock as the holders of those securities did not have a contractual obligation to share in losses. Cumulative dividends on preferred stock were added to net loss to arrive at net loss available to common stockholders.

Under the two-class method, basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding during the period, without consideration of potential dilutive securities. Diluted net loss per share is calculated by dividing net loss by the weighted-average number of shares of common stock and potential dilutive common stock equivalents outstanding during the period if the effect is dilutive. Potentially dilutive securities include warrants, stock options, RSUs and convertible preferred stock. Likewise, adjustments to the denominator are required to reflect the related dilutive shares. In all periods presented, the Company's outstanding stock options, RSUs, convertible preferred stock, common stock warrants, and the potential issuance of additional preferred shares from the Preferred Stock Tranche Obligation were excluded from the calculation of diluted net loss per share because their effects were antidilutive and the

development milestones for the issuance of additional shares from the Preferred Stock Tranche Obligation were not achieved prior to its expiration in September 2020.

Related Party Transactions

In August 2019, the Company engaged a consulting firm managed by the then acting chief financial officer of the Company for professional services related to finance and other administrative functions. For the year ended December 31, 2020, the costs incurred under this arrangement totaled $657,000 and were recorded as general and administrative expense in the accompanying statement of operations. The Company terminated its relationship with this entity in September 2020.

Segments

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the chief operating decision maker, or CODM, in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its chief executive officer. The Company has determined it operates in one segment.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period arising from transactions and other events and circumstances from non-owner sources. The Company's comprehensive loss is comprised of changes in unrealized (loss) gain on available-for-sale securities.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842)*, as amended, with guidance regarding the accounting for and disclosure of leases. The update requires lessees to recognize the liabilities related to all leases, including operating leases, with a term greater than 12 months on the balance sheet. This update also requires lessees and lessors to disclose key information about their leasing transactions. As an emerging growth company, this standard is effective for the Company for fiscal years beginning after December 15, 2021, and interim periods within annual periods beginning after December 15, 2022. Early adoption is permitted. The Company adopted this standard on January 1, 2022 and has performed an analysis on the impact of this standard and does not expect that this standard will have a material impact on its results of operations or cash flows, but that it will have a material impact on the Company's assets and liabilities as a result of the recognition of right-of-use asset and lease liabilities. The Company also expects to elect the "package of practical expedients", which permits the Company to not reassess under this standard its prior conclusions about lease identification, lease classification and initial direct costs. In addition, the Company expects to elect the short-term lease recognition exemption for all leases that qualify.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses: Measurement of Credit Losses on Financial Instruments*. ASU 2016-13 requires measurement and recognition of expected credit losses for financial assets. In April 2019, the FASB issued a clarification to ASU 2016-13 within ASU 2019-04, *Codification Improvements to Topic 326, Financial Instruments-Credit Losses, Topic 815, Derivatives and Hedging, and Topic 825, Financial Instruments*, which modified the accounting for available-for-sale securities. As an emerging growth company, ASU 2016-13 is effective for the Company for fiscal years beginning after December 15, 2022, with early adoption permitted. The Company is currently assessing the potential impact of adopting ASU 2016-13 on its financial statements and financial statement disclosures.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, which removes certain exceptions and amends certain requirements in the existing income tax guidance to ease accounting requirements. As an emerging growth company, this standard is effective for the Company for fiscal years beginning after December 15, 2021, and interim periods within annual periods beginning after December 15, 2022, and must be applied on a retrospective basis. The Company is currently evaluating the impact of this new guidance on its financial statements and financial statement disclosures but does not expect this new guidance to have a material impact on its financial statements and financial statement disclosures.

3. Fair Value Measurements

The Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible. The Company determines fair value based on assumptions that market participants would use in pricing an asset or liability in the principal or most advantageous market. When considering market participant assumptions in fair value

measurements, the following fair value hierarchy distinguishes between observable and unobservable inputs, which are categorized in one of the following three levels:

- *Level 1:* Observable inputs such as unadjusted quoted prices in active markets for identical assets or liabilities at the measurement date.
- *Level 2:* Inputs (other than quoted prices included in Level 1) that are either directly or indirectly observable for the asset or liability. These include quoted prices for similar assets or liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active.
- *Level 3:* Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values (in thousands):

	December 31, 2021			
	Level 1	Level 2	Level 3	Total
Current assets:				
Cash equivalents:				
Money market funds	$ 8,920	$ —	$ —	$ 8,920
Corporate debt securities	—	1,480	—	1,480
Commercial paper	—	2,749	—	2,749
Total cash equivalents	8,920	4,229	—	13,149
Short-term investments:				
Corporate debt securities	—	1,117	—	1,117
Commercial paper	—	41,954	—	41,954
U.S. Treasury notes	—	7,235	—	7,235
Total short-term investments	—	50,306	—	50,306
Total assets measured at fair value	$ 8,920	$ 54,535	$ —	$ 63,455

	December 31, 2020			
	Level 1	Level 2	Level 3	Total
Current assets:				
Cash equivalents:				
Money market funds	$ 15,677	$ —	$ —	$ 15,677
Corporate debt securities	—	2,500	—	2,500
Commercial paper	—	13,499	—	13,499
Total cash equivalents	15,677	15,999	—	31,676
Short-term investments:				
Corporate debt securities	—	11,588	—	11,588
Commercial paper	—	50,027	—	50,027
Total short-term investments	—	61,615	—	61,615
Total assets measured at fair value	$ 15,677	$ 77,614	$ —	$ 93,291

The following tables present information as to cost, unrealized gains and losses and fair value determination of the Company's financial assets measured at fair value on a recurring basis (in thousands):

	December 31, 2021			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Aggregate Fair Value
Current assets:				
Cash equivalents:				
Money market funds	$ 8,920	$ —	$ —	$ 8,920
Corporate debt securities	1,480	—	—	1,480
Commercial paper	2,749	—	—	2,749
Total cash equivalents	13,149	—	—	13,149
Short-term investments:				
Corporate debt securities	1,117	—	(1)	1,116
Commercial paper	41,956	6	(8)	41,954
U.S. Treasury notes	7,249	—	(13)	7,236
Total short-term investments	50,322	6	(22)	50,306
Total assets measured at fair value	$ 63,471	$ 6	$ (22)	$ 63,455

	December 31, 2020			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Aggregate Fair Value
Current assets:				
Cash equivalents:				
Money market funds	$ 15,677	$ —	$ —	$ 15,677
Corporate debt securities	2,502	—	(2)	2,500
Commercial paper	13,498	1	—	13,499
Total cash equivalents	31,677	1	(2)	31,676
Short-term investments:				
Corporate debt securities	11,588	1	(1)	11,588
Commercial paper	50,030	2	(5)	50,027
Total short-term investments	61,618	3	(6)	61,615
Total assets measured at fair value	$ 93,295	$ 4	$ (8)	$ 93,291

Money market funds are highly liquid investments which are actively traded. The pricing information on the Company's money market funds is based on quoted prices in active markets for identical securities. This approach results in the classification of these securities as Level 1 of the fair value hierarchy.

The fair value of short-term investments is determined from market pricing and other observable market inputs for similar securities obtained from various third-party data providers. The pricing services utilize industry-standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities; issuer credit spreads; benchmark securities; prepayment/default projections based on historical data; and other observable inputs. This approach results in the classification of these securities as Level 2 of the fair value hierarchy.

As of December 31, 2021 and 2020, the contractual maturities of all available-for-sale investments were less than 12 months. The Company periodically reviews the available-for-sale investments for other-than-temporary impairment loss. All investments with unrealized losses have been in a loss position for less than 12 months. As a result, the Company did not recognize any other-than-temporary impairment losses as of December 31, 2021 and 2020.

There were no transfers between Levels 1, 2 or 3 for the periods presented.

4. Balance Sheet Components

Property and Equipment, net

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

	December 31,	
	2021	2020
Manufacturing and laboratory equipment	$ 2,511	$ 2,179
Computer hardware	28	28
Office furniture and equipment	28	28
Leasehold improvement	234	234
Construction in progress	833	611
Total property and equipment, at cost	3,634	3,080
Less: accumulated depreciation	(1,653)	(1,134)
Property and equipment, net	$ 1,981	$ 1,946

Depreciation expense for the years ended December 31, 2021 and 2020 was $519,000 and $395,000, respectively.

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31,	
	2021	2020
Prepaid expenses	$ 1,866	$ 2,140
Prepaid clinical and research expenses	168	6
Interest and other receivables	21	598
Other current assets	1,353	1,463
Total prepaid expenses and other current assets	$ 3,408	$ 4,207

Other Current Liabilities

Other current liabilities consisted of the following (in thousands):

	December 31,	
	2021	2020
Salaries and benefits	$ 2,278	$ 2,302
Professional services	461	425
Deferred rent	8	27
Other	479	374
Total other current liabilities	$ 3,226	$ 3,128

5. Commitments and Contingencies

The Company enters into contracts in the normal course of business with CROs for clinical trials and CMOs for clinical supply manufacturing and with vendors for equipment, preclinical research studies, research supplies and other services and products for operating purposes. As of December 31, 2021, these commitments were approximately $0.8 million due within 3 to 15 months. These contracts generally provide for termination on notice of 60 to 90 days. During the year ended December 31, 2021, the Company terminated several contracts with its equipment vendors and CMOs. The termination of these contracts resulted in the cancellation of commitments totaling $3.7 million as of December 31, 2020. From this amount, the Company recognized $2.2 million in general and administrative expenses in the Company's statement of operations for the write-off of $1.3 million in equipment deposits and $0.9 million in other commitments and cancellation fees. As of December 31, 2021, there were no unpaid cancellation or other related costs and none are anticipated.

Operating Lease Agreements

The Company leases a facility in Baltimore, Maryland under an operating lease with a term through June 2023.

On July 29, 2021, the Company entered into a lease agreement for approximately 2,560 rentable square feet of office space in Redwood City, California. The lease commenced on August 18, 2021 with a 12-month initial term expiring on August 31, 2022. This new facility replaced the Company's existing Redwood City lease when it expired on August 31, 2021. Upon execution of the lease, the Company delivered to the lessor a sum of $31,000, consisting of a security deposit and one month's rent. The total lease obligation over the term of the lease will be approximately $0.2 million.

Rent expense for the Company's facility leases was $0.7 million for each of the years ended December 31, 2021 and 2020.

Future minimum lease payments under the Company's non–cancelable operating leases as of December 31, 2021 were as follows (in thousands):

Year ended December 31:		
2022	$	527
2023		205
Total future minimum lease payments	$	732

License Agreements

Johns Hopkins University

In June 2011, the Company entered into an Exclusive License Agreement with Johns Hopkins University, or JHU, which has been amended from time to time, such agreement as amended is referred to as the JHU Agreement. Pursuant to the JHU Agreement, JHU granted the Company an exclusive, worldwide, sublicensable license to three patent families to research, develop, make, use and sell products and provide services in any field, and a non-exclusive license to use specified know-how and materials with a provision that JHU will not grant a license to know how and materials to any other commercial entity. The JHU first patent family describes microparticles with a hydrophobic polymeric core (such as poly(lactic-co-glycolic acid), or PLGA, poly-lactic acid, or PLA, or a combination of both PLGA and PLA) and a hydrophilic coating (such as PLGA permanently linked to polyethylene glycol) to reduce inflammation for intraocular injections and their methods of use, which technology is incorporated into the Company's GB-102 and GB-401 product candidates. The JHU licensed fourth and fifth patent families cover potential future technologies.

In September 2015, the JHU Agreement was amended to include the JHU second patent family which covers sunitinib-encapsulated polymeric microparticles, including GB-102, and their use as therapeutic compositions to treat disorders of the eye. Under the terms of the amended JHU Agreement, the Company paid a one-time, non-refundable upfront fee, with a remaining amount to be paid upon the occurrence of certain events. The Company also agreed to pay an additional one-time, non-refundable fee of $100,000 on the occurrence of the first commercial sale of a product falling under the claims of a patent in the second patent family.

In April 2016, the JHU Agreement was further amended to include a third patent family which discloses a method for reducing neuronal damage in the eye that includes administration of a sustained release formulation of a dual leucine kinase inhibitor in a polymeric particle, and wherein the dual leucine kinase inhibitor may be sunitinib, and thus is relevant to both the Company's GB-102 and GB-103 product candidates. Under the terms of the amended JHU Agreement, the Company paid a one-time, non-refundable upfront fee, and a milestone payment for the grant of the first patent. The Company also agreed to use its best efforts to develop a licensed product under the third patent family and enter into a Phase I clinical trial on or before April 2019, and to have cumulatively spent several million dollars on research and development within six years of execution of the amendment.

Upon execution of the JHU Agreement in 2011, the Company paid JHU an upfront license fee in the low tens of thousands of dollars and issued to JHU a low single digit percentage of the Company's equity interests as of such date. The Company also reimbursed JHU for the prosecution and maintenance costs incurred by JHU for the licensed patent rights prior to the Company entering into the JHU Agreement, and the Company is responsible for all of the ongoing costs relating to the prosecution and maintenance of the JHU patent rights licensed to the Company. The Company also agreed to pay minimum annual royalties in the tens of thousands of dollars per year until the first commercial sale of a licensed product or service.

The JHU Agreement further requires single-digit running royalties on the Company's annual net sales, which may be reduced by 50% of any payments the Company makes to third parties for freedom to operate, up to a maximum credit of 50% of the running royalty rate otherwise due to JHU. Royalties must be paid on products that fall within a patent claim of an issued and unexpired patent or a pending patent application that has not been finally rejected or is pending for less than seven years. The Company also must pay developmental milestones for achieving certain clinical progression events, ranging from tens of thousands to hundreds of thousands dollars per event, which in the aggregate, total less than $2.0 million per product. Under the JHU Agreement, prior to the Kala Agreement renegotiation described below, the Company was responsible for paying each developmental milestone payment for the first three products to achieve such milestone, and milestones for the second and third products are reduced by 50%. The Company further agreed to pay a percentage of any sublicense consideration the Company receives.

The JHU Agreement will remain effective until (i) the later of the expiration date of the last-to-expire patents covered under the JHU Agreement or 20 years from the effective date; (ii) the termination by either party upon the bankruptcy or uncured breach of the other party or (iii) if the Company terminates the JHU Agreement, with a 90-day notification period. The Company may terminate the entire agreement or on a patent by patent basis if desired, subject to the 90-day notification period.

Milestone and royalty expenses under the JHU Agreement are classified as research and development expense and reimbursement of patent-related expenditures are classified as general and administrative expense in the statements of operations. Expense under the JHU Agreement is as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	$ 38	$ 38
General and administrative	160	165
Total JHU Agreement expense	$ 198	$ 203

Kala Pharmaceuticals, Inc.

A dispute arose between the Company, JHU and Kala Pharmaceuticals, Inc., or Kala, over rights licensed to the Company and Kala by JHU. In October 2014, the Company entered into a Settlement and License Agreement, or the Kala Agreement, with Kala and JHU, which settled all pending disputes and amended the Company's and Kala's existing license agreements with JHU and created new rights and obligations among the parties.

Under the Kala Agreement, each of Kala and the Company provided the other with a royalty-free, exclusive sublicense with respect to certain intellectual property rights granted by JHU in limited fields of use. Specifically, the Company provided Kala with an exclusive sublicense for the use of a particle with specific characteristics for delivery of a biologically active material through mucus, mucin, or a mucosal barrier (provided that such delivery does not involve administration via injection to the eye), or the Kala Field of Use, and Kala provided the Company with an exclusive sublicense to the use of a particle with specific characteristics for delivery of a biologically active material to the eye via injection (excluding such use of any particle comprising or consisting of loteprednol etabonate). Kala also agreed not to use a particle with those specific characteristics that include sunitinib in any technology licensed the Kala Field of Use under the license from the Company or JHU. Neither the Company nor Kala owe JHU any payments under its existing JHU agreement with respect to the sublicenses granted to the other. Both the Company and Kala hold rights to sublicense the Company's respective rights in connection with a future collaboration arrangement and subject to any such sublicensee being bound by the applicable terms of the Kala Agreement.

Under the Kala Agreement, JHU agreed to a number of financial concessions to both the Company and Kala. The payments under the existing JHU agreements were modified by reducing all milestones and minimum annual royalties by 25%, including the development milestone payments due for the first licensed product; the development milestone payments due for the first license product were each extended by one year; development milestone payments for the second and third licensed products were eliminated; and the commercial milestone payments for the first commercial sale of a licensed product were reduced by 50% in the United States. New sales-based milestones were added for the second and third licensed products. Upon the second licensed product under the JHU Agreement reaching a certain level of sales or receiving sublicense royalty income, the Company is required to pay $100,000 plus the amounts of the eliminated development milestones and reduced first commercial sale milestone. For the third licensed product, on reaching the same level of sales or receiving sublicense royalty income, the Company is required to pay $150,000 plus the amounts of the eliminated development milestones and reduced first commercial sale milestone. In addition, the Company, Kala and JHU released each other from any liability or claims known to Kala and the Company as of the Kala Agreement and arising out of the actions leading to, and related to the subject of, the Kala Agreement.

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

There have been no expenses under the Kala Agreement in the years ended December 31, 2021 or 2020 and no amounts payable at December 31, 2021 or 2020.

AffaMed Project Limited

In July 2019, the Company entered into a letter agreement with AffaMed Project Limited, or AffaMed, in connection with their purchase of the Company's Series C convertible preferred stock, or the AffaMed Letter. Under the AffaMed Letter, the Company granted AffaMed a right of first negotiation, or the Option, to exclusively develop, register and commercialize GB-102 solely in the territories of China, Hong Kong, Taiwan, Macau and South Korea. The Option expires upon the earlier of (i) July 31, 2021 and (ii) 60 days after the Company provides top line data from the Phase 2b ALTISSIMO trial for GB-102. AffaMed did not exercise the Option, and the Company has no further obligation to AffaMed to license rights to GB-102.

There have been no expenses under the Affamed Letter in the years ended December 31, 2021 or 2020 and no amounts payable at December 31, 2021 or 2020.

Asset Acquisition

In December 2021, the Company entered into an Assignment and Licensing Agreement with a private company, pursuant to which the Company acquired certain intellectual property rights, including patents and know-how, related to new cyclic monophosphate (cGMP) compounds for the treatment of ocular disorders.

As consideration for the intellectual property rights acquired, the Company made an upfront cash payment of $0.5 million and may be required to make additional contingent payments of up to $27.0 million in the aggregate upon achievement of certain development and regulatory milestones. Additionally, upon commercialization, the Company may be required to make tiered single-digit royalty payments based on net product sales.

As the acquired rights relate to in-process research and development activities that have no alternative future use to the Company, the upfront payment of $0.5 million was recorded as research and development expense in the accompanying statements of operations for the year ended December 31, 2021. As of December 31, 2021, no development or regulatory milestones were deemed probable of achievement and, accordingly, no amounts have been recognized in the accompanying financial statements with respect to these contingent payments.

In March 2022, the Company acquired a private company in the United States with certain gene therapy technology and preclinical data. The private company was purchased at a cost of approximately $2.0 million, including estimated transaction costs and a contingent holdback, and the Company may be required to make additional contingent payments of up to $20.0 million in the aggregate upon the achievement of certain milestones. Other than the contingent holdback release, no further payments are required until FDA approval of a product based upon the acquired assets and the sale or utilization of any priority review voucher that may be granted in connection with such approval.

Indemnification

The Company, as permitted under Delaware law and in accordance with its certification of incorporation and bylaws and pursuant to indemnification agreements with certain of its officers and directors, indemnifies its officers and directors for certain events or occurrences, subject to certain limits, which the officer or director is or was serving at the Company's request in such capacity.

The Company enters into certain types of contracts that contingently require the Company to indemnify various parties against claims from third parties. These contracts primarily relate to (i) the Company's bylaws, under which the Company must indemnify directors and executive officers, and may indemnify other officers and employees, for liabilities arising out of their relationship, (ii) contracts under which the Company must indemnify directors and certain officers and consultants for liabilities arising out of their relationship, and (iii) procurement, service or license agreements under which the Company may be required to indemnify vendors, service providers or licensees for certain claims, including claims that may be brought against them arising from the Company's acts or omissions with respect to the Company's products, technology, intellectual property or services.

From time to time, the Company may receive indemnification claims under these contracts in the normal course of business. In the event that one or more of these matters were to result in a claim against the Company, an adverse outcome, including a judgment or settlement, may cause a material adverse effect on the Company's future business, operating results or financial condition. It is not possible to determine the maximum potential amount potentially payable under these contracts since the Company has no history of prior indemnification claims and the unique facts and circumstances involved in each particular claim will be determinative.

Litigation

From time to time, the Company may become involved in legal proceedings arising in the ordinary course of business. The Company is not presently a party to any legal proceedings that it believes would have a material adverse effect on its business, operating results, financial condition or cash flows.

6. Convertible Preferred Stock and Preferred Stock Tranche Obligation

The following table summarizes outstanding convertible preferred stock as of December 31, 2019 (in thousands, except share amounts):

	Shares Authorized	Shares Outstanding	Net Carrying Value	Liquidation Preference
Series A	2,280,000	2,280,000	$ 2,280	$ 2,280
Series A-2	2,018,561	2,018,561	1,605	1,740
Series B	76,078,535	76,078,535	74,926	87,729
Series C	61,773,000	37,432,787	52,552	56,843
Total	142,150,096	117,809,883	$ 131,363	$ 148,592

In July 2019, the Company authorized the sale of up to 61,773,000 shares of its Series C Convertible Preferred Stock, or Series C, at a price of $1.4693 per share, or Series C Financing. In July and August 2019, the Company issued 37,432,787 shares of Series C for aggregate gross proceeds of $55.0 million. In connection with this financing, certain purchasers of the Series C had the option to purchase up to an additional 17,014,902 shares of Series C at a price per share of $1.4693 for a period of up to 30 days after the Company notified them of the three-month readout from the Phase 2a clinical trial of GB-102 in patients with macular edema secondary to diabetic macular edema and retinal vein occlusion, or the Preferred Stock Tranche Obligation. The Company concluded that the Preferred Stock Tranche Obligation met the definition of a freestanding financial instrument, as the rights were legally detachable and separately exercisable from the Series C. Therefore, the Company allocated the proceeds received from the issuance of shares under the Series C Preferred Stock Purchase Agreement between the Preferred Stock Tranche Obligation and the Series C. The fair value of the Preferred Stock Tranche Obligation of $2.2 million on issuance was allocated from the $55.0 million proceeds of the Series C Financing and classified as a current liability on the balance sheet as the Series C would become redeemable upon a deemed liquidation event, the occurrence of which was not within the Company's control. The Preferred Stock Tranche Obligation was remeasured at fair value at each reporting period using an option pricing valuation methodology. For the year ended December 31, 2020, the Company recognized a gain on change in fair value of preferred stock tranche obligation of $2.2 million.

In September 2020, the board of directors and the Series C investors amended the Series C stock purchase agreement such that the Preferred Stock Tranche Obligation was no longer exercisable and expired upon the effectiveness of the Company's IPO registration statement. As a result, the liability for the Preferred Stock Tranche Obligation was permanently eliminated as of September 24, 2020. Due to the low probability of the Preferred Stock Tranche Obligation being settled, the fair value immediately prior to the IPO was immaterial.

Prior to the completion of the IPO on September 24, 2020, all of the outstanding shares of convertible preferred stock automatically converted into 13,085,913 shares of common stock. Subsequent to the closing of the IPO on September 29, 2020, there were no shares of convertible preferred stock outstanding.

The rights and preferences and privileges of convertible preferred stock are described below:

Dividend Rights

The holders of Series C Preferred, in preference to holders of Series B Preferred, Series A-2 Preferred, Series A Preferred and common stock, are entitled to receive cumulative dividends on each outstanding share payable when declared by the board of directors of $0.117544 per share. After payment of such dividends on the Series C Preferred, the holders of Series B Preferred, in preference to holders of Series A-2 Preferred, Series A Preferred and common stock, are entitled to receive cumulative dividends on each outstanding share payable when declared by the board of directors of $0.06937 per share. After payment of such dividends on the Series B Preferred, the holders of Series A-2 Preferred, in preference to the holders of Series A Preferred and common stock, are entitled to receive non-cumulative dividends on each outstanding share payable when declared by the board of directors of $0.06034 per share. After payment of such dividends on the Series A-2 Preferred, the holders of Series A Preferred, in preference to the holders of common stock, are entitled to receive non-cumulative dividends on each outstanding share payable when declared by the board of directors of $0.08 per share. The board of directors has not declared any dividends to-date.

Conversion Rights

Each share of convertible preferred stock is convertible at the option of the holder, at any time after the date of issuance, into a fully paid and non-assessable share of common stock. Each share of convertible preferred stock is convertible into that number of common shares as is determined by dividing the applicable original purchase price of such share by the applicable conversion price. The conversion rate is subject to adjustment upon the occurrence of certain events. The conversion rates for the Series C Preferred, Series B Preferred and Series A-2 Preferred is 9.0058:1 and for the Series A Preferred is 8.8527:1.

All shares of the convertible preferred stock automatically convert upon the closing of a firm commitment underwritten initial public offering of common stock, in which the price per share is at least $14.56 per share, subject to adjustment, resulting in gross proceeds of at least $40.0 million. The conversion price for each series of convertible preferred stock is subject to adjustment in the event of stock split, combination, common stock dividend or distribution, reclassification, exchange, substitution, reorganization, and certain antidilution adjustments.

Liquidation Rights

In the event of any liquidation, dissolution, or winding up of the Company or a deemed liquidation event, the holders of Series C Preferred are entitled to receive, prior to any distribution made to any other class of security, an amount equal to $1.4693 per share, plus any dividends accrued and declared but unpaid. Upon distribution to holders of Series C Preferred, the holders of Series B Preferred are entitled to receive, prior to distribution to holders of Series A-2 Preferred, Series A Preferred and common stock, an amount equal to $0.991 per share, plus any dividends accrued and declared but unpaid. Upon distribution to holders of Series C Preferred and Series B Preferred, the holders of Series A-2 Preferred are entitled to receive, prior to distribution to holders of Series A Preferred and common stock, an amount equal to $0.862 per share, plus any dividends declared but unpaid. Upon distributions to the holders of Series C Preferred, Series B Preferred and Series A-2 Preferred, the holders of Series A Preferred are entitled to receive, prior to any distribution or payment to the holders of common stock, an amount equal to $1.00 per share, plus any dividends declared but unpaid. Upon the completion of the distribution to the holders of Series C Preferred, Series B Preferred, Series A-2 Preferred and Series A Preferred, any remaining assets available for distribution will be distributed among the holders of the shares of Series C Preferred, Series B Preferred, Series A-2 Preferred, Series A Preferred and common stock, on a pro rata basis on the number of shares held by each such holder, treating each share as if they had been converted to common stock immediately prior to such liquidation, dissolution or winding up of the Company.

Voting Rights

Each share of Series A Preferred has voting rights equal to the number of common shares into which the Series A Preferred can be converted. Shares of Series A-2 Preferred, Series B Preferred and Series C Preferred do not have voting rights.

The holders of Series C Preferred are entitled to elect one director of the Company; the holders of Series B Preferred are entitled to elect three directors of the Company; the holders of Series A-2 Preferred, are entitled to elect one director; the holders of common stock are entitled to elect one director; and holders of common stock and any other class or series of voting stock, exclusively and voting together as a single class on an as-converted basis, are entitled to elect one director. Holders of Series A Preferred are not entitled to a director of the Company.

Redemption Rights

Shares of Series C Preferred, Series B Preferred and Series A-2 Preferred may be redeemed at the greater of the fair market value or the original issue price for the applicable series of convertible preferred stock plus any dividends accrued but unpaid with respect to the Series C Preferred and the Series B Preferred and any dividend declared by unpaid with respect to the Series A-2 Preferred. A redemption will occur upon a written request from the holders of a majority of the then outstanding shares of Series C Preferred, voting exclusively as a separate series, and the holders of a majority of the Series B Preferred and Series A-2 Preferred, voting together on an as-converted basis, which request can be made at any time after July 2024.

Cumulative dividends and accretion of discount on Series A-2 Preferred, Series B Preferred and Series C Preferred, together the Contingently Redeemable Preferred, is not recorded until the Contingently Redeemable Preferred is probable of becoming redeemable. As of December 31, 2019, the Company has determined that the Contingently Redeemable Preferred are not currently probable of becoming redeemable and, as such, the cumulative dividend and accretion of discount on the Contingently Redeemable Preferred has not been recorded.

7. Stock-Based Compensation

2020 Equity Incentive Plan

In August 2020, the Company's board of directors and stockholders adopted the Company's 2020 Equity Incentive Plan, or the 2020 Plan, that became effective in connection with the IPO, and serves as the successor to the Company's 2015 Stock Incentive Plan, or the 2015 Plan. The Company's 2020 Plan authorizes the award of stock options, restricted stock units, or RSUs, restricted stock awards, or RSAs, stock appreciation rights, or SARs, performance awards and stock bonus awards. The Company initially reserved 1,850,000 shares of its common stock, plus any reserved shares not issued or subject to outstanding grants under the 2015 Plan on the effective date of the 2020 Plan, for issuance pursuant to awards granted under the 2020 Plan. The aggregate number of shares reserved

for sale under the 2020 Plan will increase automatically on each January 1st of 2021 through 2030 by the number of shares equal to 5% of the aggregate number of outstanding shares of the Company's common stock as of the immediately preceding December 31, or a lesser number as may be determined by the Company's board of directors.

In conjunction with adopting the 2020 Plan, the Company may not grant any additional stock-based awards under the 2015 Plan, and any shares available for issuance under the 2015 Plan were added to the shares reserved under the 2020 Plan. The 2015 Plan will continue to govern outstanding stock-based awards granted thereunder. On January 1, 2021, the aggregate number of shares reserved for issuance was increased by an additional 1,048,963 shares pursuant to the automatic share reserve increase provision of the 2020 Plan. As of December 31, 2021, there were 445,617 shares available for issuance under the 2020 Plan.

2020 Employee Stock Purchase Plan

In August 2020, the Company's board of directors and stockholders adopted the Company's 2020 Employee Stock Purchase Plan, or the ESPP, that became effective in connection with the IPO, in order to enable eligible employees to purchase shares of the Company's common stock with accumulated payroll deductions. The Company's ESPP is intended to qualify under Section 423 of the Internal Revenue Code. The Company has initially reserved 210,000 shares of its common stock for sale under the ESPP. The aggregate number of shares reserved for sale under the Company's ESPP will increase automatically on January 1st of each of the first ten calendar years after the first offering date under the ESPP by the number of shares equal to the lesser of 1% of the total outstanding shares of the Company's common stock as of the immediately preceding December 31, or a number of shares as may be determined by the Company's board of directors in any particular year. The aggregate number of shares issued over the term of the ESPP, subject to stock-splits, recapitalizations or similar events, may not exceed 2,100,000 shares of the Company's common stock.

Inducement Grants

On January 14, 2022, six newly-hired employees were granted inducement options to purchase an aggregate of 234,200 shares of the Company's common stock at an exercise price of $1.55 per share. These inducement grants were made outside of the 2020 Equity Incentive Plan in accordance with the Nasdaq Listing Rule 5635(c)(4). One-fourth of the options will vest on the one-year anniversary of the vesting commencement date and the remainder will vest in equal monthly installments over the next three years, in each case subject to the new employee's continued service with the Company. The stock options have a ten-year term and are subject to the terms and conditions of a stock option agreement covering the grant.

Stock Option Activity

The following summarizes stock option activity:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Outstanding—December 31, 2020	2,756,102	$ 8.28	8.6	$ 57,090
Granted	1,649,500	$ 3.74		
Exercised	(353,508)	$ 1.97		
Forfeited and Canceled	(274,696)	$ 12.52		
Outstanding—December 31, 2021	3,777,398	$ 6.58	8.4	$ 41,967
Options Exercisable—December 31, 2021	1,705,619	$ 5.24	7.4	$ 41,967

At December 31, 2021, the aggregate intrinsic value of options granted is calculated as the difference between the exercise price and the closing price on the same date. The aggregate intrinsic value of options exercised in the years ended December 31, 2021 and 2020 was $2.5 million and $113,000, respectively.

The aggregate fair value of options that vested during the years ended December 31, 2021 and 2020 was $4.0 million and $1.4 million, respectively. The weighted-average grant-date fair value per share of options that vested during the years ended December 31, 2021 and 2020 was $6.06 and $2.43, respectively.

Restricted Stock Units

The following table summarizes restricted stock units (RSUs) activity for the year ended December 31, 2021:

	RSUs Outstanding	
	Number of Restricted Stock Units	Weighted-Average Grant Date Fair Value Per Share
Balance - December 31, 2020	80,000	$ 16.50
Granted	988,700	$ 3.73
Vested	(25,000)	$ 16.50
Cancelled/forfeited	(74,000)	$ 3.74
Balance - December 31, 2021	969,700	$ 4.45

The fair value of RSUs is determined on the date of grant based on the market price of the Company's common stock on that date. The aggregate fair value of RSUs vested during the year ended December 31, 2021 was $0.4 million. No RSUs vested during the year ended December 31, 2020.

Fair Value of Stock Option Awards

The Company estimates the fair value of stock option awards on the grant date using Black-Scholes. The weighted-average grant date fair value per option granted during the years ended December 31, 2021 and 2020 was $2.72 and $11.90, respectively. The fair value of each award is estimated using Black-Scholes based on the following assumptions:

	Year Ended December 31,	
	2021	2020
Expected term (years)	5.1-6.1	5.0-6.1
Expected volatility	87% - 88%	85%
Risk-free interest rate	0.84%-1.12%	0.25%-0.53%
Expected dividend	—	—

Black-Scholes requires the use of subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

Expected Term: The expected term represents the period that options are expected to be outstanding and is determined using the simplified method, based on the mid-point between the vesting date and the end of the contractual term.

Expected Volatility: The expected volatility is estimated based on the average volatility for comparable publicly-traded biopharmaceutical companies over a period equal to the expected term of the stock option grants as the Company does not yet have sufficient historical trading history for its own stock. The comparable companies are chosen based on their similarities to the Company, including life cycle stage, therapeutic focus and size. The Company will continue to apply this method until a sufficient amount of historical information over a period equal to the expected term of the stock-based awards becomes available.

Risk-free Interest Rate. The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the stock option grants.

Expected Dividend: The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

Stock-Based Compensation Expense

Stock-based compensation expense is classified as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	$ 1,210	$ 390
General and administrative	4,165	1,398
Total stock-based compensation expense	$ 5,375	$ 1,788

As of December 31, 2021, the total unrecognized stock-based compensation expense related to outstanding unvested stock awards that are expected to vest was $15.4 million, which the Company expects to recognize over an estimated weighted-average term of 2.8 years.

8. Income Taxes

The Company has incurred net operating losses for all the periods presented. The Company has not reflected the benefit of any such net operating loss carryforwards in the accompanying financial statements.

The effective tax rate for the years ended December 31, 2021 and 2020 is different from the federal statutory rate primarily due to the valuation allowance against deferred tax assets as a result of insufficient sources of income. The reconciliation of the federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2021	2020
Income tax benefit at the federal statutory rate	21.0%	21.0%
State income taxes, net of federal benefit	0.6	3.2
Research and development tax credits	1.4	1.3
Other	(0.4)	(0.6)
Mark to market gain/loss	—	1.7
Change in valuation allowance	(22.6)	(26.6)
Total	—%	—%

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The principal components of the Company's net deferred tax assets consisted of the following (in thousands):

	December 31,	
	2021	2020
Deferred tax assets		
Federal and state net operating loss carryforwards	$ 34,431	$ 27,567
Research and development tax credits	5,408	4,887
Other	1,408	748
Gross deferred tax assets	41,247	33,202
Less: valuation allowance	(41,215)	(33,141)
Total deferred tax assets	32	61
Deferred tax liabilities		
Depreciation	(32)	(61)
Total deferred tax liabilities	(32)	(61)
Net deferred tax assets	$ —	$ —

The Company has incurred annual net operating losses in each year since inception. The Company has not reflected the benefit of any such net operating loss carryforwards in the financial statements. Due to the Company's history of losses, and lack of other positive evidence, the Company has determined that it is more likely than not that its net deferred tax assets will not be realized and, therefore, the net deferred tax assets are fully offset by a valuation allowance at December 31, 2021 and 2020. The Company increased its valuation allowance by $8.1 million for the year ended December 31, 2021 in order to maintain a full valuation allowance against its deferred tax assets.

As of December 31, 2021, the Company had federal net operating loss carryforwards, or NOLs, of $157.4 million and federal tax credits of $6.1 million available to offset tax liabilities. The Company's federal NOLs and federal tax credit carryforwards begin to expire in 2035 and 2036, respectively. Of the federal NOLs, $123.3 million have an indefinite life. The Company also had gross state NOLs of $23.3 million and state tax credits of $1.8 million which are available to offset state tax liabilities. The state NOLs expire in 2036 and the state tax credit carryforwards can be carried forward indefinitely. Federal and state NOLs and tax credit carryforwards are also subject to annual limitations in the event that cumulative changes in the ownership interests of significant stockholders exceed 50% over a three-year period, as defined under Sections 382 and 383 of the Internal Revenue Code of 1986. The Company has not completed an analysis to determine if the NOLs and tax credits are limited due to a change in ownership. Should there be ownership changes that occurred, the Company's ability to utilize existing carryforwards could be substantially restricted.

The Company determines its uncertain tax positions based on whether and how much of a tax benefit taken by the Company in its tax filings is more likely than not to be sustained upon examination by the relevant income tax authorities.

A reconciliation of the unrecognized tax benefit is as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Balance—beginning of year	$ 1,981	$ 1,406
Addition based on tax position related to current year	257	406
(Reduction) addition based on tax position related to prior year	(148)	169
Balance—end of year	$ 2,090	$ 1,981

The unrecognized tax benefits, if recognized, would not have an impact on the Company's effective tax rate assuming the Company continues to maintain a full valuation allowance position. Based on prior year's operations and experience, the Company does not expect a significant change to its unrecognized tax benefits over the next twelve months. The unrecognized tax benefits may increase or change during the next year for unexpected or unusual items for items that arise in the ordinary course of business. The Company has elected to include interest and penalties as a component of tax expense. During the years ended December 31, 2021 and 2020, the Company did not recognize accrued interest and penalties related to unrecognized tax benefits.

The Company files income tax returns in the U.S., California, and several other state jurisdictions. Due to net operating loss carryforwards, all years remain open for income tax examination, however, the Company is not currently under examination by any taxing authority for any open tax year.

9. Employee Retirement Plan

The Company maintains a 401(k) retirement savings plan, or 401(k) Plan. The 401(k) Plan allows employees to make contributions up to the maximum allowable by the IRS. The Company did not make any contributions to the 401(k) Plan on behalf of its employees in the years ended December 31, 2021 or 2020.

10. Net Loss Per Share Attributable to Common Stockholders

Basic and diluted net loss per common share is calculated as follows (in thousands except share and per share amounts):

	Year Ended December 31,	
	2021	2020
Net loss	$ (35,821)	$ (27,531)
Cumulative dividends on convertible preferred stock	—	(7,189)
Net loss attributable to common stockholders	$ (35,821)	$ (34,720)
Net loss per common share—basic and diluted	$ (1.69)	$ (5.25)
Weighted-average number of shares used in computing net loss per common share—basic and diluted	21,199,291	6,618,445

The following outstanding potentially dilutive shares have been excluded from the calculation of diluted net loss per share due to their anti-dilutive effect:

	As of December 31,	
	2021	2020
Stock options to purchase common stock	3,777,398	2,756,102
Restricted stock units	969,700	80,000
Warrants to purchase common stock	27,759	27,759

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

None

Item 9A. Controls and Procedures.

Evaluation of disclosure controls and procedures.

Under the supervision and with the participation of our management, including our Chief Executive Officer (our Principal Executive Officer) and our Chief Financial Officer (our Principal Financial Officer and Principal Accounting Officer), we evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of December 31, 2021. Based on our management's evaluation (with the participation of our Chief Executive Officer and our Chief Financial Officer), as of the end of the period covered by this report, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act). Our management, including our Chief Executive Officer, assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in Internal Control – 2013 Integrated Framework. Based on that assessment, our management concluded that our internal control over financial reporting was effective as of December 31, 2021.

Changes in internal control over financial reporting.

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2022 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2021.

Item 11. Executive Compensation.

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2022 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2021.

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

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2022 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2021.

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

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2022 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2021.

Item 14. Principal Accountant Fees and Services.

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2022 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2021.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this report:

1. Financial Statements

Information in response to this Item is included in Part II, Item 8 of this Annual Report on Form 10-K.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits:

Exhibit Index

Exhibit Number	Description	Form	File No.	Exhibit Filing Date	Exhibit No.	Filed/Furnished Herewith
3.1	Restated Certificate of Incorporation of Graybug Vision, Inc.	10-Q	001-39538	11/12/2020	3.1	
3.2	Restated Bylaws of Graybug Vision, Inc.	10-Q	001-39538	11/12/2020	3.2	
4.1	Form of Common Stock Certificate.	S-1/A	333-248611	9/21/2020	4.1	
4.2	Amended and Restated Investors' Rights Agreement, dated July 31, 2019, by and among the Registrant and certain of its stockholders.	S-1	333-248611	9/4/2020	4.2	
4.3	Warrant to Purchase Common Stock, dated December 11, 2019, by and between the Registrant and SG DAN Equity Holdings, LLC.	S-1	333-248611	9/4/2020	4.3	
4.4	Description of Common Stock Registered Under Section 12 of the Securities Exchange Act of 1934.	10-K	001-39538	3/5/2021	4.4	
10.1*	Form of Indemnification Agreement.	S-1	333-248611	9/4/2020	10.1	
10.2*	2020 Equity Incentive Plan and forms of award agreements.	S-1/A	333-248611	9/21/2020	10.3	
10.3*	2020 Employee Stock Purchase Plan and forms of award agreements.	S-1/A	333-248611	9/21/2020	10.4	
10.4*	2015 Stock Incentive Plan, as amended, and forms of award agreements thereunder.	S-1	333-248611	9/4/2020	10.2	
10.5*	Employment Agreement, effective as of February 1, 2019, by and between the Registrant and Frederic Guerard.	S-1	333-248611	9/4/2020	10.6	
10.6*	Offer Letter, effective as of May 7, 2020, by and between the Registrant and Parisa Zamiri.	S-1	333-248611	9/4/2020	10.8	
10.7*	Offer Letter, effective as of September 4, 2020, by and between the Registrant and Robert S. Breuil.	S-1	333-248611	9/4/2020	10.9	
10.8*	Change in Control and Severance Policy.	S-1	333-248611	9/4/2020	10.11	
10.9	Lease, dated October 8, 2019, by and between the Registrant and Ventas Beckley, LLC, as amended by that certain First Amendment to Lease, dated December 5, 2019, and that certain Second Amendment to Lease, dated June 26, 2020.	S-1	333-248611	9/4/2020	10.13	
10.10†	Exclusive License Agreement, dated June 23, 2011, by and between the Registrant and Johns Hopkins University School of Medicine, as amended.	S-1	333-248611	9/4/2020	10.14	
10.11†	Settlement and License Agreement, dated October 24, 2014, by and among the Registrant, Johns Hopkins University School of Medicine, and Kala Pharmaceuticals, Inc.	S-1	333-248611	9/4/2020	10.15	
10.12	Letter Agreement, dated July 31, 2019, by and between the Registrant and AffaMed Project Limited.	S-1	333-248611	9/4/2020	10.16	
23.1	Consent of Independent Registered Public Accounting Firm.					X

Exhibit Number	Description	Form	File No.	Exhibit Filing Date	Exhibit No.	Filed/Furnished Herewith
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.					X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
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.					X
32.2**	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	Inline XBRL Instance Document.					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)					X

† Registrant has omitted portions of the exhibit as permitted under Item 601(b)(10) of Regulation S-K.
* Indicates a management contract or compensatory plan or arrangement.
** This certification is deemed not filed for purposes of section 18 of the Exchange Act or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of the Exchange Act.

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.

GRAYBUG VISION, INC.

Date: March 10, 2022

By: /s/ Frederic Guerard

Frederic Guerard, Pharm.D.
Chief Executive Officer

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

Signature	Title	Date
/s/ Frederic Guerard Frederic Guerard, Pharm.D.	Chief Executive Officer (Principal Executive Officer)	March 10, 2022
/s/ Robert S. Breuil Robert S. Breuil	Chief Financial Officer (Principal Accounting and Financial Officer)	March 10, 2022
/s/ Christina Ackermann Christina Ackermann	Director	March 10, 2022
/s/ Eric Bjerkholt Eric Bjerkholt	Director	March 10, 2022
/s/ Gerald Cagle Gerald Cagle, Ph.D.	Director	March 10, 2022
/s/ Julie Eastland Julie Eastland	Director	March 10, 2022
/s/ Christy Shaffer Christy Shaffer, Ph.D.	Chairperson, Director	March 10, 2022

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-249033) pertaining to the 2020 Equity Incentive Plan, 2020 Employee Stock Purchase Plan and 2015 Stock Incentive Plan of Graybug Vision, Inc.,

(2) Registration Statement (Form S-8 No. 333-254522) pertaining to the 2020 Equity Incentive Plan of Graybug Vision, Inc.

of our report dated March 10, 2022, with respect to the financial statements of Graybug Vision, Inc. included in this Annual Report (Form 10-K) of Graybug Vision, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Redwood City, California
March 10, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Frederic Guerard, certify that:

1. I have reviewed this Form 10-K of Graybug Vision, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 10, 2022

By: /s/ Frederic Guerard

Frederic Guerard, Pharm.D.
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Robert S. Breuil, certify that:

1. I have reviewed this Form 10-K of Graybug Vision, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 10, 2022

By: /s/ Robert S. Breuil

Robert S. Breuil
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Graybug Vision, Inc. (the "Company") on Form 10-K for the period ending December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 10, 2022

By: /s/ Frederic Guerard

Frederic Guerard, Pharm.D.
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Graybug Vision, Inc. (the "Company") on Form 10-K for the period ending December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 10, 2022

By: /s/ Robert S. Breuil

Robert S. Breuil
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)