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 April 30, 2020
OR

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

Commission File Number 001-36830

KalVista Pharmaceuticals, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**20-0915291**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
55 Cambridge Parkway Suite 901 East Cambridge, Massachusetts	**02142**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (857) 999-0075

Title of Each Class	Trading Symbol	Name of Exchange on Which Registered
Common Stock, $0.001 par value per share	**KALV**	**The Nasdaq Stock Market LLC**

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

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

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 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, smaller reporting company, or an emerging growth company. See the definition of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

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

The aggregate market value of common stock held by non-affiliates of the registrant calculated based on the closing price of $10.60 of the registrant's common stock as reported on The NASDAQ Global Market on October 31, 2019, the last business day of the registrant's most recently completed second quarter, was $164,278,175.

The number of shares of Registrant's Common Stock outstanding as of June 24, 2020 was 17,847,224.

DOCUMENTS INCORPORATED BY REFERENCE

Information required in responses to Part III of Form 10-K is hereby incorporated by reference to portions of the Registrant's Proxy Statement for the Annual Meeting of Stockholders to be held in 2020. The Proxy Statement will be filed by the Registrant with the Securities and Exchange Commission no later than 120 days after the end of the Registrant's fiscal year ended April 30, 2020.

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PART I

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical fact are "forward-looking statements" for purposes of this Annual Report on Form 10-K. These forward-looking statements may include, but are not limited to, statements regarding our current and future nonclinical, preclinical and clinical development activities, anticipated impacts of the COVID-19 pandemic, our future results of operations and financial position, business strategy, market size, potential growth opportunities, the efficacy and safety profile of our product candidates, expected timing and results of our clinical trials, and receipt and timing of potential regulatory designations, approval and commercialization of product candidates. In some cases, forward-looking statements may be identified by terminology such as "believe," "may," "will," "should," "predict," "goal," "strategy," "potentially," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect," "seek" and similar expressions and variations thereof. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in the "Risk Factors" section and elsewhere in this Annual Report on Form 10-K. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this report to conform these statements to actual results or to changes in our expectations, except as required by law.

As used in this Annual Report on Form 10-K, the terms "KalVista," "the Company," "we," "us," and "our" refer to KalVista Pharmaceuticals, Inc. and, where appropriate, its consolidated subsidiaries, unless the context indicates otherwise.

Item 1. Business.

Overview

We are a clinical stage pharmaceutical company focused on the discovery, development and commercialization of small molecule protease inhibitors for diseases with significant unmet need. Our first product candidates are inhibitors of plasma kallikrein being developed for two indications: hereditary angioedema ("HAE") and diabetic macular edema ("DME"). We apply our insights into the chemistry of proteases and, with our current programs, the biology of the plasma kallikrein system, to develop small molecule oral inhibitors with high selectivity, potency and bioavailability that we believe will make them successful treatments for disease. We have created a structurally diverse portfolio of oral plasma kallikrein inhibitors and advanced multiple drug candidates into clinical trials in order to create what we believe will be best-in-class oral therapies for these two indications.

Our primary focus is currently on developing oral plasma kallikrein inhibitors for HAE, for which we have two drug program candidates in clinical trials. HAE is a rare and potentially life-threatening condition with symptoms that include episodes of debilitating and often painful swelling in the skin, gastrointestinal tract or airways. Despite having multiple therapies approved, we believe HAE patients are in need of alternatives that better meet their objectives for quality of life and ease of disease control. Currently marketed therapies are all administered by injection, which patients can find challenging despite their efficacy because they can be painful, time consuming

to deliver and difficult to store. We anticipate that there will be strong interest in safe and effective, orally delivered, small molecule treatments, and our strategy is to develop oral drug candidates for both on-demand and prophylactic use with the goal of providing patients with a complete set of oral options to treat their disease.

Our strategy is based upon extensive patient, physician and payer research to identify the key needs in the market. According to our analysis, oral therapy remains the highest unmet need, with 93% of patients surveyed by KalVista expressing a willingness to switch to oral therapy for both on-demand and prophylactic use. Importantly however, the survey data shows that patients are not prepared to accept significantly reduced efficacy or safety with a switch to oral therapy, and so we place a high degree of emphasis on advancing program candidates that we believe can compare favorably to existing approved therapies in both those dimensions.

We have advanced the first of our candidates, KVD900, into later stage clinical development as potential on-demand therapy for HAE attacks, with a Phase 2 clinical trial expected to complete in the second half of 2020. This trial is being conducted in approximately 20 sites in Europe and the U.S., and is intended to complete 50 HAE patients in a placebo-controlled, crossover study designed to evaluate the safety and efficacy of KVD900 in treatment of HAE attacks. We believe that KVD900 displays an attractive profile for on-demand therapy, with a rapid uptake of the drug to very high blood levels, and with no concerning safety signals observed to date in any clinical trials, including no treatment-related gastrointestinal adverse events. The 600mg dose used in our ongoing Phase 2 trial yields maximal concentrations more than 100 times the level we believe is required for clinical efficacy, with effective concentrations reached in as little as 10 minutes after dosing. We believe this pharmacokinetic profile compares favorably to the existing injected therapies, which show no faster absorption and generally much lower peak levels of drug concentration. Our pharmacodynamic analysis of samples collected from volunteers following administration of KVD900 shows high levels of plasma kallikrein inhibition for as long as 12 hours after a single dose, and near complete inhibition of plasma kallikrein for as long as six hours. This data, combined with the level of inhibition of plasma kallikrein activity by exogenously added KVD900 in HAE patient plasma tested in a separate assay, leads us to believe that a single dose of KVD900 may inhibit plasma kallikrein in patients experiencing an acute HAE attack sufficiently to provide a therapeutic alternative that is superior to current treatments. KVD900 has received Fast Track designation from the U.S. Food and Drug Administration ("FDA").

In early 2020, we announced the selection of KVD824 as our next oral program to be developed, in this case for prophylactic treatment of HAE. Based on a first-in-human study we conducted in 2019, we believe that KVD824 can achieve the profile necessary for a twice-daily treatment for prevention of HAE attacks, which also remains an area of high unmet need. We are currently conducting additional clinical studies intended to optimize the formulation and exposure profile of KVD824, following which we plan to commence a Phase 2 clinical trial in the second half of 2020 to evaluate the safety and efficacy of KVD824 as a potential oral prophylactic treatment for HAE.

KVD824 was chosen as our next oral HAE candidate because it offers the opportunity to tailor an exposure profile which delivers the strong and sustained inhibition of plasma kallikrein required for a successful prophylactic treatment. KVD824 is a potent inhibitor of plasma kallikrein in vitro (<10nM) and in whole human plasma assays (<80nM). The first-in-human study of KVD824 showed very high exposures and essentially complete suppression of plasma kallikrein activity with good tolerability following single and multiple dosing. Our initial development plan for KVD824 is focused on twice-daily dosing to ensure trough concentrations are maintained well above the target required to maximize efficacy. Our patient surveys indicate this schedule causes no reduction in attractiveness of oral therapy, with 88% of patients saying they would accept twice-daily dosing.

The second indication we are pursuing is DME. DME is the leading cause of moderate vision loss in most developed countries and diabetes, the underlying cause of DME, is the leading cause of blindness among American adults according to the Center for Disease Control and Prevention. Our DME program is initially focused on the development of an intravitreally administered small molecule plasma kallikrein inhibitor, KVD001. We believe intravitreal plasma kallikrein inhibitors may be an effective alternative therapy to vascular endothelial growth factor ("VEGF") inhibitors and further improve visual acuity and decrease macular thickening. In 2019 we completed a Phase 2 clinical trial of KVD001 in patients with DME and we also intend to develop an oral plasma kallikrein inhibitor to treat DME. An oral treatment may provide the opportunity to reduce treatment burden, treat patients earlier in disease progression, and provide a convenient and readily accessible treatment option for DME.

The Phase 2 clinical trial of KVD001 evaluated the safety and efficacy of two dose levels (3μg and 6μg) of KVD001 compared to a sham control in 129 DME patients who had previously been treated with anti-VEGF therapy, and still had significant edema and reduced visual acuity. The study was conducted at 38 sites in the United States, and consisted of four intravitreal injections or sham administered over three months with a three month follow up period. The primary efficacy endpoint of change in best corrected visual acuity ("BCVA") at 16 weeks compared to sham was not met. The 6μg dose showed a difference of +2.6 letters versus sham, which was not statistically significant (p=0.223), and the 3μg dose showed a difference of +1.5 letters (p=0.465). No significant differences were observed in the secondary endpoints of central subfield thickness or the diabetic retinopathy severity scale. KVD001 was generally safe and well tolerated with no drug-related serious adverse events. In the overall study population, KVD001 demonstrated a protection against vision loss. In the sham treated group, 54.5% of patients experienced a reduction in vision compared to 32.5% in the 6μg dose (p=0.042). The study also included a pre-specified subgroup analysis investigating the impact of baseline visual acuity on response. After excluding those patients with the most severe vision loss (visual acuity of <55 letters at baseline), the remaining 70% of the total patient population showed a difference in BCVA compared to sham of 4.9 letters (p=0.056) at the 6μg dose. As many as 40% of DME patients may not respond adequately to VEGF inhibitor treatment, and we believe that KVD001 may offer these patients protection against further vision loss.

In October 2017, our wholly-owned, U.K. based subsidiary KalVista Pharmaceuticals Limited and Merck Sharp & Dohme Corp. ("Merck") entered into an option agreement (the "Option Agreement") under which we granted to Merck an option to acquire KVD001 through a period following completion of a Phase 2 clinical trial. We also granted to Merck a similar option to acquire investigational orally delivered molecules for DME (the "Oral DME Compounds") through a period following the completion of a Phase 2 clinical trial. Under the terms of the Option Agreement, Merck paid to us a non-refundable upfront fee of $37.0 million in November 2017. Merck also invested approximately $9.1 million in a separate private placement transaction of common shares that closed concurrently with the Option Agreement. In February 2020, Merck notified us that those options would not be exercised. As a result, we have retained all the rights and intellectual property that were subject to the Option Agreement, and Merck has no further rights or obligations to us, and we have no obligations to Merck. We continue to believe that the results of the KVD001 Phase 2 study suggest a patient population in which plasma kallikrein inhibition may yield vision benefits, and we intend to explore further development opportunities for this and oral DME programs over time.

Strategy

Key elements of our strategy include:

- *Apply our deep scientific expertise in the area of serine proteases to develop novel oral therapies for indications with high unmet need.* Our core scientific team has decades of experience working on protease inhibitors and developing compounds with high potency, selectivity and bioavailability. We have assembled a team of chemists and biologists who have demonstrated the ability to design and formulate multiple drug candidate programs from a broad variety of chemical classes, as indicated by our extensive intellectual property portfolio. Our initial focus is specifically on development of plasma kallikrein inhibitors for HAE and DME; however, we believe our scientific capabilities also can be applied to other proteases to develop therapies for diseases with high unmet need and orphan indications.
- *Advance multiple HAE product candidates into clinical development.* We intend to develop best-in-class oral therapies for HAE and, to accomplish that goal, we plan to develop drug candidates for both on-demand and prophylactic use to provide patients with a complete set of oral options to treat their disease. KVD900 has been chosen to advance to later stage development as an on-demand therapy for acute HAE attacks, and a Phase 2 clinical trial in HAE patients is expected to complete in the second half of 2020. KVD824 was selected in 2020 as our next oral candidate and we plan to commence a Phase 2 clinical trial to evaluate KVD824's potential as an oral prophylactic treatment for HAE in the second half of 2020.

- *Continue to advance our DME programs, including developing an oral therapy.* KVD001, our first product candidate to treat DME, completed a Phase 2 clinical trial in the second half of 2019. We also intend to develop an oral therapy for this indication, which we believe could dramatically improve the standard of care for patients, since all current therapies are delivered by injection into the eye.
- *Grow our capabilities internally as well as through strategic partnerships.* We intend to retain ownership and control of our pipeline programs to key milestones. For certain indications, such as HAE, that can be addressed by a focused organization, we intend to keep all program rights and develop internal sales and marketing capabilities. For programs that address larger markets or require greater infrastructure or resources, we may seek a partner that can provide those capabilities. Decisions on whether, and when, to engage in partnerships or collaborations will be based upon our evaluations of the relative risks and rewards of those collaborations at each point in the development cycle.

Plasma Kallikrein in HAE and DME

Plasma kallikrein is a serine protease enzyme that is a key early mediator of inflammation and edema. The body modulates the inflammatory effects of plasma kallikrein through a circulating inhibitor protein called C1-esterase inhibitor ("C1-INH"). Most patients with HAE have genetic mutations that lead to C1-INH deficiency, which results in an inability to control activated plasma kallikrein in affected tissues. This excessive activation leads to inflammation, edema, and pain.

Published laboratory work has shown that the vitreous fluid of the eye is also a site of increased plasma kallikrein in DME. In diabetic patients, the retina is one of a few tissues in which edema develops. Under normal circumstances the eye is protected from the diffusion of plasma proteins by an effective blood vessel barrier. In diabetes this barrier becomes less effective and allows plasma proteins such as plasma kallikrein to enter the retina and vitreous. While C1-INH can also to enter by the same route, animal models of DME have shown that the concentration of C1-INH in the vitreous fluid is insufficient to fully suppress the effects of plasma kallikrein on retinal edema. Over time, this edema leads to retinal damage that causes blindness.

Hereditary Angioedema

Disease Overview

HAE is a rare and potentially life-threatening genetic condition that occurs in about 1 in 10,000 to 1 in 50,000 people, according to published information from an HAE patient advocacy group. Excessive plasma kallikrein activation that is not sufficiently controlled by C1-INH leads to HAE attacks, which can vary with regard to the affected tissue or organ and severity. HAE attacks include episodes of intense swelling usually in the skin, gastrointestinal tract or airways. They often lead to temporary disfiguration of various body parts including the hands, feet, face, body trunk, and genitals. In addition, patients often have bouts of excruciating abdominal pain, nausea and vomiting that is caused by swelling in the intestinal wall. Airway swelling is particularly dangerous and can lead to death by asphyxiation.

Attacks can occur spontaneously although they often are associated with anxiety, stress, minor trauma, surgery, or illnesses. Commonly patients are alerted to an impending attack by prodromal symptoms which include rash, fatigue, and muscle aches. Trauma to the oral cavity caused by dental procedures makes HAE patients particularly vulnerable to airway attacks. The frequency of HAE attacks is highly variable, with some patients having attacks several times per week and others very infrequently. Population studies have shown that the median number of attacks per month for patients is approximately one, and approximately 90% of patients have two or fewer attacks per month. Although life-threatening airway swelling is rare, at least half of HAE patients have experienced at least one such attack and airway attacks remain a major cause of mortality in HAE patients. The severity of attacks is unpredictable and not related to their underlying frequency. A patient with only one attack per year can nevertheless be at risk of suffering a laryngeal attack.

HAE is an autosomal dominant disease, meaning that a defect in only one copy of the gene leads to symptoms and that it occurs at similar rates in both males and females. The most common cause of HAE is a defect or mutation in the gene responsible for the production of C1-INH. While HAE can result from the inheritance of a defective gene from a parent, a number of cases also arise from spontaneous mutations. Patients with C1-INH-related disease are classified as Type 1 or Type 2; Type 1 is the most common form and results in low levels of circulating C1-INH and Type 2 results in production of a low function protein. An additional form of HAE, sometimes called normal C1-INH HAE, can occur in patients with normal levels of C1-INH for a variety of reasons including mutations in genes for Factor 12, plasminogen or angiopoetin. Moreover, bradykinin-induced acute attacks of angioedema can occur idiopathically in individuals for which a hereditary cause has not yet been identified. Excessive formation of bradykinin can also be caused by increased circulation of estrogens, reduced elimination of bradykinin, or through use of drugs such as ACE inhibitors.

C1-INH is a natural plasma-borne protein that is an inhibitor of multiple serine proteases in both the complement and kallikrein kinin systems. C1-INH is the predominant physiological inhibitor of plasma kallikrein, and thereby suppresses the generation of bradykinin, a potent hormone produced by plasma kallikrein, that activates its receptors on blood vessels to increase vascular leakage. Uncontrolled plasma kallikrein activity leads to the edema that is the hallmark of HAE. Selective plasma kallikrein inhibitors and a bradykinin receptor antagonist are approved therapies for HAE. As such, plasma kallikrein is a clinically validated target for HAE and previous studies have demonstrated that plasma kallikrein inhibition can both treat and prevent HAE attacks.

Current Treatments and Market Opportunities

There are a number of marketed and development stage therapeutics for HAE which provide evidence that inhibition of plasma kallikrein activity will give therapeutic benefit in HAE. Takyzyro® is a monoclonal antibody against plasma kallikrein indicated for prophylaxis to prevent attacks of HAE. The prescribing information recommends subcutaneous administration every two weeks, though dosing at more extended intervals may be considered in some patients. Ecallantide (Kalbitor®) is a small protein inhibitor of plasma kallikrein that is approved for treatment of acute attacks of HAE. While effective, ecallantide has been associated with cases of anaphylaxis and its approval by the FDA includes a black box warning limiting its administration to healthcare professionals. Other therapies provide C1-INH replacement to control plasma kallikrein levels. Marketed C1-INH replacement therapies include Cinryze® and Haegarda® for prophylaxis, and Berinert® for treatment of acute attacks, all of which are purified from human plasma, and Ruconest® which is a recombinant product also for treatment of acute attacks. Icatibant (Firazyr®) is a synthetic peptide-based antagonist that blocks the activity of bradykinin and is indicated for treatment of acute attacks. All of these products are administered by injection, which is typically less convenient for patients and has the potential to reduce compliance. As a result of the lifelong nature of HAE and the challenges related to taking many of the injected therapies, patient surveys consistently indicate an overwhelming desire of patients for an oral therapy. We believe that a safe and effective oral agent has the potential to transform treatment for this disease. We also believe that opportunities exist for both acute and prophylactic treatments, and we intend to develop drug candidates for both on-demand and prophylactic use, with the goal of providing patients with a complete set of oral options to treat their disease.

We believe a further future market opportunity may exist in treatment of normal C1-INH HAE. Estimates of the size of this patient population vary widely, but we believe that the nature of normal C1-INH HAE disease may make prophylaxis less attractive for these patients than a safe and rapidly effective on-demand plasma kallikrein inhibitor therapy.

Our Portfolio of HAE Programs

Our strategy is to evaluate and develop multiple oral molecules in pursuit of best-in-class therapies for HAE patients, with an initial focus on treatment of Type 1 and Type 2 HAE. We have promoted multiple molecules into clinical testing and are pursuing additional candidates in order to expand the universe of properties and increase the likelihood of delivery of one or more best-in-class treatments for HAE. The first of these product candidates being evaluated in later stage clinical trials is KVD900. KVD900 is in a Phase 2 clinical trial as a potential on-demand treatment for HAE attacks that is expected to complete in the second half of 2020. Our second oral treatment in development for HAE is KVD824. We plan to commence a Phase 2 clinical trial in the second half of 2020 intended to evaluate KVD824 as a potential oral prophylactic treatment for HAE.

KVD900

The first clinical study of KVD900 was a multi-part trial consisting of a single ascending dose phase, a formulation cross-over phase, and investigation of food effect in 84 healthy, male volunteers. Doses up to 600 mg were tested in this study using both capsule and tablet formulation, with the tablet as the intended formulation for future development. Data from the single ascending dose phase of the study showed that KVD900 tablets were rapidly absorbed into the bloodstream and achieved blood levels that we believe are sufficient for efficacy within as little as 10 minutes at the higher dose levels, and essentially complete inhibition of plasma kallikrein was observed within 30 minutes. Food effect studies showed little impact of fed state on the pharmacodynamic profile of KVD900 tablets, delivering 95% inhibition within 30 minutes.

There were no severe adverse events ("SAE") reported. On active treatment, 22 of the 23 reported adverse events ("AE") were mild; a moderate AE of headache was reported in the 10 mg dose group and considered unrelated to treatment. There was one gastrointestinal AE reported during the study which occurred three days post dosing and was considered unrelated to treatment. There were no clinically significant changes in vital signs, electrocardiogram ("ECG") or safety laboratory findings. Single doses of KVD900 up to 600 mg were generally well-tolerated in this study.

Evidence from studies using therapies approved for the treatment of acute HAE attacks shows that earlier treatment has a powerful impact on the efficacy outcomes. Despite clear evidence that early treatment markedly reduces attack duration, treatment is often delayed. In one outcome study of 207 HAE attacks, attack duration was 2.75-fold shorter when treatment was administered within 1 hour of attack onset (6.1 hours versus 16.8 hours (p<0.001)), yet treatment was administered more than 1 hour after attack onset in nearly 60% of attacks, and for 30% of attacks treatment was administered more than five hours after attack onset. We believe this delay in administration is due to many factors including the inconvenience of preparation and administration as well as the discomfort of injectable therapies. An oral therapy has the potential to overcome these and lower the barrier for treatment for patients. The combination of the rapid uptake of KVD900 to very high blood levels and the likelihood of earlier dosing by patients, could lead to much better disease management and prevention of attacks reaching the critical stage of significant swelling and discomfort. We therefore believe that a safe, oral on-demand treatment has the potential to become a preferred alternative for patients currently using injectable treatments, including both acute and prophylactic therapies.

Based upon the results of the Phase 1 study, we are currently dosing KVD900 in a Phase 2 clinical trial intended to evaluate KVD900 as an on-demand treatment for HAE attacks. This trial is investigating the safety and efficacy of KVD900 in at least 50 Type 1 and Type 2 HAE patients, conducted at approximately 20 sites in Europe and the U.S. During the first part of this two-part study, patients receive a single 600 mg dose of KVD900 while not having an attack to explore pharmacokinetic and pharmacodynamic profiles. All patients then enter part two of the study, which is a randomized, blinded, crossover investigation of the efficacy of KVD900 versus placebo. Each patient treats two attacks with trial medication, one with KVD900 and one with placebo in a randomized, blinded sequence. Following randomization, patients are given the first treatment of the sequence to take home. At the onset of an attack, patients call their doctor to confirm the attack has started and take their treatment within one hour of the recorded onset. Patients then return to the clinic to receive the alternative treatment and proceed to treat a second attack in an identical manner. Patients have access to their normal, acute treatment as required. The primary endpoint is time to use of standard of care and the secondary endpoints are comprised of several different symptom severity scores. Data is expected from this trial in the second half of 2020.

In the first calendar quarter of 2020 we completed a multiple dose study of KVD900 that was designed to explore the safety and pharmacokinetics of repeat dosing over differing timeframes. A total of 42 healthy male and female subjects were included in the study, consisting of 30 active and 12 placebo. Study subjects received a total dose of 1800mg KVD900 given as 3x600mg doses at intervals of 8 hours (6 active, 2 placebo), 4 hours (6 active, 2 placebo) or 2 hours (18 active and 8 placebo).

The study showed that dosing every two hours achieved maximum concentrations of KVD900 approximately three times the maximum concentration of a single 600mg dose. All reported AEs were mild and resolved without intervention. The incidence of AEs was similar between KVD900-treated and placebo-treated cohorts. The protocol also included continuous cardiac monitoring of subjects. There was no clinically significant effect of KVD900 treatment on any ECG parameters.

Based upon this study, we believe there are no concerns about the potential for multiple dosing of KVD900, including on short intervals.

KVD824

In 2019, we announced the initiation of a first-in-human study for our next clinical stage oral plasma kallikrein inhibitor, KVD824. This study included single ascending dose, multiple ascending dose, and food effect cohorts, at dose levels ranging from 10 mg to 1,280 mg. The single ascending dose part of the study demonstrated dose-dependent increases in exposure, achieving mean C_{max} concentrations of over 9,000 ng/ml at the highest dose studied. The multiple ascending dose part of the study was conducted at doses from 80 mg up to 640 mg twice per day for 5 days. Exposures were consistent between days 1 and 5 at all dose levels. Examination of the blinded safety data across all cohorts, both single and multiple dose, revealed no significant changes in vital signs, ECG or safety laboratory results, there were no dose-limiting tolerability or safety signals reported and all subjects completed the study.

Based on preclinical and clinical work conducted, we believe that KVD824 can achieve the profile necessary for a twice-daily treatment for prevention of HAE attacks, which also remains an area of high unmet need. We are currently undertaking additional clinical studies to optimize the formulation and dosing profile of KVD824. Following that activity, we plan to commence a Phase 2 clinical trial intended to evaluate KVD824 as a potential oral prophylactic treatment for HAE in the second half of 2020.

Diabetic Macular Edema

Disease Overview

DME occurs as a complication of diabetes and is caused by the breakdown of the endothelial barrier function in the retina, resulting in the accumulation of fluid in the macula. This leads to edematous thickening of the macula region of the retina and loss of visual acuity, potentially leading to blindness. DME is a major complication associated with diabetes, affecting an estimated 26% of type 1 diabetic patients after 14 years of the disease, and an estimated 29% over their lifetime; 17% of type 1 diabetic patients were estimated to develop clinically significant macular edema over their lifetime. Approximately 900,000 patients in the United States have active DME and are at serious risk of vision loss, according to a study published in 2015.

The current standard of care for DME in the United States is therapy directed against VEGF, a hypoxia-induced protein that stimulates the growth of blood vessels in the retina. FDA approved anti-VEGF therapies for DME are ranibizumab (Lucentis®) and aflibercept (Eylea®). Both of these products are administered via intravitreal injection at roughly monthly intervals. In addition to treatment by these two products, a large fraction of patients is treated with bevacizumab (Avastin®), another therapy that works through the same mechanism of binding to VEGF but has not been approved for ophthalmic use. Bevacizumab is priced based on its application in oncology and off-label use by retinal specialists typically results in treatment at a fraction of the cost seen with both ranibizumab and aflibercept. Patients are also treated with laser therapy in some circumstances.

A number of other drug therapies are used to treat DME, including corticosteroid anti-inflammatories such as triamcinolone acetonide, fluocinolone, and dexamethasone. These drugs also are administered via intravitreal injection. Sustained release versions of fluocinolone (Illuvien®) and dexamethasone (Ozurdex®) have been approved for use in DME, substantially reducing the number of injections required to obtain and maintain clinical responses. These novel corticosteroid formulations led to 15-letter improvements in visual acuity in approximately 20-30% of patients. Corticosteroid treatment, however, is associated with a dramatic increase in cataract formation and a rise in intraocular pressure, reducing the attractiveness of these agents as potential therapies in many patients.

In a recent large, multi-center clinical trial in DME patients, anti-VEGF therapy led to approximately 20% of patients improving their visual acuity by 15 letters or more after a median of 9 or 10 intravitreal injections, leaving a significant portion of the patients with inadequate control of their disease. Further, in one study conducted for an approved anti-VEGF, 40% of patients displayed minimal improvement in visual acuity following anti-VEGF therapy after months of treatment.

Research into the biology underlying DME by our scientific team has identified plasma kallikrein as a potential novel target for this indication. KalVista scientists were the first to identify increased concentrations of plasma kallikrein in vitreous fluid samples obtained from individuals with diabetic retinopathy and DME and have pioneered the development of plasma kallikrein inhibitors for the treatment of this disease. Our group has established preclinical models to investigate the role of plasma kallikrein in both VEGF-independent and VEGF-mediated DME as well as for underlying pathologies associated with diabetic retinopathy. We have used this in-depth knowledge of the plasma kallikrein system, diabetic retinopathy, and clinical ophthalmology to evaluate the effects of orally available plasma kallikrein inhibitors for the treatment of DME. Using a pharmacology platform, originally developed and validated using plasma kallikrein knockout mice at the Joslin Diabetes Center and Harvard Medical School, we have screened and characterized the pharmacodynamic effects of KalVista's oral plasma kallikrein inhibitors. We were the first to demonstrate that plasma kallikrein inhibition and gene knockout are protective against VEGF-induced retinal edema.

Using subcutaneously implanted osmotic pumps we have quantified the dose-dependent pharmacodynamic effect of plasma kallikrein inhibitors on VEGF-induced retinal edema and have correlated these effects with both plasma and retinal drug concentrations. Moreover, using gavage we have characterized the pharmacokinetic and pharmacodynamics effects of orally administered plasma kallikrein inhibitors on retinal edema. These models and protocols have enabled detailed characterization and comparison of the effects of multiple oral plasma kallikrein inhibitors on retinal edema.

KVD001

Our first potential DME therapy is KVD001. KVD001 is a potent inhibitor of human plasma kallikrein with a Ki of approximately 10 nM and a high degree of selectivity against a broad range of other proteases. We have developed KVD001 for intravitreal injection because we believe that trials using this delivery modality will provide a relatively early and direct proof-of-concept since the molecule is delivered directly to the site of edema. Since other products such as anti-VEGF therapies are also delivered intravitreally, we believe this will be accepted by both physicians and patients and will not lead to any competitive disadvantages. Another inherent advantage of intravitreal administration is that there is very limited systemic exposure, thus reducing potential systemic safety concerns.

In December 2019 we announced data from a Phase 2 trial for KVD001. This study evaluated the safety and efficacy of two dose levels (3µg and 6µg) of KVD001 compared to a sham control in 129 DME patients who had previously been treated with anti-VEGF therapy, and still had significant edema and reduced visual acuity. The study was conducted at 38 sites in the United States and consisted of four intravitreal injections or sham administered over three months with a three month follow up period. The primary efficacy endpoint of change in best corrected visual acuity ("BCVA") at 16 weeks compared to sham was not met. The 6µg dose showed a difference of +2.6 letters versus sham, which was not statistically significant (p=0.223), and the 3µg dose showed a difference of +1.5 letters (p=0.465). No significant differences were observed in the secondary endpoints of central subfield thickness or the diabetic retinopathy severity scale. KVD001 was generally safe and well tolerated with no drug-related serious adverse events. In the overall study population, KVD001 demonstrated a protection against vision loss. In the sham treated group 54.5% of patients experienced a reduction in vision compared to 32.5% in the 6µg dose (p=0.042). The study also included a pre-specified subgroup analysis investigating the impact of baseline visual acuity on response. After excluding those patients with the most severe vision loss (visual acuity of <55 letters at baseline), the remaining 70% of the total patient population showed a difference in BCVA compared to sham of 4.9 letters (p=0.056) at the 6µg dose. As many as 40% of DME patients may not respond adequately to VEGF inhibitor treatment, and we believe that KVD001 may offer these patients protection against further vision loss.

The KVD001 program and our planned future oral DME programs were subject to an Option Agreement with Merck. Under the terms of the agreement, Merck had a defined period following receipt of a clinical data package including the results of the Phase 2 trial for KVD001, to determine whether to exercise its option to acquire KVD001 and to maintain its option on the oral DME programs. In February 2020, Merck notified us that those options would not be exercised. As a result, we have retained all the rights and intellectual property that were subject to the Option Agreement, and Merck has no further rights or obligations to us, and we have no obligations to Merck. We continue to believe that the results of the KVD001 Phase 2 study suggest a patient population in which plasma kallikrein inhibition may yield vision benefits, and we intend to explore further development opportunities for this and oral DME programs over time.

Potential for Oral DME Therapies

In parallel with the clinical development of our intravitreal product candidate KVD001, we intend to identify and advance plasma kallikrein inhibitors as oral therapies for DME. We believe that a safe and effective oral therapy has the potential to transform the treatment of DME which to date has been dominated by drug therapies that must be injected intravitreally. Future trials in DME with oral plasma kallikrein inhibitors may focus on the treatment of earlier stage disease, a stage at which intravitreal injections are not a desirable solution due to their inherently invasive nature and consequent risk of adverse reactions.

Additional Earlier Stage Programs

In addition to our clinical stage candidates, we are continually conducting preclinical development work on multiple additional drug candidates in order to achieve our goal of creating best-in-class oral plasma kallikrein inhibitors for HAE therapy, as well as for the treatment of DME. We currently have multiple additional compounds in preclinical testing. We routinely terminate earlier stage programs for any number of reasons that lead us to believe they will not achieve our objectives, and our medicinal chemistry team is constantly developing new potential candidates. We believe this capacity to develop large numbers of candidate compounds is key to success in drug development and represents a core strategic asset of the Company.

Competition

In treating HAE, we expect to face competition from several FDA-approved therapeutics, including Takhzyro and Cinryze, marketed by Takeda Pharmaceuticals Company Limited ("Takeda") in the United States and Europe for the prevention of angioedema attacks in adults and adolescents; Firazyr, marketed by Takeda in the United States, Europe and certain other geographic territories for the treatment of acute angioedema attacks in adult patients; Kalbitor, an injectable plasma kallikrein inhibitor marketed by Takeda for the resolution of acute attacks in adolescent and adult HAE patients; Berinert, marketed by CSL Behring for treatment of acute abdominal, facial or laryngeal attacks of HAE in adults and adolescents, and Haegarda, also marketed by CSL Behring, for prophylaxis; and Ruconest, marketed by Pharming Group for the treatment of acute angioedema attacks in adult patients. We are also aware of two companies that are engaged in the clinical development of oral plasma kallikrein inhibitors for use as prophylaxis in HAE patients, BioCryst Pharmaceuticals, Inc. and Attune Pharmaceuticals, Inc.

In treating DME, we expect to face competition from several FDA-approved therapeutics, including anti-VEGF therapies Lucentis, marketed by Roche Holding AG ("Roche") and Novartis International AG ("Novartis"), Eylea, marketed by Regeneron Pharmaceuticals ("Regeneron"), and off-label use of Avastin from Roche. We also face competition from various corticoid steroids including extended release formulations Iluvien, marketed by Alimera Sciences, Inc., and Ozurdex, marketed by Allergan plc. We further expect to compete with generic corticosteroids such as fluocinolone acetonide, and dexamethasone and we are aware of a number of other companies that have product candidates in early clinical trials, including Novartis, GlaxoSmithKline plc, Boehringer Ingelheim, Roche, Regeneron, Ohr Pharmaceutical, Inc., Aerpio Therapeutics, Oxurion NV and Allegro Ophthalmics, LLC. We also believe that Oxurion continues to develop an intravitreally delivered plasma kallikrein inhibitor for the treatment of DME.

Intellectual Property

Our success substantially depends on our ability to obtain and maintain patents and other forms of intellectual property rights for our product candidates, methods used to manufacture our product candidates and methods for treating patients using our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. As of April 30, 2020, we are the owner of thirteen U.S. patents expiring between 2023 and 2037, absent any extensions, as well as nine pending U.S. patent applications and four pending US provisional applications. Any patents issuing from the foregoing owned or licensed U.S. patent applications are expected to expire in between 2034 and 2038, absent any adjustments or extensions. As of April 30, 2020, we owned a total of 165 pending foreign applications and 257 patents in multiple jurisdictions. Any issued patents, or those issuing from these foreign patent applications, are expected to expire between 2023 and 2039, absent any adjustments or extensions. As of April 30, 2020, we also controlled twelve pending international applications that, if issued, are expected to expire between 2038 and 2040, absent any adjustments or extensions.

KVD001 is covered by U.S. patents, U.S. patent applications and U.S. provisional applications covering composition of matter, methods of treatment, solid form and clinical formulations. The anticipated expiration dates of these patents, patents arising from applications, or patents arising from applications claiming priority from provisional applications, range from 2032 to 2040, absent any adjustments or extensions. KVD001 is also covered by European patents with the European Patent Office ("EPO"), European patent applications, and an additional expected European patent application claiming priority from a U.S. provisional application, covering composition of matter, medical use, solid form and clinical formulations. The anticipated expiration dates of these European patents, or European patents arising from applications, range from 2032 to 2040 absent any extensions.

Our portfolio of oral plasma kallikrein inhibitors, including KVD900 and KVD824, is covered by U.S. patents, U.S. patent applications and U.S. provisional applications, and pending international applications covering composition of matter, methods of treatment, solid form and clinical formulations and the anticipated expiration dates of these patents, patents arising from those applications, or patents arising from applications claiming priority from provisional applications range from 2034 to 2040, absent any adjustments or extensions. Our portfolio of oral plasma kallikrein inhibitors, including KVD900 and KVD824, is also covered by EPO patents, European patent applications, and expected European patent applications claiming priority from U.S. provisional applications, covering composition of matter, medical use, solid form and clinical formulations. The anticipated expiration dates of these European patents, or European patents arising from applications, range from 2034 to 2040 absent any extensions.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country.

We also use other forms of protection, such as trademark, copyright and trade secret protection for our intellectual property, particularly where we do not believe patent protection is appropriate or obtainable. We require our employees, consultants, contractors and other advisors to execute nondisclosure and assignment of invention agreements upon commencement of their respective employment or engagement. In addition, we also require confidentiality or service agreements from third parties that receive confidential information or materials.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the United Kingdom and European Union, 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 the FDA. The Federal Food, Drug, and Cosmetic Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as clinical hold, FDA refusal to approve pending new drug applications ("NDA"), 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 United States typically involves preclinical laboratory and animal tests, the submission to the FDA of an Investigational New Drug ("IND") application, which must become effective before clinical testing may commence in the United States, 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 approval requirements prior to marketing a pharmaceutical product 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 manufacturing process, as well as toxicity studies in animals 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 and good manufacturing practice ("cGMP"). The results of preclinical testing are submitted to the FDA as part of an IND along with the information on product chemistry, manufacturing and controls, and a proposed clinical trial protocol. For the initial IND submission, a 30-day waiting period after the submission of the IND is required prior to the commencement of the clinical trial in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. For subsequent clinical trial protocols submitted to the IND, there is no mandated review time for FDA. Longer duration pre-clinical studies, for example animal tests of reproductive toxicology and carcinogenicity, if required, will be conducted and submitted to the IND throughout the development of the product until sufficient data is available to support submission of an NDA. Clinical trials involve the administration of the investigational 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 ("GCP"), an international standard designed to protect the rights, safety and well-being of trial subjects 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 the FDA as part of the IND.

The 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 trial protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board ("IRB"), for approval prior to the start of the clinical trial. 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 product is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on 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 dose, and to identify common adverse effects and safety risks. If a compound 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 the FDA to evaluate the overall benefit risk relationship of the drug and to provide adequate information for the labeling of the product. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial with other confirmatory evidence may

be sufficient in rare instances where the trial is a large multicenter trial demonstrating internal consistency and a statistically persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious or life-threatening outcome and confirmation of the result in a second trial would be practically or ethically impossible.

The manufacturer of an investigational drug in a Phase 2 or 3 clinical trial for a serious or life- threatening disease is required to make available, 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 the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of all preclinical and clinical data, including pharmacology and toxicology results, and the results of other testing and a compilation of data relating to the product's chemistry, manufacture and controls. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to an application user fee, and once approved, the NDA is also subject to annual product and establishment user fees. These fees are typically increased annually. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most such applications for standard review drug products are reviewed within ten months of the date the FDA files the NDA; most applications for priority review drugs are reviewed within six months of the date the FDA files the NDA. Priority review can be applied to a drug that the FDA determines has the potential to treat a serious or life-threatening condition and, if approved, would be a significant improvement in safety or effectiveness compared to available therapies. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

After the FDA evaluates the NDA and the compliance of manufacturing facilities with GMP, 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 the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction, the FDA will issue an approval letter. The FDA has committed to reviewing such additional data 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 the indication being supported. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy ("REMS") if it is considered that additional measures are needed to ensure that the benefits of the drug outweigh the potential risks. REMS can include the use of medication guides and communication plans for healthcare professionals, and elements to assure safe use ("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 product. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the product'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. 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 the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Foreign clinical studies to support an NDA

The FDA will accept as support for marketing approval of a product (NDA) well-designed, well-conducted, clinical studies conducted outside of the United States if the studies have been conducted in accordance with the exact same standards of GCP, as required in the United States, and the protocol was submitted to the IND. FDA may validate the data from the study through an onsite inspection, if necessary. Clinical studies conducted outside the United States are subject to the same rigorous regulatory controls as the United States (see "— Europe / rest of world government regulation" below).

A sponsor or applicant who wishes to rely on a non-IND foreign clinical study to support an IND must submit documentation to the FDA to demonstrate compliance with GCP. The FDA may also request to inspect a foreign clinical study site to confirm compliance.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a compound with the potential to treat a rare disease or condition, generally a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a product available in the United States for such disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested prior to submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the compound and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process of an NDA. The first NDA applicant to receive FDA approval for a drug product containing a compound that has FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that drug product for that orphan indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market a drug product containing the same active moiety for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. A product is clinically superior if it is safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a drug product containing a different active moiety for the same disease or condition, or the same drug product for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA user fee.

Fast Track Designation and Priority Review

The FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Fast track designation may be granted for products that are intended to treat a serious or life-threatening disease or condition for which there is no effective treatment and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. Any product submitted to FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review.

Priority review may be granted for products that are intended to treat a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. FDA will attempt to direct additional resources to the evaluation of an application designated for priority review in an effort to facilitate the review.

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 on the website www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, trial 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 clinical development programs as well as clinical trial design.

Pediatric information

Under the Pediatric Research Equity Act ("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 product is safe and effective. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any drug product for an indication for which orphan designation has been granted.

Post-approval requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, the 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 only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug product manufacture, packaging, and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Other U.S. healthcare laws and compliance requirements

In the United States, our 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 and Medicaid Services ("CMS"), other divisions of the U.S. Department of Health and Human Services (such as the Office of Inspector General), the U.S. Department of Justice ("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 ("HIPAA"), and similar state laws, each as amended, as applicable.

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 certain common activities from prosecution or other regulatory sanctions. 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. In addition, the statutory exceptions and regulatory safe harbors are subject to change.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, the "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 price 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 ("HITECH"), and its implementing regulations, imposes requirements 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 to CMS 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. Moreover, the Drug Supply Chain Security Act imposes new obligations on manufacturers of pharmaceutical products related to product tracking and tracing. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products.

In order to distribute products commercially, we must comply 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. Certain local jurisdictions also require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Sales and marketing activities are also potentially subject to federal and state consumer protection and unfair competition laws.

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including without limitation, significant civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, imprisonment, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Coverage, pricing and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third party payors provide coverage, and establish adequate reimbursement levels for such products. In the United States, third party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. The process for determining whether a third party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. 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 FDA-approved products for a particular indication. Third party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of its products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. 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 for the product. Adequate third party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on its investment in product development.

Different pricing and reimbursement schemes exist in other countries. In the EU, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. The downward pressure on health care costs has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on healthcare pricing. Coverage policies and third party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare reform

In March 2010, the President signed into law the ACA, which has the potential to substantially change healthcare financing and delivery by both governmental and private insurers, and significantly impacts the pharmaceutical and biotechnology industry. The ACA will impact existing government healthcare programs and will result in the development of new programs.

Among the ACA provisions of importance to the pharmaceutical industries, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs apportioned among these entities according to their market share in some government healthcare programs that began in 2011;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals beginning in 2014 and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected;
- requirements to report certain financial arrangements with physicians and teaching hospitals; and
- a requirement to annually report certain information regarding drug samples that manufacturers and distributors provide to physicians.

The current U.S. presidential administration and Congress have sought, and we expect will continue to seek, to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. Since January 2017, the current U.S. presidential administration has issued two executive orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. For example, on October 12, 2017, the current U.S. presidential administration issued an executive order that expands the use of association health plans and allows anyone to purchase short-term health plans that provide temporary, limited insurance. This executive order also calls for the halt of federal payments to health insurers for cost-sharing reductions previously available to lower-income Americans to afford coverage. There is still uncertainty with respect to the impact this executive order could have on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017, among other things, includes a provision repealing, 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". On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. While the Texas U.S. District Court Judge, as well as the current U.S. presidential administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA. Additionally, on January 22, 2018, the current U.S. presidential administration signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". There is still uncertainty with respect to the impact the current U.S. presidential administration and the Congress may have, if any, and any changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the ACA. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least $1.2 trillion for fiscal years 2012 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect beginning on April 1, 2013 and will stay in effect through 2025 unless additional Congressional action is taken. Additionally, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals and imaging centers. 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 products, if approved, and, accordingly, our financial operations.

There has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the current President's budget proposals for fiscal years 2019 and 2020 contain further drug price control measures that could be enacted during the budget process or in other future legislation. Further, the current President released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has already started soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical 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. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent the generation revenue, attainment profitability, or commercialization of products. In addition, it is possible that there will be further legislation or regulation that could harm the business, financial condition and results of operations.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act ("FCPA") prohibits any U.S. individual or business from paying, offering, or 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 accounting provisions requiring us 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.

Additional regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Europe / rest of world government regulation

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we obtain FDA approval of a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial application must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the clinical trial application is approved in accordance with a country's requirements, clinical trial development may proceed. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country in the European Union. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of a drug product under European Union regulatory systems, we must submit a marketing authorization application ("MAA"). The documentation submitted to the FDA in support of an NDA in the United States is almost identical to that required in the European Union, with the exception of, among other things, country-specific document requirements. For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we or our potential collaborators fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Other regulations

We are subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees

As of April 30, 2020, we had a total of 56 full-time employees, of whom 23 were located in the United States and 33 were located in the United Kingdom. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We have not experienced any work stoppages and consider our relations with employees to be good.

Corporate Information

Our principal executive offices are located at 55 Cambridge Parkway, Ste 901E, Cambridge, MA 02142, and our telephone number is (857) 999-0075. Our website address is www.kalvista.com. The information contained on, or that can be accessed through, our website is not a part of this report. We have included our website address in this report solely as an inactive textual reference.

Available Information

We file annual, quarterly, and current reports, proxy statements, and other documents with the Securities and Exchange Commission ("SEC") under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), which are available on our corporate website at www.kalvista.com as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Also, the SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding issuers, including us, that file electronically with the SEC. The public can obtain any documents that we file with the SEC at www.sec.gov. The information posted on or accessible through these websites are not incorporated into this filing.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K, including the consolidated financial statements, the notes thereto and the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this Annual Report on Form 10-K before deciding whether to invest in shares of 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 deem immaterial may also become important factors that adversely affect our business. If any of the following risks actually occur, our business, financial condition, results of operations and future prospects could be materially and adversely affected. In that event, the market price of our stock could decline, and you could lose part or all of your investment.

Risks Related to Our Business

The novel strain of coronavirus, SARS-CoV-2 ("COVID-19") outbreak has caused, and has the potential to further cause, disruptions in our business, financial condition and results of operations, including the execution of our clinical development activities and the use and sufficiency of our existing cash.

The outbreak of COVID-19 has evolved into a global pandemic. We have multiple clinical development activities, including our ongoing Phase 2 clinical trial for KVD900, that are being conducted primarily in Europe. Several European nations, in particular Italy, have implemented quarantines or other containment measures in response to the ongoing coronavirus outbreak, which have limited our ability to access patients and physicians at certain local clinical centers that are participating in these development activities. This has led to delays in our clinical development programs, particularly for KVD900. Should these clinical facilities continue to experience disruptions, or should patients or physicians be unable to continue their participation, on either a temporary or permanent basis, our clinical development activities could be significantly additionally delayed. We may also experience delays or difficulties with respect to our clinical trials as a result of delays in clinical site initiations and the enrollment of patients in our future clinical trials, including difficulties in recruiting clinical site investigators and clinical site staff due to the COVID-19 pandemic. Any such delays to our planned clinical trial timelines could also impact the use and sufficiency of our existing cash reserves, and we may be required to raise additional capital earlier than we had previously planned. We may be unable to raise additional capital if and when needed, which may result in further delays or suspension of our development plans. If we are able to raise additional capital, challenging and uncertain economic conditions can make capital raising costly and dilutive.

Further, the extent to which the COVID-19 pandemic impacts our ability to procure resources, raw materials or components necessary for our research studies or preclinical or clinical development will depend on unpredictable future developments, including new information that may emerge about the severity of the coronavirus and the actions to contain the coronavirus or treat its effects, among others.

Additionally, our operations have been, and may continue to experience disruptions, such as due to temporary closure of our offices or those of our suppliers and suspension of services, which may materially and adversely affect our development timelines, and our business, financial condition and results of operations.

Further, infections and deaths related to COVID-19 are also disrupting certain healthcare and healthcare regulatory systems globally. Such disruptions could divert healthcare resources away from, or materially delay review by, the FDA and comparable foreign regulatory agencies. As a result of the FDA's updated industry guidance for conducting clinical trials issued on March 18, 2020, we may experience delays in or temporary suspension of the enrollment of patients in our ongoing clinical trials. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of our clinical trial or delay in regulatory review resulting from such disruptions could materially adversely affect the development and study of KVD900 and KVD824.

The spread of COVID-19, which has caused a broad impact globally, including restrictions on travel and quarantine policies put into place by businesses and governments, may have a material adverse effect on our business. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, it has already caused, and is likely to result in further, significant disruption of global financial markets and the trading prices for our common stock and other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic, which may reduce our ability to access capital either at all or on favorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the global effort to control COVID-19 infections could materially and adversely affect our business and the value of our common stock.

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

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses as we focused on our discovery efforts and developing our product candidates. We expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To date, we have financed our operations primarily through sales of our stock and the Option Agreement and associated private placement. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue clinical development of our current product candidates;
- seek to identify additional product candidates;
- acquire or in-license other products and technologies or enter into collaboration arrangements with regards to product discovery;
- initiate clinical trials for additional product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- continue to incur increased costs as a result of operating as a public company.

To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This will require us to be successful in a range of challenging activities, including completing clinical trials of our product candidates, obtaining marketing approval for these product candidates and manufacturing, marketing and selling those products for which we may obtain marketing approval. We may never succeed in these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our business and could impair our ability to raise capital, maintain our discovery and preclinical development efforts, expand our business or continue our operations and may require us to raise additional capital that may dilute the ownership interest of common stockholders. A decline in the value of our business could also cause stockholders to lose all or part of their investment.

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

We are a clinical stage company and our operations to date have been limited to organizing and staffing, business planning, raising capital, acquiring and developing the technology, identifying potential product candidates, undertaking up to Phase 2 clinical studies of our most advanced product candidates, KVD900 and KVD001. We have not yet demonstrated our ability to successfully complete large-scale, pivotal 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. Substantial time is required to develop a new medicine from the time it is discovered to when it is available for treating patients. Consequently, any predictions made about our future success or viability based on our limited operating history to date may not be as accurate as they could be if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. Upon regulatory approval of our product candidates, we will need to transition from a company with a research focus to a company capable of supporting and scaling commercial activities. We may not be successful in such a transition.

We will need substantial additional funding. If we are unable to raise capital when needed, we may need to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in parallel with our ongoing activities, particularly as we continue our discovery and preclinical development collaborations to identify new clinical candidates and initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will need to obtain substantial additional funding for our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our discovery and preclinical development programs or any future commercialization efforts.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings and debt financings. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

Risks Related to the Discovery and Development of Our Product Candidates

We are early in our development efforts. If we or our collaborators are unable to successfully develop and commercialize one or more of our compounds, or if we experience significant delays in doing so, the business will be materially harmed.

We currently do not have any products that have gained regulatory approval. We have invested substantially all of our efforts and financial resources in identifying potential drug candidates and funding our preclinical and clinical studies. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our clinical stage product candidates.

We have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

- execute ongoing clinical development activities;
- successfully complete any clinical trials beyond Phase 2;
- move other product candidates into development;
- obtain required regulatory approvals for the development and commercialization of one or more of our product candidates;
- maintain, leverage and expand our intellectual property portfolio;
- manufacture a commercial scale product or arrange for a third party to do so on our behalf;
- build and maintain robust sales, distribution and marketing capabilities for successful product commercialization, either on our own or in collaboration with strategic partners;

- gain market acceptance for one or more of our product candidates;
- develop and maintain any strategic relationships we elect to enter into; and
- manage our spending as costs and expenses increase due to drug discovery, preclinical development, clinical trials, regulatory approvals and commercialization.

If we are unsuccessful in accomplishing these objectives, we may not be able to successfully develop and commercialize KVD900, KVD001 or other product candidates, and our business will suffer.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We have not yet commercialized our product candidates and the historical failure rate in clinical drug development of product candidates in our industry is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of its product candidates in humans. Clinical testing is expensive, difficult to design and implement and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Further, the results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. 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. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval.

We may experience delays in our clinical trials and we do not know whether planned clinical trials will begin or enroll subjects on time, need to be redesigned or be completed on schedule, if at all. There can be no assurance that the FDA, Medicines & Healthcare products Regulatory Agency (the "MHRA"), the U.K. regulatory authority, or the European Medicines Agency (the "EMA") will not put any of our product candidates on clinical hold in the future. 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 product candidates. Clinical trials may be delayed, suspended or prematurely terminated for a variety of reasons, such as:

- delay or failure in reaching agreement with the FDA, MHRA, EMA or a comparable foreign regulatory authority on a trial design that we want to execute;
- delay or failure in obtaining authorization to commence a trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical study;
- delays in reaching, or failure to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- inability, delay, or failure in identifying and maintaining a sufficient number of trial sites, many of which may already be engaged in other clinical programs;
- delay or failure in recruiting and enrolling suitable subjects to participate in a trial, including due to the COVID-19 pandemic;
- delay or failure in having subjects complete a trial or return for post-treatment follow-up, including due to the COVID-19 pandemic;
- clinical sites and investigators deviating from trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial;
- the withdrawal of the United Kingdom from the European Union could materially impact the regulatory regime with respect to clinical trials in the United Kingdom or the European Union;

- lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional clinical studies and increased expenses associated with the services of its clinical research organizations ("CROs") and other third parties;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- we may experience delays or difficulties in the enrollment of patients that our product candidates are designed to target;
- our third party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have difficulty partnering with experienced CROs that can identify patients that our product candidates are designed to target and run our clinical trials effectively;
- regulators or IRBs may require that we or our investigators 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;
- there may be political factors surrounding the approval process, such as government shutdowns, political instability or global pandemics such as the COVID-19 pandemic;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate, including due to the COVID-19 pandemic; or
- there may be changes in governmental regulations or administrative actions.

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 positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings that would reduce the potential market for our products or inhibit our ability to successfully commercialize our products;
- be subject to additional post-marketing restrictions and/or 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 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 and may harm our business and results of operations.

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 and expenses for development of our product candidates could increase.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to demonstrate safety and efficacy. We are conducting clinical trials of KVD900 and KVD824, and we do not know whether planned or ongoing clinical trials will enroll subjects in a timely fashion, require redesign of essential trial elements or be completed on our projected schedule. In particular, because we are focused on patients with HAE, which is a rare disease, our ability to enroll eligible patients in trials may be limited or may result in slower enrollment than we anticipate. In addition, competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Global pandemics, such as COVID-19, could also negatively affect site initiation, as well as recruitment and retention, at sites in a region or city whose health care system becomes overwhelmed due to the COVID-19 pandemic. For example, as a result of COVID-19, several of our clinical trial sites in Europe have paused enrollment or are not prioritizing clinical trial activities or allowing enrollment, and of those sites still conducting clinical trial activities, the availability for patients to visit sites and have screening conducted may be limited.

Patient enrollment is affected by other factors including:

- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same disease indication;
- the patient referral practices of physicians;
- the proximity and availability of clinical trial sites for prospective patients;
- any delays and difficulties in enrollment due to the COVID-19 pandemic;
- ambiguous or negative interim results of our clinical trials, or results that are inconsistent with earlier results;
- feedback from the FDA, MHRA, EMA, IRBs, data safety monitoring boards, or a comparable foreign regulatory authority, or results from earlier stage or concurrent preclinical and clinical studies, that might require modifications to the protocol;
- decisions by the FDA, MHRA, EMA, IRBs, a comparable foreign regulatory authority or us, or recommendations by data safety monitoring boards, to suspend or terminate clinical trials at any time for safety issues or for any other reason; and
- unacceptable risk-benefit profile or unforeseen safety issues or adverse effects.

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

If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary

dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, or at all, the commercialization of our products may be delayed or never achieved and, as a result, our stock price may decline.

If serious adverse events or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit the development of some of our product candidates.

If our product candidates are associated with undesirable effects in preclinical or clinical trials or have characteristics that are unexpected, we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. There are risks inherent in the intravitreal administration of drugs like KVD001 which can cause injury to the eye and other complications. Our HAE programs, including KVD900 and KVD824, are still in the early stage of clinical testing and we have not yet determined what, if any, significant side effects may occur from dosing. Additional or more severe side effects may be identified for all our programs through further clinical studies. These or other drug-related side effects could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may significantly harm our business, financial condition and prospects.

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

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates must be approved by the FDA pursuant to an NDA in the United States and by the EMA and similar regulatory authorities outside the United States prior to commercialization. The process of obtaining marketing approvals, both in the United States and abroad, is expensive and takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have no experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third party CROs to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude us from obtaining marketing approval or prevent or limit commercial use. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may also cause delays in or prevent the approval of an application.

Additionally, on December 31, 2019, the United Kingdom officially withdrew from the European Union, commonly referred to as Brexit. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the final resolution of the withdrawal of the United Kingdom from the European Union could materially impact the regulatory regime with respect to the approval of KVD900 or any of our other product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing KVD900 or any of our other product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for KVD900 or any of our other product candidates, which could significantly and materially harm our business.

Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

We may seek orphan drug exclusivity for some of our product candidates, and we may be unsuccessful.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a disease with a patient population of fewer than 200,000 individuals in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug for the same indication during the period of exclusivity. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective, if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a different drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

A Fast Track designation by the FDA may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval.

The FDA has granted fast track designation for KVD900 for the treatment of HAE. We may also seek fast track designation for other indications or for some of our other product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot assure that the FDA would decide to grant it. Even though we have received fast track designation for KVD900 for the treatment of HAE, or even if we receive fast track designation for other indications or for our other product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs that have received fast track designation have failed to obtain drug approval.

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

In order to market and sell our products in the European Union and many other jurisdictions, we or our third party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain MHRA or FDA approval. The regulatory approval process outside the United Kingdom and United States generally includes all of the risks associated with obtaining, respectively, MHRA or 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 approved for sale in that country.

We, or these third parties, may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the MHRA or 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. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Our product candidates and the activities associated with their development and commercialization, including their testing, manufacture, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA, MHRA, and other regulatory authorities. In the United States, these requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, including periodic inspections by the FDA and other regulatory authority, requirements regarding the distribution of samples to physicians and recordkeeping.

The FDA, or other regulatory authorities, may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products and if we promote our products beyond their approved indications, we may be subject to enforcement action for off-label promotion. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may 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 marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

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 prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

As an example, the ACA, was signed into law in 2010 but has continued to be the subject of legislative efforts at revision and repeal. The ACA included a substantial number of major changes to the healthcare system that impact our business, and several other legislations since then, as well as ongoing efforts, have continued to create a complicated planning and operating environment for companies in our industry.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate 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 business could be materially harmed.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We 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. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also 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 its use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed its 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 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 the 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 discovery, preclinical development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

As with all companies, we are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we may establish, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a material and adverse effect on our business, financial condition, results of operations and prospects, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, integrity oversight and reporting obligations, or reputational harm.

Risks Related to the Commercialization of Our Product Candidates

Even if any of our product candidates receives marketing approval, we 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.

If any of our product candidates receives marketing approval, we may nonetheless fail to gain sufficient market acceptance by physicians, patients, third party payors and others in the medical community. In addition, physicians, patients and third party payors may prefer other novel products to ours. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety and potential advantages and disadvantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- 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 availability of third party coverage and adequate reimbursement, including patient cost-sharing programs such as copays and deductibles;
- the ability to develop or partner with third-party collaborators to develop companion diagnostics;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

In addition, in order to commercialize any product candidates, we must build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If we are unable to enter into such arrangements when needed on acceptable terms or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval or any such commercialization may experience delays or limitations. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. In addition, our ability to compete may be affected in many cases by insurers or other third party payors seeking to encourage the use of generic products. Generic products are expected to become available over the coming years, potentially creating pricing pressure. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products.

Many of the companies against which we are competing or 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.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health

maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new medicines are typically made by the CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS. Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third party payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market.

In addition, many private payors contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of our products.

Our ability to obtain services, reimbursement or funding may be impacted by possible reductions in federal spending in the United States as well as globally.

U.S. federal government agencies currently face potentially significant spending reductions. Under the Budget Control Act of 2011, the failure of Congress to enact deficit reduction measures of at least $1.2 trillion for the years 2013 through 2021 triggered automatic cuts to most federal programs. These cuts would include aggregate reductions to Medicare payments to providers of up to two percent per fiscal year, which went into effect beginning on April 1, 2013 and will stay in effect through 2025 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, which was enacted on January 1, 2013, among other things, reduced Medicare payments to several providers, including hospitals and imaging centers. The full impact on our business of these automatic cuts is uncertain. Additionally, the Coronavirus Aid, Relief, and Economic Security ("CARES") Act enacted in 2020 may result in future spending reductions and cuts to federal programs.

If government spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell any products we may develop. Any reductions in government spending in countries outside the United States may also impact us negatively, such as by limiting the functioning of international regulatory agencies in countries outside the United States or by eliminating programs on which we may rely.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend 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 or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently hold $10,000,000 in product liability insurance coverage in the aggregate, with a per incident limit of $10,000,000, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Dependence on Third Parties

We have entered, and may in the future seek to enter, into collaborations with third parties for the development and commercialization of our product candidates. If we fail to enter into such collaborations, or such collaborations are not successful, we may not be able to capitalize on the market potential of our product candidates.

Biopharmaceutical companies are our prior and likely future collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements. For example, in 2017, we entered into a collaboration with Merck, under which we granted to Merck an option to acquire KVD001 through a period following completion of a Phase 2 clinical trial, as well as an option to our planned future oral DME programs; such options expired in February 2020. We expect that in any future collaboration agreements, we would have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Moreover, our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for any 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. 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 our development program or one

or more of our other development programs, delay our potential development schedule or reduce the scope of research activities, or increase our expenditures and undertake discovery or preclinical development activities at our own expense. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development activities, we may not be able to further develop our product candidates or continue to develop our product candidates and our business may be materially and adversely affected.

Future collaborations we may enter into may involve the following risks:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, may divert resources or create competing priorities;
- collaborators may delay discovery and preclinical development, provide insufficient funding for product development of targets selected by us, stop or abandon discovery and preclinical development for a product candidate, repeat or conduct new discovery and preclinical development for a product candidate;
- 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 than our products;
- 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 development of its product candidates;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the discovery, preclinical 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 be time-consuming and expensive;
- collaborators may not properly maintain or defend their intellectual property rights or intellectual property rights licensed to us or may use their 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.

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

If our collaborations do not result in the successful development of products or product candidates, product candidates could be delayed and we may need additional resources to develop product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this proxy statement also apply to the activities of our collaborators.

We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and we expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products at an acceptable cost and quality, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate facilities for the manufacture of our product candidates, and we do not have any manufacturing personnel. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing and we do not have backup sources of supply established for our candidates. We review the manufacturing process for each of our candidates and assess the risk to supply and, as appropriate, establish multiple manufacturers and/or establish stock levels to support future activities and do not believe we are currently substantially dependent on any one third party. Despite the drug substance and product risk management, this reliance on third parties presents a risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. Furthermore, if any third-party in the supply chain for materials used in the production of our product candidates are adversely impacted by restrictions resulting from the COVID-19 pandemic, our supply chain may be disrupted, limiting the ability of our third-party manufacturers to manufacture our product candidates for our clinical trials. If our third-party manufacturers were to encounter any manufacturing difficulties or delays due to resource constraints as a result of COVID-19 pandemic, our ability to provide our product candidates to patients in clinical trials, or to provide product for treatment of patients once approved, would be jeopardized.

Any performance failure on the part of our existing or future manufacturers of drug substance or drug products could delay clinical development or marketing approval. If current suppliers cannot supply us with our Phase 2 requirements as agreed, we may be required to identify alternative manufacturers, which would lead us to incur added costs and delays in identifying and qualifying any such replacement.

The formulation used in early studies frequently is not a final formulation for commercialization. Additional changes may be required by the FDA or other regulatory authorities on specifications and storage conditions. These may require additional studies and may delay our clinical trials.

We expect to rely on third party manufacturers or third party collaborators for the manufacture of commercial supply of any other product candidates for which our collaborators or we obtain marketing approval.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

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

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

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

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

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

We may not successfully engage in strategic transactions, including any additional collaborations we seek, which could adversely affect our ability to develop and commercialize product candidates, impact our cash position, increase our expenses and present significant distractions to our management. The terms of any collaborations may also have impacts on other aspects of our business.

From time to time, we may consider strategic transactions, such as collaborations, acquisitions of companies, asset purchases and out- or in-licensing of product candidates or technologies that we believe will complement or augment our existing business. In particular, we will evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biotechnology or biopharmaceutical companies. The competition for collaborators is intense, and the negotiation process is time-consuming and complex. Any new collaboration may be on terms that are not optimal for us, and we may not be able to maintain any new collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product candidate do not meet expectations or the collaborator terminates the collaboration. 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 strategic partners. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the strategic partner's resources and expertise, the terms and conditions of the proposed collaboration and the proposed strategic partner's evaluation of a number of factors. These factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. Moreover, even if we acquire assets with promising markets or technologies, we may not be able to realize the benefit of acquiring such assets due to an inability to successfully integrate them with our existing technologies and we may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic acquisition that delay or prevent us from realizing their expected benefits or enhancing our business.

We cannot assure you that following any such collaboration, or other strategic transaction, we will achieve the expected synergies to justify the transaction. For example, such transactions may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions would entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. Also, such strategic alliance, joint venture or acquisition may be prohibited. Collaborations may also have potential impact on other aspects of our business.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks that would have a material and adverse effect on our business, financial condition, results of operations and prospects. Conversely, any failure to enter any additional collaboration or other strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches the market.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain intellectual property protection for our technology and products or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States, the European Union, and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates. This patent portfolio includes issued patents and pending patent applications covering compositions of matter and methods of use.

The patent prosecution process is expensive and time-consuming, and 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, and 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 discovery and preclinical development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, India and China do not allow patents for methods of treating the human body. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. If a third party has also filed a United States patent application prior to the effective date of the relevant provisions of the America Invents Act (i.e. before March 16, 2013) covering our product candidates or a similar invention, we may have to participate in an adversarial proceeding, known as an interference, declared by the USPTO to determine priority of invention in the United States. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the European Union, the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Moreover, we may be subject to a third party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

The risks described elsewhere pertaining to our patents and other intellectual property rights also apply to the intellectual property rights that we license, and any failure to obtain, maintain and enforce these rights could have a material adverse effect on our business. In some cases we may not have control over the prosecution, maintenance or enforcement of the patents that we license, and our licensors may fail to take the steps that we believe are necessary or desirable in order to obtain, maintain and enforce the licensed patents. Any inability on our part to protect adequately our intellectual property may have a material adverse effect on our business, operating results and financial position.

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 USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. 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 may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Because competition in our industry is intense, competitors may infringe or otherwise violate our issued patents, patents of our licensors or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringed their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. We may also elect to enter into license agreements in order to settle patent infringement claims or to resolve disputes prior to litigation, and any such license agreements may require us to pay royalties and other fees that could be significant. 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.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and

pharmaceutical industries. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We seek to protect our confidential proprietary information, in part, by entering into confidentiality and invention or patent assignment agreements with our employees and consultants, however, we cannot be certain that such agreements have been entered into with all relevant parties. Moreover, to the extent we enter into such agreements, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate them, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Employee Matters, Facilities, Managing Growth and Macroeconomic Conditions

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 the principal members of our management, scientific and clinical team. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of our management team, other key employees and other scientific and medical advisors, including due to illness resulting from COVID-19, and our inability to find suitable replacements, could result in delays in product development and harm our business.

Recruiting and retaining qualified scientific, clinical, manufacturing, 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 discovery and preclinical 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 provide services 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 and regulatory 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 drug development, regulatory affairs and, if any of our product candidates receive marketing approval, sales, marketing and distribution. 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 the limited experience of our management team in managing a company with 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.

The U.K. vote to leave the European Union, known as Brexit, could negatively impact our business and operations.

The majority of our scientific operations are based in the United Kingdom and we have received significant funding through United Kingdom government sources and tax credits. In addition, we have used the United Kingdom as our European location for interactions with European Union regulatory authorities related to clinical development and other activities executed or planned in the European Union. On December 31, 2019 the UK officially withdrew from the European Union, although many of the details of future interactions between the United Kingdom and European Union remain unresolved. There are many risks and uncertainties associated with this process, including whether Brexit has a negative economic impact on either the United Kingdom or the European Union member states, or interactions with the European Union regulatory regime are changed as a result of Brexit, any of which could have an adverse impact on our business or future operations. For additional risks related to Brexit, see "*—If we are not able to obtain, or if there are delays in obtaining required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.*"

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

Our operations, and those of our CROs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, such as the COVID-19 pandemic, and other natural or man-made disasters or business interruptions, for which we may not have insurance coverage. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. In particular, the potential effects on our business due to the COVID-19 pandemic may be significant and could materially harm our business, operating results and financial condition. We rely on third-party manufacturers to produce and process our product candidates. Our ability to obtain supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. Our operations and financial condition could suffer in the event of a natural or man-made disaster near our headquarters in Cambridge, Massachusetts or our research facility in Porton Down, United Kingdom.

Unstable or unfavorable global market and economic conditions may have adverse consequences on our business, financial condition and stock price.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. We cannot assure you that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy and stock price may be adversely affected by any such economic downturn, volatile business environment or large-scale unpredictable or unstable market conditions, including a prolonged government shutdown or as a result of a global pandemic such as the COVID-19 pandemic. While the potential economic impact brought by and the duration of the pandemic may be difficult to assess or predict, it has already caused, and is likely to result in further, significant disruption of global financial markets, which may reduce our ability to access capital either at all or on favorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the spread of COVID-19 could materially and adversely affect our business and the value of our common stock.

If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

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

Our internal computer systems and those of our CROs, collaborators and third parties on whom we rely are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Furthermore, we have little or no control over the security measures and computer systems of our third party collaborators. In May 2019, we were notified by one of our vendors that they suffered a security breach and some of our data was among the information stolen by an unknown third party. We have taken certain actions in response to that theft and we do not anticipate significant disruption to our business or future prospects. However, in the future, if such an event were to occur and lead to exposure of sensitive information or cause interruptions in our operations or our third party collaborators, it could result in a material disruption of our drug development programs and potential financial losses. For example, the loss of research data could delay development of our product candidates and the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and we may incur substantial costs to attempt to recover or reproduce the data. If any disruption or security breach resulted in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and/or the further development of our product candidates could be delayed or impaired.

We also depend on our information technology infrastructure for communications among our personnel, contractors, consultants and vendors. System failures or outages, including any potential disruptions due to significantly increased global demand on certain cloud based systems during the COVID-19 pandemic, could also compromise our ability to perform these functions in a timely manner, which could harm our ability to conduct business or delay our financial reporting.

Risks Related to Ownership of Our Common Stock

Our stock price is volatile and our stockholders may not be able to resell shares of our common stock at or above the price they paid.

The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, many of which are beyond our control. In addition, the trading prices for our common stock and other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. Factors affecting the market price of our common stock include those discussed in this "Risk Factors" section of this Annual Report on Form 10-K and others such as:

- announcement of a strategic transaction or other significant events for us or our competitors;
- our decision to initiate a clinical trial or not to initiate a clinical trial;
- announcements of significant changes in our business or operations, including the decision not to pursue drug development programs;
- additions or departures of key personnel;
- adverse results or delays in clinical trials;
- changes in reimbursement or third party coverage of treatments for HAE or DME, or changes to treatment recommendations or guidelines applicable to the treatment of HAE or DME;
- announcements relating to collaboration partnerships or other strategic transactions undertaken by us;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to any of our product candidates;
- any adverse changes to our relationship with any manufacturers or suppliers;
- the success of our testing and clinical trials;
- the success of our efforts to acquire or license or discover additional product candidates;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;
- FDA or other regulatory actions affecting us or our industry or other healthcare reform measures in the United States, the United Kingdom or the European Union;
- changes in financial estimates or recommendations by securities analysts;
- trading volume of our common stock;

- sales of our common stock by us, our executive officers and directors or our stockholders in the future;
- general economic and market conditions and overall fluctuations in the United States equity markets, including due to global pandemics such as COVID-19; and
- other events or factors, many of which are beyond our control.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse 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. If any analysts who cover us issue an adverse regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If any of these 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 our stock price or trading volume to decline.

We incur significant costs as a result of operating as a public company, and our management devotes substantial time to compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business.

We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Exchange Act, and regulations regarding corporate governance practices. The listing requirements of The NASDAQ Global Market require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel have devoted, and will continue to need to devote, a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations increase our legal and financial compliance costs and make some activities more time consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

We are subject to Section 404 of The Sarbanes-Oxley Act of 2002 ("Section 404"), and the related rules of the SEC which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. Effective April 27, 2020, the SEC adopted amendments to the "accelerated filer" and "large accelerated filer" definitions in Rule 12b-2 under the Securities and Exchange Act of 1934. The amendments exclude from the "accelerated filer" and "large accelerated filer" definitions an issuer that is eligible to be a smaller reporting company and that had annual revenues of less than $100 million in the most recent fiscal year for which audited financial statements are available. We determined that our Company does not meet the accelerated or large accelerated filer definitions as of April 30, 2020. For so long as we remain a smaller reporting company and a non-accelerated filer, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies, including, but not limited to, not being

required as a non-accelerated filer to comply with the auditor attestation requirements of Section 404(b). An independent assessment by our independent registered public accounting firm of the effectiveness of internal control over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

During the course of the review and testing of our internal control for the purpose of providing the reports required by these rules, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal control over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Market or other adverse consequences that would materially harm our business.

In addition, if we lose our status as a "non-accelerated filer," we will be required to have our independent registered public accounting firm attest to the effectiveness of internal control over financial reporting. If our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting once we are an accelerated filer or a large accelerated filer, investors may lose confidence in the accuracy and completeness of our financial reports, and the market price of our common stock could be negatively affected.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquirer or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least 66 2/3% of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of at least 66 2/3% of the shares entitled to vote at an election of directors to adopt, amend or repeal certain provisions of our bylaws and our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;

- the requirement that a special meeting of stockholders may be called only by or at the direction of our board of directors pursuant to a resolution adopted by a majority of the total number of directors that our board of directors would have if there were no vacancies, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us. In addition, these provisions would apply even if we were to receive an offer that some stockholders may consider beneficial.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- we will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.
- the rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.
- we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

Our ability to use our net operating losses to offset future taxable income, if any, may be subject to certain limitations.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" (generally defined as a greater than 50-percentage-point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three-year period) is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. We have experienced ownership changes that substantially limit our use of the NOLs available to us for U.S. federal income tax purposes. If we undergo additional ownership changes (some of which changes may be outside our control), our ability to utilize

our NOLs could be further limited by Section 382 of the Code. Our NOLs may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs. Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating U.S. federal taxable income. We have incurred net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the U.S. federal taxable income necessary to utilize our NOLs.

The Tax Cuts and Jobs Act of 2017, or the TCJA, changed both the federal deferred tax value of the net operating loss carryforwards and the rules of utilization of federal net operating loss carryforwards. Under the TCJA, net operating loss carryforwards generated in years after 2017 will only be available to offset 80% of future taxable income in any single year but will not expire. However, the Coronavirus Aid, Relief, and Economic Security (CARES) Act temporarily repealed the 80% taxable income limitation for tax years beginning before January 1, 2021; net operating loss carried forward generated from 2018 or later and carryforwards to taxable years beginning after December 31, 2020 will be subject to the 80% limitation. Also, under the CARES Act, net operating losses arising in 2018, 2019 and 2020 can be carried back 5 years.

We do not currently intend to pay dividends on our common stock, and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, our stockholders are not likely to receive any dividends on their common stock for the foreseeable future. Since we do not intend to pay dividends, our stockholders' ability to receive a return on their investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters is located in Cambridge, Massachusetts where we occupy approximately 2,700 square feet of office space under a five-year lease. We maintain approximately 8,800 square feet of office and research laboratory space in Porton Down, United Kingdom, under a ten-year lease, as well as approximately 4,600 square feet of additional office and research laboratory space in the same location under an eight-year lease. We also maintain approximately 1,000 square feet of leased research laboratory space in Boston, Massachusetts.

We believe that our current and planned facilities are adequate to meet our needs for the foreseeable future, and that, should it be needed, suitable additional space will be available to accommodate any such expansion of our operations.

Item 3. Legal Proceedings.

From time to time, we may become involved in various lawsuits and legal proceedings which arise in the ordinary course of business. We are currently not aware of any such legal proceedings or claims that we believe will have a material adverse effect on our business, financial condition or operating results.

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 "KALV."

Holders

As of June 24, 2020, there were 32 holders of record of our common stock. The actual number of holders 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.

Dividends

We have never declared or paid cash dividends on our capital stock. We do not expect to pay dividends on our common stock for the foreseeable future. Instead, we anticipate that all of our earnings, if any, will be used for the operation and growth of our business. Any future determination to declare cash dividends would be subject to the discretion of our board of directors and would depend upon various factors, including our results of operations, financial condition and capital requirements, restrictions that may be imposed by applicable law and our contracts and other factors deemed relevant by our board of directors.

Recent Sales of Unregistered Securities

None.

Item 6. Selected Financial Data.

The following selected financial data should be read in conjunction with the Consolidated Financial Statements and the Notes thereto and the section captioned "Management's Discussion and Analysis of Financial Condition and Results of Operations," included elsewhere in this Annual Report on Form 10-K.

The Balance Sheet Data at April 30, 2020 and 2019 and the Statement of Operations Data for each of the three years ended April 30, 2020, 2019, and 2018 have been derived from the audited Consolidated Financial Statements for such years, included elsewhere in this Annual Report on Form 10-K. The Balance Sheet Data at April 30, 2018, 2017, and 2016, and the Statement of Operations Data for each of the two years in the period ended April 30, 2017 and 2016 have been derived from audited consolidated financial statements for such years not included in this Annual Report on Form 10-K.

	For the Years Ended April 30,				
	2020	2019	2018	2017	2016
	(in thousands, except share and per share data)				
Consolidated Statement of Operations Data:					
Revenue	$ 12,690	$ 16,127	$ 8,394	$ 1,504	$ 2,133
Operating expenses					
Research and development	40,194	35,021	18,237	12,666	14,661
General and administrative	13,029	10,926	8,862	11,177	2,653
Total operating expenses	53,223	45,947	27,099	23,843	17,314
Operating loss	(40,533)	(29,820)	(18,705)	(22,339)	(15,181)
Total other income	11,293	9,128	2,900	3,736	3,745
Loss before income taxes	(29,240)	(20,692)	(15,805)	(18,603)	(11,436)
Income tax (benefit) expense	(124)	124	—	—	—
Net loss	$ (29,116)	$ (20,816)	$ (15,805)	$ (18,603)	$ (11,436)
Net loss per share, basic and diluted	$ (1.64)	$ (1.38)	$ (1.53)	$ (4.47)	$ (26.17)
Weighted average common shares outstanding, basic and diluted	17,748,666	15,080,863	10,321,780	4,646,764	591,298

	April 30,				
	2020	2019	2018	2017	2016
			(in thousands)		
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 15,789	$ 32,006	$ 51,055	$ 30,950	$ 21,764
Property and equipment, net	2,043	2,413	1,836	97	74
Working capital	80,976	97,494	36,164	31,180	21,422
Total assets	92,529	118,132	61,389	34,345	24,745
Total liabilities	8,777	21,394	34,136	3,018	3,249
Stockholders' equity (deficit)	83,752	96,738	27,253	31,327	(37,112)

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

The following discussion and analysis should be read in conjunction with our audited consolidated financial statements and the related notes that appear elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Exchange Act. These statements are often identified by the use of words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "estimate," or "continue," and similar expressions or variations. These statements are based on the belief and assumptions of our management based on information currently available to management, reflecting our current expectations that involve risks and uncertainties. Actual results and the timing of certain events may differ materially from those discussed or implied in these forward-looking statements due to a number of factors, including, but not limited to, the impact of the current COVID-19 pandemic on our business and future financial performance, and those set forth in the section entitled "Risk Factors" and elsewhere in this Annual Report on Form 10-K. You should review the risk factors for a more complete understanding of the risks associated with an investment in our securities. For further information regarding forward-looking statements, please refer to the "Special Note Regarding Forward-Looking Statements" at the beginning of Part I of this Annual Report on Form 10-K. Our fiscal year end is April 30, and references throughout this Annual Report to a given fiscal year are to the twelve months ended on that date.

Management Overview

We are a clinical stage pharmaceutical company focused on the discovery, development and commercialization of small molecule protease inhibitors for diseases with significant unmet need. Our first product candidates are inhibitors of plasma kallikrein being developed for two indications: hereditary angioedema ("HAE") and diabetic macular edema ("DME"). We apply our insights into the chemistry of proteases and, with our current programs, the biology of the plasma kallikrein system, to develop small molecule inhibitors with high selectivity, potency and bioavailability that we believe will make them successful treatments for diseases.

We have created a structurally diverse portfolio of oral plasma kallikrein inhibitors and advanced multiple drug candidates into clinical trials in order to create best-in-class oral therapies for both HAE and DME. Our most advanced program for HAE is KVD900, which is being developed as a potential on-demand oral therapy for treatment of HAE attacks. KVD900 is currently being evaluated in a Phase 2 clinical trial which we expect to provide data in the second half of 2020. KVD824 is our next oral program to be developed for HAE and we plan to commence a Phase 2 clinical trial intended to evaluate KVD824 as a twice-daily potential oral prophylactic treatment for HAE in the second half of 2020.

In the case of DME, in December 2019 we announced data from a Phase 2 trial for KVD001, an intravitreally delivered plasma kallikrein inhibitor. This study evaluated the safety and efficacy of two dose levels (3µg and 6µg) of KVD001 compared to a sham control in 129 DME patients who had previously been treated with anti-VEGF therapy, and still had significant edema and reduced visual acuity. The study was conducted at 38 sites in the United States, and consisted of four intravitreal injections or sham administered over three months with a three month follow up period. The primary efficacy endpoint of change in best corrected visual acuity ("BCVA") at 16 weeks compared to sham was not met.

We have devoted substantially all our efforts to research and development, including clinical trials of our product candidates. We have not completed the development of any product candidates. Pharmaceutical drug product candidates, like those being developed by us, require approvals from the FDA or foreign regulatory agencies prior to commercial sales. There can be no assurance that any product candidates will receive the necessary approvals, and any failure to receive approval or delay in approval may have a material adverse impact on our business and financial results. We are subject to a number of risks and uncertainties similar to those of other life science companies developing new products, including, among others, the risks related to the necessity to obtain adequate additional financing, to successfully develop product candidates, to obtain regulatory approval of product candidates, to comply with government regulations, to successfully commercialize our potential products, to the protection of proprietary technology and to our dependence on key individuals.

The extent of the impact of COVID-19 on our operational and financial performance will depend on certain developments, including the duration and spread of the outbreak, impact on our clinical studies, employee or industry events, and effect on our suppliers and manufacturers, or impact on the healthcare systems, all of which are uncertain and cannot be predicted. We may experience constrained supplies of our product candidates or, with respect to our clinical trials, delays in enrollment, site initiation, participant dosing, distribution of clinical trial materials, study monitoring and data analysis that could materially adversely impact our business, results of operations and overall financial performance in future periods. Any such delays to our planned clinical timelines for KVD900 and KVD824 could also impact the use and sufficiency of our existing cash reserves, and we may be required to raise additional capital earlier than we had previously planned. We may be unable to raise additional capital if and when needed, which may result in further delays or suspension of our development plans. As of the filing date of this Annual Report on Form 10-K, the extent to which COVID-19 may impact our financial condition, results of operations or guidance is uncertain. The effect of the COVID-19 pandemic will not be fully reflected in our results of operations and overall financial performance until future periods. See the section entitled "Risk Factors" included elsewhere in this report for further discussion of the possible impact of the COVID-19 pandemic on our business.

We have funded operations primarily through the issuance of stock, the Option Agreement and associated private placement. As of April 30, 2020, we had an accumulated deficit of $121.6 million and $67.7 million of cash, cash equivalents and available for sale securities. Our working capital is anticipated to fund our operations for at least the next twelve months from the date the audited consolidated financial statements are issued.

Financial Overview

Revenue

Our revenue consists of upfront fees from the Option Agreement, which was recognized as revenue using an input method of performance completed to date comparing the total effort incurred with our estimate of total effort required to perform the R&D activities. All of the revenues recognized in the accompanying financial statements have been recognized from deferred revenue that existed at the beginning of the period. No future revenue exists under the Option Agreement.

Research and Development Expenses

Research and development expenses primarily consist of costs associated with our research activities, including the preclinical and clinical development of product candidates. We contract with clinical research organizations to manage our clinical trials under agreed upon budgets for each study, with oversight by our clinical program managers. All research and development costs are expensed as incurred.

Costs for certain research and development activities, such as manufacturing development activities and clinical studies are recognized based on the contracted amounts adjusted for the percentage of work completed to date. Payments for these activities are based on the terms of the contractual arrangements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheets as prepaid or accrued expenses. We defer and capitalize non-refundable advance payments made for research and development activities until the related goods are delivered or the related services are performed.

We expect to continue to incur substantial expenses related to development activities for the foreseeable future as we conduct clinical development, manufacturing and toxicology studies. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials, additional drug manufacturing requirements, and later stage toxicology studies such as carcinogenicity studies. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming. The probability of success for each product candidate is affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability. Accordingly, we may never succeed in achieving marketing approval for any of our product candidates.

Completion dates and costs for clinical development programs as well as our research program can vary significantly for each current and future product candidate and are difficult to predict. As a result, we cannot estimate with any degree of certainty the costs associated with development of our product candidates at this point in time. We anticipate making determinations as to which programs and product candidates to pursue and how much funding to direct to each program and product candidate on an ongoing basis in response to the scientific success of early research programs, results of ongoing and future clinical trials, our ability to enter into collaborative agreements with respect to programs or potential product candidates, as well as ongoing assessments as to the commercial potential of each current or future product candidate.

General and Administrative Expenses

General and administrative expenses consist primarily of the costs associated with general management, obtaining and maintaining our patent portfolio, professional fees for accounting, auditing, consulting and legal services, and general overhead expenses.

We expect ongoing general and administrative expenses to increase in the future as we expand our operating activities, maintain and expand the patent portfolio and incur additional costs associated with the management of a public company and maintain compliance with exchange listing and requirements of the SEC. These potential increases will likely include management costs, legal fees, accounting fees, directors' and officers' liability insurance premiums and expenses associated with investor relations, among others.

Other Income

Other income consists of bank and investment interest, research and development tax credits from the United Kingdom government's tax incentive programs set up to encourage research and development in the United Kingdom, and realized and unrealized exchange rate gains/losses on cash held in foreign currencies and transactions settled in foreign currencies.

Income Taxes

We historically have incurred net losses and had no corporation tax liabilities. We file U.S. Federal tax returns, as well as certain state returns. We also file returns in the United Kingdom. Under the U.K. government's research and development tax incentive scheme, we have incurred qualifying research and development expenses and filed claims for research and development tax credits in accordance with the relevant tax legislation. The research and development tax credits are paid out to us in cash and reported as other income.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States ("U.S. GAAP"). The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of our financial statements and the reported revenue and expenses during the reported periods. We evaluate these estimates and judgments, including those described below, on an ongoing basis. We base our estimates on historical experience, known trends and events, contractual milestones and 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. See also Note 2, Summary of Significant Accounting Policies to our Consolidated Financial Statements included in this Annual Report on Form 10-K, which discusses the significant assumptions used in applying our accounting policies. Those accounting policies and estimates that we deem to be critical are as follows:

Revenue Recognition

We recognize revenue from research and development arrangements. In accordance with Accounting Standards Codification ("ASC") 606, "Revenue from Contracts with Customers," revenue is recognized when a customer obtains control of promised goods or services. The amount of revenue recognized reflects the consideration to which we expect to be entitled to receive in exchange for these goods and services.

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, we must apply judgment to determine whether promised goods and services are capable of being distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

The transaction price is determined based on the consideration to which we will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, we estimate the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in our judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis unless the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The consideration to be received is allocated among the separate performance obligations based on relative standalone selling prices.

We satisfy performance obligations either over time or at a point in time. Revenue is recognized over time if either: (1) the customer simultaneously receives and consumes the benefits provided by the entity's performance, (2) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced or, (3) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer. ASC 606 requires us to select a single revenue recognition method for the performance obligation that faithfully depicts our performance in transferring control of the goods and services. The guidance allows for two methods to measure progress toward complete satisfaction of a performance obligation, depending on the facts and circumstances:

Output methods - recognize revenue on the basis of direct measurements of the value to the customer of the goods or services transferred to date relative to the remaining goods or services promised under the contract (e.g., surveys of performance completed to date, appraisals of results achieved, milestones reached, time elapsed, and units of produced or units delivered); and

Input methods - recognize revenue on the basis of the entity's efforts or inputs to the satisfaction of a performance obligation (e.g., resources consumed, labor hours expended, costs incurred, or time elapsed) relative to the total expected inputs to the satisfaction of that performance obligation.

Licenses of intellectual property: If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we must consider the nature of the intellectual property to which the customer will have rights (i.e., access at a point in time or benefit of intellectual property enhancements over time). We recognize revenue from non-refundable, up-front fees allocated to the license at a point in time or over the period the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined

performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes development and regulatory milestone payments for promised goods and services, we evaluate the circumstances of whether the milestones will be reached and estimates the amount to be included in the transaction price that will not cause a significant revenue reversal. With the expiration of the Option Agreement, there are no outstanding milestones.

Up-front payments: Up-front payments and fees are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until we perform our obligations under these arrangements. Amounts payable to us are recorded as accounts receivable when our right to consideration is unconditional. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

Preclinical and Clinical Trial Accruals

We base our accrued expenses related to clinical trials on estimates of patient enrollment and related expenses at clinical investigator sites as well as estimates for services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical trials on our behalf. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us and based on contracted amounts applied to the level of patient enrollment and activity according to the clinical trial protocol. 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.

If we do not identify costs that we have begun to incur, or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

Results of Operations

This section of this Annual Report on Form 10-K generally discusses fiscal years 2020 and 2019 items and year-to-year comparisons between fiscal years 2020 and 2019. Discussions of fiscal years 2019 items and year-to-year comparisons between fiscal years 2019 and 2018 that are not included in this Annual Report on Form 10-K can be found in Part II, Item 7 of our Annual Report on Form 10-K for the fiscal year ended April 30, 2019, which was filed with the SEC on July 16, 2019.

Year Ended April 30, 2020 Compared to Year Ended April 30, 2019

The following table sets forth the key components of our results of operations for the years ended April 30, 2020 and 2019:

	Years Ended April 30,		Increase
	2020	2019	(Decrease)
	(in thousands)		
Income			
Revenue	$ 12,690	$ 16,127	$ (3,437)
Operating Expenses			
Research and development expenses	40,194	35,021	5,173
General and administrative expenses	13,029	10,926	2,103
Other income			
Interest, exchange rate gain and other income	11,293	9,128	2,165

Revenue. Revenue was $12.7 million in the year ended April 30, 2020 compared to $16.1 million in the prior year. The decrease of $3.4 million was due to the decrease in the deferred revenue recognized and the expiration of the Option Agreement in February 2020. No future revenue remains under the Option Agreement.

Research and Development Expenses. Research and development expenses were $40.2 million in the year ended April 30, 2020 compared to $35.0 million in the prior year. The increase of $5.2 million was primarily due to an increase of $5.9 million in spending on KVD900 and an increase of $5.4 million in spending on preclinical activities. The increased costs were offset by a decrease of $5.5 million related to KVD001 and $0.7 million related to KVD824, compared to the prior year. The impact of exchange rates on research and development expenses was a decrease of approximately $1.0 million compared to the prior year, which is reflected in the figures above.

Research and development expenses by major programs or categories were as follows:

	Years Ended April 30,		Increase (Decrease)	
	2020	2019		
	(in thousands)			
KVD001	$ 4,719	$ 10,169	$ (5,450)	-54%
KVD900	10,441	4,529	5,912	131%
KVD824	4,857	5,583	(726)	-13%
Preclinical activities	20,177	14,740	5,437	37%
Total	$ 40,194	$ 35,021	$ 5,173	15%

We have changed the presentation of the research and development expenses by major program for the year ended April 30, 2020 compared to year ended April 30, 2019. We believe that the new categories more accurately reflect how we categorize and track our research and development spending.

Expenses for the KVD001 program decreased primarily due to the completion of the KVD001 Phase 2 clinical trial. We anticipate that expenses will continue to decline as we determine next steps for the program.

Expenses for the KVD900 program increased primarily due to the ongoing Phase 2 clinical trial as well as other non-clinical expenses for manufacturing and toxicology related to preparation for later stage development. We anticipate that these expenses will increase above current levels as we continue the Phase 2 trial and continue to prepare for later stage development of KVD900.

Expenses for the KVD824 program decreased primarily due to a decrease in toxicology expenses. We anticipate that the expenses for the KVD824 program will increase above current levels as we conduct further activities to support later stage development of KVD824 and initiate additional clinical trials.

Expenses for preclinical activities increased due to additional projects and increased headcount compared to the same period in the prior year. We anticipate that expenses will continue at or below current levels over the near term as a result of prioritization of our clinical activities.

General and Administrative Expenses. General and administrative expenses were $13.0 million in the year ended April 30, 2020 compared to $10.9 million in the prior fiscal year. The increase of $2.1 million was primarily due to an increase of $0.9 million in compensation related expenses, an increase of $0.4 million in commercial planning expenses, an increase of $0.3 million in professional fees, an increase of $0.3 million in insurance costs, an increase of $0.1 million in depreciation expense, and an increase of $0.1 million of other administrative expenses, compared to the prior year. We anticipate that expenses will continue at or above current levels as we continue to support the growth of the Company.

Other Income. Other income was $11.3 million for the year ended April 30, 2020 compared to $9.1 million in the prior fiscal year. The increase of $2.2 million was primarily due to an increase of $1.9 million in income from research and development tax credits, an increase in interest income of $0.4 million, an increase in realized gains from available for sale securities of $0.3 million, offset by a decrease in foreign currency exchange rate gains of $0.4 million from transactions denominated in foreign currencies in our U.K. subsidiary, compared to the prior year.

Liquidity and Capital Resources

We have incurred losses since inception and cash outflows from operating activities for the year ended April 30, 2020 and 2019. As of April 30, 2020, we had received cumulative equity funding totaling $155.9 million and revenue of $37.0 million from the Option Agreement. We had an accumulated deficit of $121.6 million as of April 30, 2020. We anticipate that we will continue to incur net losses for the foreseeable future as we continue the research and development efforts on our product candidates, hire additional staff, including clinical, scientific, operational and financial and management personnel.

Cash Flows

The following table shows a summary of the net cash flow activity for the years ended April 30, 2020 and 2019:

	Years Ended April 30,	
	2020	2019
	(in thousands)	
Cash flows used in operating activities	$ (44,816)	$ (36,365)
Cash flows provided by (used in) investing activities	16,753	(69,422)
Cash flows provided by financing activities	11,584	87,943
Effect of exchange rate changes on cash	262	(1,205)
Net decrease in cash and cash equivalents	$ (16,217)	$ (19,049)

Net cash used in operating activities

Net cash used in operating activities was $44.8 million for the year ended April 30, 2020 and primarily consisted of a net loss of $29.1 million adjusted for stock-based compensation of $4.4 million, an increase in the research and development tax credit receivable of $5.8 million, a decrease in deferred revenue of $12.7 million, and other changes in net working capital. The research and development tax credit receivable increased due to higher eligible spending compared to the prior year. Deferred revenue decreased due to the expiration of the Option Agreement and recognition of the remaining deferred revenue. Net cash used in operating activities was $36.4 million for the year ended April 30, 2019 and primarily consisted of a net loss of $20.8 million adjusted for stock-based compensation expense of $3.0 million, an increase in the research and development tax credit receivable of $4.9 million, a decrease in deferred revenue of $16.1 million, and other changes in net working capital. The increase in cash used in operating activities was due to increased spending, primarily on research and development activities during the year ended April 30, 2020 compared to the prior fiscal year.

Net cash provided by (used in) investing activities

Net cash provided by investing activities was $16.8 million for the year ended April 30, 2020 and consisted of sales and maturities of marketable securities of $66.8 million offset by purchases of marketable securities of $49.8 million and acquisitions of property and equipment of $0.2 million. Net cash used in investing activities was $69.4 million for the year ended April 30, 2019 and consisted of the purchase of marketable securities of $79.9 million and acquisitions of property and equipment of $1.1 million offset by sales and maturities of marketable securities of $11.5 million.

Net cash provided by financing activities

Net cash provided by financing activities was $11.6 million for the year ended April 30, 2020 and primarily consisted of the sale of common stock pursuant to an existing at-the-market sales agreement. Net cash provided by financing activities was $87.9 million for the year ended April 30, 2019 and primarily consisted of proceeds from the sale of common stock through a private placement transaction in August 2018 and a public offering in September 2018.

Operating Capital Requirements

To date, we have not generated any revenues from the sale of products, and we do not have any products that have been approved for commercialization. We do not expect to generate significant product revenue unless and until we obtain regulatory approval for, and commercialize, one of our current or future product candidates. We anticipate that we will continue to incur losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, product candidates, and begin to commercialize any approved products. We are subject to all of the risks inherent in the development of new therapeutic products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We currently anticipate that, based upon our operating plans and existing capital resources, we have sufficient funding to operate for at least the next 12 months.

Until such time, if ever, as we can generate substantial revenues, we expect to finance our cash needs through a combination of equity and debt financings, collaborations, strategic partnerships and licensing arrangements. To the extent that additional capital is raised through the sale of stock or convertible debt securities, the ownership interest of existing stockholders will be diluted, and the terms of these newly issued securities may include liquidation or other preferences that adversely affect the rights of common stockholders. Debt financing, if available, may involve agreements that include increased fixed payment obligations and covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends, selling or licensing intellectual property rights and other operating restrictions that could adversely impact our ability to conduct business. Additional fundraising through collaborations, strategic partnerships or licensing arrangements with third parties may require us to relinquish valuable rights to product candidates, including our other technologies, future revenue streams or research programs, or grant licenses on terms that may not be favorable. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate product development or future commercialization efforts or grant rights to develop and commercialize other product candidates even if we would otherwise prefer to develop and commercialize such product candidates internally.

Contractual Obligations and Commitments

We enter into contracts in the normal course of business with contract research organizations and clinical trial sites for the conduct of clinical trials, preclinical and clinical studies, professional consultants and other vendors for clinical supply manufacturing or other services. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments in Note 8, Commitments and Contingencies to the consolidated financial statements included in this Annual Report on Form 10-K. Contractual obligations related to the expected future costs to be incurred to complete the ongoing toxicology studies and clinical trials, which have cancellation provisions, total $3.6 million at April 30, 2020. There were no long-term debt payment obligations as of April 30, 2020.

The table below summarizes our non-cancelable lease commitments:

	Payments Due by Period (In thousands)				
Contractual Obligations	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
Lease obligations	$ 2,024	$ 679	$ 622	$ 284	$ 439

As a result of the terms of grant income received in prior years, upon successful regulatory approval and following the first commercial sale of certain products, we will be required to pay royalty fees of up to $1 million within 90 days of the first commercial sale of the product subject to certain caps and follow on payments depending upon commercial success and type of product. Given the stage of development of the current pipeline of products it is not possible to predict with certainty the amount or timing of any such liability.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Recent Accounting Pronouncements

For information regarding recent accounting pronouncements, please refer to Note 2, Summary of Significant Accounting Policies to our consolidated financial statements contained in this Annual Report on Form 10-K.

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

Interest Rate Risk

Because of the short-term nature of the bank deposit arrangements and the very low interest rates prevailing in the United Kingdom and the United States, a sudden change in market interest rates would not be expected to have a material impact on our financial condition and/or results of operations. We do not believe that our cash or cash equivalents have significant risk of default or illiquidity.

We invest in marketable securities in accordance with our investment policy. The primary objectives of our investment policy are to preserve capital, maintain proper liquidity to meet operating needs and maximize yields. We invest our excess cash in securities issued by financial institutions, commercial companies, and government agencies that management believes to be of high credit quality in order to limit the amount of credit exposure. Some of the securities we invest in may have market risk. This means that a change in prevailing interest rates may cause the principal amount of the investment to fluctuate.

Our investment exposure to market risk for changes in interest rates relates to the increase or decrease in the amount of interest income we can earn on our portfolio, changes in the market value due to changes in interest rates and other market factors as well as the increase or decrease in any realized gains and losses. Our investment portfolio includes only marketable securities and instruments with active secondary or resale markets to help ensure portfolio liquidity. An increase or decrease in interest rates along the entire interest rate yield curve would not significantly affect the fair value of our interest sensitive financial instruments, but may affect our future earnings and cash flows. We generally intend to hold our fixed income investments to maturity and therefore do not expect that our operating results, financial position or cash flows will be materially impacted due to a sudden change in interest rates. However, our future investment income may fall short of expectations due to changes in interest rates, or we may suffer losses in principal if forced to sell securities which have declined in market value due to changes in interest rates or other factors, such as changes in credit risk related to the securities' issuers. To minimize this risk, we schedule our investments to have maturities that coincide with our expected cash flow needs, thus avoiding the need to redeem an investment prior to its maturity date. Accordingly, we do not believe that we have material exposure to interest rate risk arising from our investments. We have not realized any significant losses from our investments.

Foreign Exchange Rate Risk

We maintain cash balances primarily in both U.S. Dollars ("USD") and British Pound Sterling ("GBP") to fund ongoing operations and manage foreign exchange risk. Cash, cash equivalents and marketable securities as of April 30, 2020 was composed of $15.8 million in cash and cash equivalents which consisted of readily available checking and bank deposit accounts held primarily in both USD and GBP and $51.9 million of USD denominated marketable securities. As of April 30, 2020, 75% of cash and cash equivalents were held in USD and 25% in GBP. We currently incur significant expense denominated in foreign currencies, primarily in GBP. We do not currently engage in exchange rate hedging or other similar activities to address our exchange rate risk. A 10% change in the exchange rate would result in an immaterial net gain or loss.

Effects of Inflation

We do not believe that inflation and changing prices had a significant impact on the results of operations for any periods presented herein.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed are listed in Item 15 of this Annual Report on Form 10-K and incorporated herein by reference.

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

As required by Rule 13a-15(b) under the Exchange Act of 1934, our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures as of April 30, 2020. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of April 30, 2020 our Chief Executive Officer and Chief Financial Officer have concluded that, as of April 30, 2020, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. GAAP. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management, with the participation of our principal executive officer and principal financial officer, assessed the effectiveness of our internal control over financial reporting as of April 30, 2020. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in its 2013 *Internal Control – Integrated Framework*. Based on our assessment, our management has concluded that, as of April 30, 2020, our internal control over financial reporting is effective based on those criteria.

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. Effective April 27, 2020, the SEC adopted amendments to the "accelerated filer" and "large accelerated filer" definitions in Rule 12b-2 under the Exchange Act. The amendments exclude from the accelerated and large accelerated filer definitions an issuer that is eligible to be a smaller reporting company and that had annual revenues of less than $100 million in the most recent fiscal year for which audited financial statements are available. We determined that our Company does not meet the accelerated or large accelerated filer definitions as of April 30, 2020. For as long as we remain a non-accelerated filer, we intend to take advantage of the exemption permitting us not to comply with the requirement under Section 404(b) of the Sarbanes-Oxley Act of 2002 that our independent registered public accounting firm provide an attestation on the management's assessment of the effectiveness of our internal control over financial reporting.

Changes in Internal Controls over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended April 30, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting, even though most of our employees are working remotely due to the COVID-19 pandemic. We are continually monitoring and assessing the COVID-19 pandemic on our internal controls to minimize the impact on the operating effectiveness.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by the Item is set forth in our 2020 Proxy Statement to be filed with the SEC within 120 days of April 30, 2020, and is incorporated by reference into this Annual Report on Form 10-K.

Item 11. Executive Compensation.

The information required by the Item is set forth in our 2020 Proxy Statement to be filed with the SEC within 120 days of April 30, 2020, and is incorporated by reference into this Annual Report on Form 10-K.

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

The information required by Item 403 of Regulation S-K is set forth in our 2020 Proxy Statement to be filed with the SEC within 120 days of April 30, 2020, and is incorporated by reference into this Annual Report on Form 10-K.

Securities Authorized for Issuance under Equity Compensation Plans

The following table provides information as of April 30, 2020, with respect to the shares of our common stock that may be issued under our existing equity compensation plans.

Plan Category	Number of Securities to be Issued upon Exercise of Outstanding Options, Warrants and Rights (a)	Weighted-average Exercise Price of Outstanding Options, Warrants and Rights (b)	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by stockholders (1)(2)	2,240,622	$ 13.53	1,217,413
Equity compensation plans not approved by stockholders (3)	80,055	$ 8.49	—
Total	2,320,677		1,217,413

(1) Includes 158,475 shares subject to options issued pursuant to the Carbylan 2015 Incentive Plan, 160,092 shares subject to options issued pursuant to the Enterprise Management Incentives Plan and 1,922,055 shares subject to options issued pursuant to the 2017 Equity Incentive Plan. The 2017 Equity Incentive Plan contains provisions that provide for automatic increases to the authorized number of shares as of January 1st of each year of the first ten calendar years during the term of such plan, by the lesser of (a) 4% of the issued and outstanding shares of stock on the last day of the immediately preceding calendar year and (b) such number of shares as approved by our board of directors. There are 942,122 shares available for future issuance under the 2017 Equity Incentive Plan as of April 30, 2020. In January 2019, the board of directors authorized the first offering period under the 2017 Employee Stock Purchase Plan to run from February 15, 2019 to June 30, 2019. All subsequent offering periods will run for six month periods ending June 30 and December 31 of each year. The 2017 Employee Stock Purchase Plan contains provisions that provide for automatic increases to the authorized number of shares as of January 1st for the first ten calendar years after the first Offering Date (as defined therein) by the number of shares equal to one percent of the total number of outstanding shares of common stock on the immediately preceding December 31 (rounded down to the nearest whole share) or a lesser number of shares determined by our board of directors. There are 275,291 shares of common stock available for future issuance under the 2017 Employee Stock Purchase Plan as of April 30, 2020.

(2) Shares reserved for issuance under the 2017 Equity Incentive Plan may be granted as restricted stock, restricted share units and other equity awards, as well as for grants of stock options and stock appreciation rights.

(3) Consists of options issued pursuant to inducement grants.

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

The information required by the Item is set forth in our 2020 Proxy Statement to be filed with the SEC within 120 days of April 30, 2020, and is incorporated by reference into this Annual Report on Form 10-K.

Item 14. Principal Accounting Fees and Services.

The information required by the Item is set forth in our 2020 Proxy Statement to be filed with the SEC within 120 days of April 30, 2020, and is incorporated by reference into this Annual Report on Form 10-K.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K:

(1) *Consolidated Financial Statements.* See Index to Financial Statements beginning on page F-1 of this Annual Report, which are incorporated by reference.

(2) *Financial Statement Schedules.* All schedules have been omitted because the information required to be presented in them is not applicable or is shown in the financial statements or related notes.

(3) *Exhibits.* We have filed, or incorporated into this Annual Report on Form 10-K by reference, the exhibits listed on the accompanying Exhibit Index.

(b) *Exhibits.*

Exhibit Number	Description of Document	Incorporated by reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
3.1	Amended and Restated Certificate of Incorporation.	8-K	001-36830	3.1	April 16, 2015	
3.2	Certificate of Amendment to the Restated Certificate of Incorporation.	8-K	001-36830	3.1	November 23, 2016	
3.3	Certificate of Amendment (Name Change) to the Restated Certificate of Incorporation.	8-K	001-36830	3.2	November 23, 2016	
3.4	Amended and Restated Bylaws, as amended as of June 10, 2020 (Redline version).					X
4.1	Form of Common Stock Certificate.	S-1/A	333-201278	4.2	January 23, 2015	
4.2	Registration Rights Agreement, dated June 15, 2016, by and among the Registrant and the Sellers.	8-K	001-36930	10.1	November 23, 2016	
4.3	Description of Registrant's Securities	10-K	001-36830	10.24	July 16, 2019	
10.1#	Form of Indemnification Agreement.	S-1	333-201278	10.14	December 29, 2014	
10.2#	Carbylan 2015 Incentive Plan and forms of award agreements.	S-1/A	333-201278	10.3	January 23, 2015	
10.3#	2017 Equity Incentive Plan.	DEF 14A	001-36830	Appendix A	March 2, 2017	
10.4#	2017 Employee Stock Purchase Plan.	DEF 14A	001-36830	Appendix B	March 2, 2017	
10.5#	Amended and Restated Employment Agreement between the Registrant and T. Andrew Crockett, dated June 26, 2019.	10-K	001-36830	10.5	July 16, 2019	
10.6#	Amended and Restated Employment Agreement between the Registrant and Benjamin L. Palleiko, dated June 26, 2019.	10-K	001-36830	10.6	July 16, 2019	
10.7#	Forms of Equity Agreements under the 2017 Equity Incentive Plan.	8-K	001-36830	99.1	June 29, 2018	
10.8	Office Lease Agreement by and between the Registrant and 55 Cambridge Parkway, LLC, dated May 30, 2017.	10-K	001-36830	10.12	July 27, 2017	

Exhibit Number	Description of Document	Incorporated by reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
10.9	Underlease by and between the Registrant and Wiltshire Council, dated April 30, 2018.	8-K	001-36830	10.1	May 2, 2018	
10.10#	Amended and Restated Executive Employment Agreement dated June 26, 2019, by and between the Registrant and Andreas Maetzel.	10-K	001-36830	10.13	July 16, 2019	
10.11#	Enrollment/Change Form under the 2017 Employee Stock Purchase Plan.	S-8	333-237059	99.4	March 10, 2020	
10.12#	Service Agreement dated November 1, 2015, by and between KalVista. Pharmaceuticals Ltd and Dr. Christopher M. Yea.	10-K	001-36830	10.15	July 30, 2018	
10.13#	Amendment, dated January 31, 2019, to the Service Agreement dated November 1, 2015 by and between KalVista. Pharmaceuticals Ltd and Dr. Christopher M. Yea.	10-Q	001-36830	10.1	March 14, 2019	
10.14#	Equity Acceleration Letter, dated March 11, 2019 by and between KalVista Pharmaceuticals Ltd and Dr. Christopher M. Yea.	10-Q	001-36830	10.2	March 14, 2019	
10.15	Sales Agreement dated March 29, 2019 by and between KalVista. Pharmaceuticals Ltd and Cantor Fitzgerald & Co.	8-K	001-36830	1.1	March 29, 2019	
10.16#	Amended and Restated Executive Employment Agreement by and between Registrant and Edward Feener.	10-K	001-36830	10.21	July 16, 2019	
10.17#	Executive Employment Agreement by and between Registrant and Michael Smith.	10-K	001-36830	10.22	July 16, 2019	
10.18#	Amendment, dated June 26, 2019, to the Service Agreement dated November 1, 2015 by and between KalVista. Pharmaceuticals Ltd and Dr. Christopher M. Yea.	10-K	001-36830	10.23	July 16, 2019	
21.1	Subsidiaries of the Registrant.					X
23.1	Consent of Deloitte & Touche LLP.					X
24.1	Power of Attorney. (See signature page hereto.)					X
31.1	Certification of Principal Executive Officer, pursuant to Rule 13a-14(a)/15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
31.2	Certification of Principal Financial Officer, pursuant to Rule 13a-14(a)/15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
32.1*	Certification of Chief Executive Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X

Exhibit Number	Description of Document	Incorporated by reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
32.2*	Certification of Chief 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	XBRL Instance Document.					X
101.SCH	XBRL Taxonomy Extension Schema Document.					X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document.					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.					X

Management contract or compensatory plan or arrangement.

* This certification is deemed not filed for purpose 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 or the Exchange Act.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

KalVista Pharmaceuticals, Inc.

Date: July 1, 2020

By: /s/ T. Andrew Crockett
T. Andrew Crockett
Chief Executive Officer

Date: July 1, 2020

By: /s/ Benjamin L. Palleiko
Benjamin L. Palleiko
Chief Business Officer and Chief Financial Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Thomas Andrew Crockett and Benjamin L. Palleiko, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ T. Andrew Crockett T. Andrew Crockett	Chief Executive Officer and Director (Principal Executive Officer)	July 1, 2020
/s/ Benjamin L Palleiko Benjamin L. Palleiko	Chief Business Officer and Chief Financial Officer (Principal Financial and Accounting Officer)	July 1, 2020
/s/ Martin Edwards Martin Edwards, M.D.	Director and Chairman	July 1, 2020
/s/ Albert Cha Albert Cha, M.D., Ph.D.	Director	July 1, 2020
/s/ Arnold Oronsky Arnold L. Oronsky, Ph.D.	Director	July 1, 2020
/s/ Brian J.G. Pereira Brian J.G. Pereira, M.D.	Director	July 1, 2020
/s/ Daniel Soland Daniel Soland	Director	July 1, 2020
/s/ Edward W. Unkart Edward W. Unkart	Director	July 1, 2020

KALVISTA PHARMACEUTICALS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of KalVista Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of KalVista Pharmaceuticals, Inc. and subsidiaries (the "Company") as of April 30, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows for each of the three years in the period ended April 30, 2020, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of April 30, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended April 30, 2020, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

/s/ Deloitte & Touche LLP

Boston, Massachusetts
July 1, 2020

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

KALVISTA PHARMACEUTICALS, INC.
Consolidated Balance Sheets
April 30, 2020 and 2019
(in thousands except share and per share amounts)

	2020	2019
Assets		
Current assets:		
Cash and cash equivalents	$ 15,789	$ 32,006
Marketable securities	51,925	68,805
Research and development tax credit receivable	16,527	11,315
Prepaid expenses and other current assets	4,455	3,420
Total current assets	88,696	115,546
Property and equipment, net	2,043	2,413
Right of use assets	1,612	—
Other assets	178	173
Total assets	$ 92,529	$ 118,132
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,677	$ 2,860
Accrued expenses	5,455	5,647
Deferred revenue - current portion	—	9,545
Lease liability - current portion	588	—
Total current liabilities	7,720	18,052
Long-term liabilities:		
Deferred revenue - net of current portion	—	3,342
Lease liability - net of current portion	1,057	—
Total long-term liabilities	1,057	3,342
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Common stock, $0.001 par value, 100,000,000 authorized		
Shares issued and outstanding: 17,845,599 at April 30, 2020 and 17,277,750 at April 30, 2019	18	17
Additional paid-in capital	207,208	191,123
Accumulated deficit	(121,592)	(92,476)
Accumulated other comprehensive loss	(1,882)	(1,926)
Total stockholders' equity	83,752	96,738
Total liabilities and stockholders' equity	$ 92,529	$ 118,132

See notes to consolidated financial statements.

KALVISTA PHARMACEUTICALS, INC.
Consolidated Statements of Operations and Comprehensive Loss
Years Ended April 30, 2020, 2019 and 2018
(in thousands, except share and per share amounts)

	2020	2019	2018
Revenue	$ 12,690	$ 16,127	$ 8,394
Operating expenses:			
Research and development	40,194	35,021	18,237
General and administrative	13,029	10,926	8,862
Total operating expenses	53,223	45,947	27,099
Operating loss	(40,533)	(29,820)	(18,705)
Other income:			
Interest income	1,830	1,397	82
Foreign currency exchange gain (loss)	(367)	49	(1,574)
Other income	9,830	7,682	4,392
Total other income	11,293	9,128	2,900
Loss before income taxes	(29,240)	(20,692)	(15,805)
Income tax (benefit) expense	(124)	124	—
Net loss	$ (29,116)	$ (20,816)	$ (15,805)
Other comprehensive income (loss):			
Foreign currency translation adjustments	59	(1,257)	1,534
Unrealized holding gains on available-for-sale securities	285	440	—
Reclassification adjustment for realized (gain) on available for sale securities included in net loss	(300)	—	—
Comprehensive loss	$ (29,072)	$ (21,633)	$ (14,271)
Net loss per share to common stockholders, basic and diluted	$ (1.64)	$ (1.38)	$ (1.53)
Weighted average common shares outstanding, basic and diluted	17,748,666	15,080,863	10,321,780

See notes to consolidated financial statements.

KALVISTA PHARMACEUTICALS, INC.
Consolidated Statements of Changes in Stockholders' Equity
Years Ended April 30, 2020, 2019 and 2018
(in thousands, except share and per share amounts)

	Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Loss	Equity
Balance at May 1, 2017	9,713,042	$ 10	$ 89,815	$ (55,855)	$ (2,643)	$ 31,327
Issuance of ordinary shares	1,070,589	1	9,100	—	—	9,101
Issuance of common stock from exercise of stock options	16,264	—	36	—	—	36
Stock-based compensation expense	—	—	1,060	—	—	1,060
Net loss	—	—	—	(15,805)	—	(15,805)
Foreign currency translation adjustment	—	—	—	—	1,534	1,534
Balance at April 30, 2018	10,799,895	11	100,011	(71,660)	(1,109)	27,253
Issuance of common stock	6,382,320	6	87,904	—	—	87,910
Issuance of common stock from exercise of stock options	95,535	—	242	—	—	242
Stock-based compensation expense	—	—	2,966	—	—	2,966
Net loss	—	—	—	(20,816)	—	(20,816)
Foreign currency translation adjustment	—	—	—	—	(1,257)	(1,257)
Unrealized holding gains from available-for-sale securities, net of reclassification for realized gains	—	—	—	—	440	440
Balance at April 30, 2019	17,277,750	17	191,123	(92,476)	(1,926)	96,738
Issuance of common stock, net of issuance costs of $123	527,221	1	11,421	—	—	11,422
Issuance of common stock from exercise of stock options	40,628	—	216	—	—	216
Stock-based compensation expense	—	—	4,448	—	—	4,448
Net loss	—	—	—	(29,116)	—	(29,116)
Foreign currency translation adjustment	—	—	—	—	59	59
Unrealized holding gains from available for sale securities	—	—	—	—	285	285
Reclassification adjustment for realized (gain) on available-for-sale securities included in net loss	—	—	—	—	(300)	(300)
Balance at April 30, 2020	17,845,599	$ 18	$207,208	$ (121,592)	$ (1,882)	$ 83,752

See notes to consolidated financial statements.

KALVISTA PHARMACEUTICALS, INC.
Consolidated Statements of Cash Flows
Years Ended April 30, 2020, 2019 and 2018
(in thousands)

	2020	2019	2018
Cash flows from operating activities:			
Net loss	$ (29,116)	$ (20,816)	$ (15,805)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:			
Depreciation and amortization	512	378	180
Stock-based compensation expense	4,448	2,966	1,060
Realized gain from sale of marketable securities	(300)	(23)	—
Non-cash operating lease expense	13	—	—
Amortization of premium on available for sale securities	193	—	—
Foreign currency exchange (gain) loss	74	(80)	(651)
Changes in operating assets and liabilities:			
Research and development tax credit receivable	(5,781)	(4,883)	(4,256)
Grants and other receivables	—	—	319
Prepaid expenses and other current assets	(1,112)	(1,979)	(746)
Other assets	(5)	—	(123)
Accounts payable	(1,004)	1,534	217
Accrued expenses	(48)	2,665	1,132
Deferred revenue	(12,690)	(16,127)	29,231
Net cash (used in) provided by operating activities	(44,816)	(36,365)	10,558
Cash flows from investing activities:			
Purchases of available for sale securities	(49,797)	(79,889)	—
Sales and maturities of available for sale securities	66,770	11,548	—
Acquisition of property and equipment	(220)	(1,081)	(1,427)
Net cash provided by (used in) investing activities	16,753	(69,422)	(1,427)
Cash flows from financing activities:			
Issuance of common stock, net of offering expenses	11,422	87,910	9,137
Issuance of common stock from equity incentive plans	216	242	—
Finance lease principal payments	(54)	(209)	(151)
Net cash provided by financing activities	11,584	87,943	8,986
Effect of exchange rate changes on cash and cash equivalents	262	(1,205)	1,988
Net (decrease) increase in cash and cash equivalents	(16,217)	(19,049)	20,105
Cash and cash equivalents, beginning year	32,006	51,055	30,950
Cash and cash equivalents, end of year	$ 15,789	$ 32,006	$ 51,055
Supplemental disclosures of cash flow information:			
Right of use assets obtained in exchange for operating lease liabilities	$ 309	$ —	$ —
Capital leases	$ —	$ —	$ 513
Acquisition of property and equipment in accounts payable	$ —	$ —	$ 291

See notes to consolidated financial statements.

Note 1. Description of Business and Basis of Presentation

KalVista Pharmaceuticals, Inc. (together with its subsidiaries, "KalVista" or the "Company") is a clinical stage pharmaceutical company focused on the discovery, development and commercialization of small molecule protease inhibitors for diseases with significant unmet need. The Company's first product candidates are inhibitors of plasma kallikrein being developed for two indications: hereditary angioedema ("HAE") and diabetic macular edema ("DME"). The Company applies its insights into the chemistry of proteases and, with current programs, the biology of the plasma kallikrein system, to develop small molecule inhibitors with high selectivity, potency and bioavailability that it believes will make them successful treatments for HAE and DME.

KalVista has created a structurally diverse portfolio of oral plasma kallikrein inhibitors and advanced multiple drug candidates into clinical trials in order to create best-in-class oral therapies for both HAE and DME. The Company is currently evaluating KVD900 in a Phase 2 clinical study as a potential on-demand therapy for acute HAE attacks, which is expected to complete in the second half of 2020. KVD824 is KalVista's next oral program to be developed for HAE, and the Company plans to commence a Phase 2 clinical trial intended to evaluate KVD824 as a twice-daily potential oral prophylactic treatment for HAE in the second half of 2020. In the case of DME, the Company is initially developing a plasma kallikrein inhibitor which is administered directly into the eye and anticipates ultimate development of orally delivered drugs.

The KVD001 program, which was the lead DME candidate, as well as KalVista's planned future oral DME programs were subject to an option agreement with Merck Sharpe & Dohme Corp. ("Merck") entered into in 2017 (the "Option Agreement"). Under the terms of the Option Agreement, Merck had a defined period following receipt of a clinical data package including the results of the Phase 2 trial for KVD001, which were announced in December 2019, to determine whether to exercise its option to acquire KVD001 and to maintain its option on the oral DME programs. In February 2020, Merck notified the Company that those options would not be exercised. As a result, KalVista has retained all the rights and intellectual property that were subject to the Option Agreement, Merck has no further rights or obligations to the Company and the Company has no obligations to Merck.

The Company's headquarters is located in Cambridge, Massachusetts, with research activities located in Porton Down, United Kingdom and Boston, Massachusetts.

The Company has devoted substantially all of its efforts to research and development, including clinical trials of its product candidates. The Company has not completed the development of any product candidates. Pharmaceutical drug product candidates, like those being developed by the Company, require approvals from the U.S. Food and Drug Administration ("FDA") or foreign regulatory agencies prior to commercial sales. There can be no assurance that any product candidates will receive the necessary approvals and any failure to receive approval or delay in approval may have a material adverse impact on the Company's business and financial results. The Company has not yet commenced commercial operations. The Company is subject to a number of risks and uncertainties similar to those of other life science companies developing new products, including, among others, the risks related to the necessity to obtain adequate additional financing, to successfully develop product candidates, to obtain regulatory approval of product candidates, to comply with government regulations, to successfully commercialize its potential products, to the protection of proprietary technology and to the dependence on key individuals.

The Company has funded its operations primarily through the issuance of stock and the Option Agreement. As of April 30, 2020, the Company had an accumulated deficit of $121.6 million and cash, cash equivalents and marketable securities totaling $67.7 million. The Company's working capital, primarily cash and marketable securities, is anticipated to fund the Company's operations for at least 12 months beyond the date of issuance of the consolidated financial statements.

The Company will need to expend substantial resources for research and development, including costs associated with the clinical testing of its product candidates and will need to obtain additional financing to fund its operations and to conduct trials for its product candidates. The Company will seek to finance future cash needs through equity offerings, future grants, corporate partnerships and product sales.

The Company has never been profitable and has incurred significant operating losses in each year since inception. Cash requirements may vary materially from those now planned because of changes in the Company's focus and direction of its research and development programs, competitive and technical advances, patent developments, regulatory changes or other developments. Additional financing will be required to continue operations after the Company exhausts its current cash resources and to continue its long-term plans for clinical trials and new product development. There can be no assurance that any such financing can be obtained by the Company, or if obtained, what the terms thereof may be, or that any amount that the Company is able to raise will be adequate to support the Company's working capital requirements until it achieves profitable operations. If adequate additional working capital is not secured when needed, the Company may be required to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible and/or suspend or curtail planned research programs. Any of these actions could materially harm the Company's business and prospects.

The outbreak of COVID-19 has evolved into a global pandemic. The extent of the impact of COVID-19 on the Company's operational and financial performance will depend on certain developments, including the duration and spread of the outbreak, impact on clinical studies, employee or industry events, and effect on suppliers and manufacturers, or impact on the healthcare systems, all of which are uncertain and cannot be predicted. The Company has experienced and may continue to experience constrained supplies of product candidates or, with respect to the Company's clinical trials, delays in enrollment, site initiation, participant dosing, distribution of clinical trial materials, study monitoring and data analysis that could materially adversely impact the Company's business, results of operations and overall financial performance in future periods. Any such delays to the Company's planned clinical timelines for KVD900 and KVD824 could also impact the use and sufficiency of existing cash reserves, and the Company may be required to raise additional capital earlier than previously planned. The Company may be unable to raise additional capital if and when needed, which may result in further delays or suspension of our development plans. The extent to which COVID-19 may impact the Company's financial condition, results of operations or cash flows is uncertain. The impact of COVID-19 could have a material adverse impact on the Company's operations and will continue to be monitored closely.

Note 2. Summary of Significant Accounting Policies

Principles of consolidation: The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Use of estimates: The preparation of consolidated financial statements in conformity with U.S. generally accepted accounting principles ("U.S. GAAP") requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, and disclosure of contingent assets and liabilities, at the date of the consolidated financial statements, and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from these estimates.

Foreign currency: The functional currency of the Company's UK subsidiary is the British Pound Sterling. Assets and liabilities of the foreign subsidiary are translated using the exchange rate existing on each respective balance sheet date. Revenues and expenses are translated using average exchange rates prevailing throughout the year. The translation adjustments resulting from this process are included as a component of the accumulated other comprehensive loss. In addition, the Company engages in transactions and holds balances denominated and settled in currencies other than the functional currency, and transaction gains or losses are recorded in the consolidated statement of operations.

Segment Reporting: The chief operating decision maker, the CEO, manages the Company's operations as a single operating segment for the purposes of assessing performance and making operating decisions.

Cash and cash equivalents: Cash and cash equivalents consist of bank deposits and money market accounts. Cash equivalents are carried at cost which approximates fair value due to their short-term nature. The Company considers all highly-liquid investments with an original maturity of 90 days or less to be cash equivalents.

The Company maintains its cash and cash equivalent balances with financial institutions that management believes are of high credit quality. The Company's cash and cash equivalent accounts at times may exceed federally insured limits. The Company has not experienced any losses in such accounts. The Company believes it is not exposed to any significant credit risk of cash and cash equivalents.

Research and development tax credit receivable: The research and development tax credit receivable consists of research and development expenses that have been claimed as research and development tax credits in accordance with the relevant U.K. tax legislation. These refundable tax credits are payable to the Company in cash and are carried on the consolidated balance sheet at the amount claimed and expected to be received from the U.K. government within the next 12 months.

Property and equipment: Property and equipment are stated at cost less accumulated depreciation. Expenditures for repairs and maintenance are charged to expense as incurred. Upon retirement or sale, the costs of the assets disposed of and the related accumulated depreciation are eliminated from the accounts and any resulting gain or loss is reflected in the statement of operations. Depreciation is provided using the straight-line method over the estimated useful lives of the assets, which are as follows:

Asset Classification	Estimated Useful Life
Machinery and equipment	1-5 Years
Computer equipment	3-4 Years
Motor vehicles	4 Years
Leasehold improvements	5 Years or term of lease, if shorter

The Company assesses the impairment of long-lived assets whenever events or changes in circumstances indicate that the carrying value of such assets, or asset groups, may not be recoverable. Whenever events or changes in circumstances suggest that the carrying amount of long-lived assets may not be recoverable, the future undiscounted cash flows expected to be generated by the asset, or asset groups, from its use or eventual disposition is estimated. If the sum of the expected future undiscounted cash flows is less than the carrying amount of those assets, or asset groups, an impairment loss is recognized based on the excess of the carrying amount over the fair value of the assets, or asset groups.

Revenue recognition: The Company recognizes revenue from research and development arrangements. In accordance with Accounting Standards Codification ("ASC") 606, "*Revenue from Contracts with Customers*," revenue is recognized when a customer obtains control of promised goods or services. The amount of revenue recognized reflects the consideration to which the Company expects to be entitled to receive in exchange for these goods and services.

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, the Company must apply judgment to determine whether promised goods and services are capable of being distinct and distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in the Company's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis unless the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The consideration to be received is allocated among the separate performance obligations based on relative standalone selling prices.

The Company satisfies performance obligations either over time or at a point in time. Revenue is recognized over time if either: (1) the customer simultaneously receives and consumes the benefits provided by the entity's performance, (2) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced or (3) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer. ASC 606 requires the Company to select a single revenue recognition method for the performance obligation that faithfully depicts the Company's performance in transferring control of the goods and services. The guidance allows for two methods to measure progress toward complete satisfaction of a performance obligation, depending on the facts and circumstances:

Output methods - recognize revenue on the basis of direct measurements of the value to the customer of the goods or services transferred to date relative to the remaining goods or services promised under the contract (e.g., surveys of performance completed to date, appraisals of results achieved, milestones reached, time elapsed, and units of produced or units delivered); and

Input methods - recognize revenue on the basis of the entity's efforts or inputs to the satisfaction of a performance obligation (e.g., resources consumed, labor hours expended, costs incurred, or time elapsed) relative to the total expected inputs to the satisfaction of that performance obligation.

Licenses of intellectual property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company must consider the nature of the intellectual property to which the customer will have rights (i.e., access at a point in time or benefit of intellectual property enhancements over time). The Company recognizes revenue from non-refundable, up-front fees allocated to the license at a point in time/over the period the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the measure of progress at each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes development and regulatory milestone payments for promised goods and services, the Company evaluates the circumstances of whether the milestones will be reached and estimates the amount to be included in the transaction price that will not cause a significant revenue reversal. Upon expiration of the Option Agreement, there are no outstanding milestones that can be reached.

Up-front payments: Up-front payments and fees are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until the Company performs its obligations under these arrangements. Amounts payable to the Company are recorded as accounts receivable when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

Contract Balances: The Company recognizes a contract asset when the Company transfers goods or services to a customer before the customer pays consideration or before payment is due, excluding any amounts presented as a receivable (i.e., accounts receivable). A contract asset is an entity's right to consideration in exchange for goods or services that the entity has transferred to a customer. The contract liabilities (i.e., deferred revenue) primarily relate

to contracts where the Company has received payment but has not yet satisfied the related performance obligations. The advance consideration received from customers for research and development services and/or licenses is a contract liability, recorded as deferred revenue, until the underlying performance obligations are transferred to the customer.

Research and development: Research and development costs are expensed as incurred and include, but are not limited to:

- Employee-related expenses including salaries, benefits, travel, and share-based compensation expense for research and development personnel;
- Costs associated with preclinical and development activities;
- Costs associated with regulatory operations.

Costs for certain research and development activities, such as manufacturing development activities and clinical studies are recognized based on the contracted amounts adjusted for the percentage of work completed to date. Payments for these activities are based on the terms of the contractual arrangements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheets as prepaid or accrued expenses. The Company defers and capitalizes non-refundable advance payments made by the Company for research and development activities until the related goods are delivered or the related services are performed.

Income taxes: The Company accounts for income taxes using an asset and liability approach. Under this method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective income tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The Company evaluates the realizability of its deferred tax assets and establishes a valuation allowance when it is more likely than not that all or a portion of deferred tax assets will not be realized. The Company has provided a full valuation allowance on its deferred tax assets.

Relative to accounting for uncertainties in tax positions, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. For those tax positions where it is more likely than not that a tax benefit will be sustained, the Company records the largest amount of tax benefit with a greater than 50% likelihood of being realized upon ultimate settlement with a taxing authority having full knowledge of all relevant information. For those income tax positions where it is not more likely than not that a tax benefit will be sustained, the Company does not recognize a tax benefit in the financial statements.

The Company recognizes interest and penalties related to uncertain tax positions, if any, as a component of income tax expense. As the Company has no uncertain tax positions, there were no interest or penalties charges recognized in the statement of operations for any years.

Stock-based compensation: The Company accounts for stock-based compensation arrangements at fair value. The fair value is recognized over the period during which the recipient is required to provide services (usually the vesting period), on a straight-line basis. Forfeitures are recognized as they are incurred.

Net Loss per Share: Basic net loss per share is computed by dividing the net loss by the weighted average number of common shares outstanding during the period. Diluted net loss per share is computed by dividing net loss by the sum of the weighted average number of common shares and the number of potential dilutive common share equivalents outstanding during the period. Potential dilutive common share equivalents consist of the incremental common shares issuable upon the exercise of share options and awards.

Potential dilutive common share equivalents consist of:

	April 30,		
	2020	2019	2018
Stock options and awards	2,320,677	1,784,338	388,366

In computing diluted earnings per share, common share equivalents are not considered in periods in which a net loss is reported, as the inclusion of the common share equivalents would be anti-dilutive. As a result, there is no difference between the Company's basic and diluted loss per share in the periods presented.

Fair value measurement: The Company classifies fair value measurements using a three level hierarchy that prioritizes the inputs used to measure fair value. This hierarchy requires entities to maximize the use of observable inputs and minimize the use of unobservable inputs. The three levels of inputs used to measure fair value are as follows: Level 1, quoted market prices in active markets for identical assets or liabilities; Level 2, observable inputs other than quoted market prices included in Level 1, such as quoted market prices for markets that are not active or other inputs that are observable or can be corroborated by observable market data; and 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, including certain pricing models, discounted cash flow methodologies and similar techniques that use significant unobservable inputs. These fair values are obtained from independent pricing services, which utilize Level 1 and Level 2 inputs.

The following tables summarize the cash equivalents and marketable securities measured at fair value on a recurring basis as of April 30, 2020 and 2019:

	Level 1	Level 2	Level 3	Balance at April 30, 2020
Cash equivalents	$ 650	$ —	$ —	$ 650
Marketable securities:				
Corporate debt securities	—	39,216	—	39,216
U.S. government agency securities	—	12,709	—	12,709
	$ 650	$ 51,925	$ —	$ 52,575

	Level 1	Level 2	Level 3	Balance at April 30, 2019
Cash equivalents	$ 30,044	$ 1,962	$ —	$ 32,006
Marketable securities:				
Corporate debt securities	—	56,487	—	56,487
U.S. government agency securities	—	12,318	—	12,318
	$ 30,044	$ 70,767	$ —	$ 100,811

Recently adopted accounting pronouncements: The Company adopted ASC 842, *Leases* ("ASC 842"), using the modified retrospective approach, effective May 1, 2019. The Company elected the package of practical expedients permitted under the transition guidance within the new standard which allows the Company to not reassess previous accounting conclusions around whether arrangements are or contain leases, the classification of its existing leases as of the transition date, and the treatment of initial direct costs. In addition, the Company elected the practical expedient not to apply the recognition requirements in the lease standard to short-term leases (a lease that at commencement date has a lease term of 12 months or less and does not contain a purchase option that the lessee is reasonably certain to exercise) and the practical expedient that permits lessees to make an accounting policy election (by class of underlying asset) to account for each separate lease component of a contract and its associated non-lease components as a single lease component.

As a result of the adoption of the new lease accounting standard, the Company recognized operating lease assets and operating lease liabilities of $1.9 million, respectively on May 1, 2019. The adoption of the standard had no impact to the Company's consolidated statement of operations or cash flows.

Note 3. Marketable Securities

The objectives of the Company's investment policy are to ensure the safety and preservation of invested funds, as well as to maintain liquidity sufficient to meet cash flow requirements. The Company invests its excess cash in securities issued by financial institutions, commercial companies, and government agencies that management believes to be of high credit quality in order to limit the amount of its credit exposure. The Company has not realized any significant losses from its investments.

The Company classifies all of its investments as available for sale. Unrealized gains and losses on investments are recognized in accumulated comprehensive loss, unless an unrealized loss is considered to be other than temporary, in which case the unrealized loss is charged to operations. The Company periodically reviews its investments for other than temporary declines in fair value below cost basis and whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. The Company believes the individual unrealized losses represent temporary declines primarily resulting from interest rate changes. Realized gains and losses are included in other income in the consolidated statements of operations and comprehensive loss and are determined using the specific identification method with transactions recorded on a trade date basis.

The following tables summarize the fair value of the Company's investments by type as of April 30, 2020 and 2019:

	April 30, 2020			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Corporate debt securities	$ 38,922	$ 295	$ (1)	$ 39,216
Obligations of the U.S. Government and its agencies	12,534	175	—	12,709
Total investments	$ 51,456	$ 470	$ (1)	$ 51,925

	April 30, 2019			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Corporate debt securities	$ 56,083	$ 405	$ (1)	$ 56,487
Obligations of the U.S. Government and its agencies	12,282	36	—	12,318
Total investments	$ 68,365	$ 441	$ (1)	$ 68,805

The following table summarizes the scheduled maturity for the Company's investments at April 30, 2020:

	April 30, 2020
Maturing in one year or less	$ 32,391
Maturing after one year through two years	11,698
Maturing after two years	7,836
Total investments	$ 51,925

Note 4. Property and Equipment

At April 30, 2020 and 2019, property and equipment consisted of (in thousands):

	2020	2019
Laboratory equipment	$ 1,543	$ 1,391
Office equipment	36	36
Furniture & fixtures	185	175
Leasehold improvements	1,647	1,707
Total property and equipment at cost	3,411	3,309
Less: Accumulated depreciation	(1,368)	(896)
Property and equipment, net	$ 2,043	$ 2,413

For the years ended April 30, 2020, 2019 and 2018, depreciation expense was $512,000, $378,000 and $180,000, respectively.

Note 5. Accrued Expenses

At April 30, 2020 and 2019, accrued expenses consisted of (in thousands):

	2020	2019
Accrued research expense	$ 2,821	$ 3,065
Accrued compensation	2,333	1,949
Accrued professional fees	173	186
Other accrued expenses	128	447
Total accrued expenses	$ 5,455	$ 5,647

Note 6. Merck Arrangement

On October 6, 2017, the Company's wholly-owned U.K. based subsidiary KalVista Pharmaceuticals Limited ("KalVista Limited") and Merck entered into the Option Agreement. Under the terms of the Option Agreement, the Company, through KalVista Limited, granted to Merck an option to acquire KVD001 through a period following completion of a Phase 2 clinical trial. The Company, through KalVista Limited, also granted to Merck a similar option to acquire investigational orally delivered molecules for DME (the "Oral DME Compounds") through a period following the completion of a Phase 2 clinical trial. The Company, through KalVista Limited, also granted to Merck a non-exclusive license to use the compounds solely for research purposes, and was required to use its diligent efforts to develop the two compounds through the completion of Phase 2 clinical trials. The Company's development efforts under the Option Agreement were governed by a joint steering committee consisting of equal representatives from the Company and Merck.

Under the terms of the Option Agreement, Merck paid a non-refundable upfront fee of $37 million to KalVista Limited in November 2017.

The Company evaluated the revenue arrangement in accordance with the provisions of ASC 606 upon the adoption of this guidance on May 1, 2018. The Company determined that the revenue arrangement contained the following promised services: (i) a non-exclusive license to use the two compounds solely for research purposes, (ii) research and development services related to the development of KVD001 through completion of a Phase 2 clinical trial, and (iii) research and development services related to the development of the Oral DME Compounds.

The Company further determined that the research license granted is not distinct from the respective research and development services, as the license could not be used on its own by Merck for its intended purpose of developing and commercializing KVD001 and the Oral DME Compounds and is significantly interdependent with the respective research and development services. As a result, the research license was combined with the respective research and development services for KVD001 and the Oral DME Compounds as two performance obligations.

The amounts allocated to each performance obligation were recognized as revenue using an input method of performance completed to date comparing the total effort incurred with the Company's estimate of total effort required to perform the R&D services for each respective performance obligation. For the fiscal years ended April 30, 2020, 2019 and 2018, the Company recognized approximately $12.7 million, $16.1 million, and $8.0 million of revenue with respect to the arrangement with Merck, all of which was recognized from the deferred revenue balance.

On February 10, 2020, the Company announced that the Option Agreement had expired. As a result of the expiration, KalVista has no further obligations to Merck. The Company has retained full ownership of all of its DME intellectual property in additional to its oral HAE portfolio. The Company concluded that the performance obligations were completed in the fourth quarter of the fiscal year ended April 30, 2020. As a result, the Company recognized the remaining $3.8 million of deferred revenue from the Option Agreement, after which no additional revenue remains.

Note 7. Stock-Based Compensation

The Company has three plans that provide for equity-based compensation. Two are legacy plans for which no further grants are to be made. As of April 30, 2020, 942,122 stock options remain available for grant under the 2017 Equity Incentive Plan ("2017 Plan"). There are 3,538,090 shares of the Company's common stock that are reserved for issuance upon exercise or settlement of stock options or other awards under all plans.

Initial awards generally vest 25% after one year and then ratably on a monthly basis over the next three years. Recurring grants typically vest on a monthly basis over four years. Stock option grants expire after ten years.

The Company recognizes stock-based compensation expense over the requisite service period based on the grant date fair value of the award. The Company has elected to use the Black-Scholes option pricing model to determine the fair value of awards granted. The determination of the fair value of stock-based awards utilizing the Black-Scholes model is affected by the share price and a number of assumptions, including expected volatility, expected life, risk-free interest rate and expected dividends. Due to insufficient history of the Company's stock price, the stock-price volatility assumption is based on the historical volatility of a peer group of publicly traded companies. The expected life of the awards is estimated based on the simplified method. The risk-free interest rate assumption is based on observed interest rates appropriate for the terms of the awards. The dividend yield assumption is based on history and expectation of paying no dividends. Forfeitures have not been material in the periods presented.

The fair value of the share-based awards was measured with the following weighted-average assumptions for the fiscal years ended April 30:

	2020	2019	2018
Risk-free interest rate	2.06	2.90	1.94
Expected life of the options	6.25 years	6.25 years	6.25 years
Expected volatility of the underlying stock	81.1%	77.2%	76.9%
Expected dividend rate	0%	0%	0%

Stock-based compensation was reflected in the Company's consolidated statement of operations and comprehensive loss as follows (in thousands):

	Year ended April 30,		
	2020	2019	2018
Research and development	$ 1,944	$ 2,005	$ 320
General and administrative	2,504	961	740
Total stock-based compensation expense	$ 4,448	$ 2,966	$ 1,060

A summary of option activity for the year ended April 30, 2020 and changes during the years then ended is presented below:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding at May 1, 2019	1,739,338	$ 9.95	8.47	$ 22,807
Exercised	(37,494)	4.39		
Granted	586,500	22.90		
Cancelled	(12,667)	19.89		
Outstanding at April 30, 2020	2,275,677	$ 13.32	7.83	$ 4,899
Exercisable at April 30, 2020	1,157,171	$ 9.73	7.25	$ 3,931
Vested and expected to vest at April 30, 2020	2,275,677	$ 13.32	7.83	$ 4,899

The weighted-average grant date fair value of stock options granted during the years ended April 30, 2020, 2019 and 2018 was $15.76, $9.62, and $4.87, respectively. The total intrinsic value (the amount by which the fair market value exceeded the exercise price) of stock options exercised during the years ended April 30, 2020, 2019 and 2018 was $431,000, $950,000 and $131,000, respectively. The total cash received by the Company as a result of employee stock option exercises during the years ended April 30, 2020, 2019 and 2018 was $216,000, $242,000, and $36,000, respectively. The Company has 45,000 performance-based restricted stock unit awards outstanding as of April 30, 2020. The performance period for these awards ends June 30, 2022.

As of April 30, 2020, there was $10.2 million of unrecognized compensation expense related to unvested awards, which is expected to be recognized over a weighted-average period of 2.3 years.

Note 8. Commitments and Contingencies

Clinical Studies: The Company enters into contractual agreements with contract research organizations in connection with preclinical and toxicology studies and clinical trials. Amounts due under these agreements are invoiced to the Company on predetermined schedules during the course of the studies and clinical trials and are not refundable regardless of the outcome. The Company has a contractual obligation related to the expected future costs to be incurred to complete the ongoing preclinical studies and clinical trials. The remaining commitments, which have cancellation provisions, totaled $3.6 million at April 30, 2020.

Indemnification: In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for general indemnification. The Company's exposure under these agreements is unknown because it involves future claims that may be made against the Company but have not yet been made. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. However, the Company may record charges in the future as a result of these indemnification obligations. No amounts associated with such indemnifications have been recorded to date.

Contingencies: From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business activities. The Company accrues a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. There were no contingent liabilities requiring accrual at April 30, 2020 and 2019.

As a result of the terms of grant income received in prior years, upon successful regulatory approval and following the first commercial sale of certain products, the Company will be required to pay royalty fees of up to $1 million within 90 days of the first commercial sale of the product subject to certain caps and follow on payments depending upon commercial success and type of product. Given the stage of development of the current pipeline of products it is not possible to predict with certainty the amount, if any or timing of any such liability.

Note 9. Leases

The Company has a lease agreement for approximately 2,700 square feet of space for its headquarters located in Cambridge, Massachusetts that commenced in September 2017 for a term of five years.

In April 2018, the Company entered into a lease agreement for approximately 8,800 square feet of office and research laboratory space located in Porton Down, United Kingdom for a term of ten years. In February 2020, the Company entered into a lease agreement, pursuant to which the Company leases approximately 4,600 square feet of additional office and research laboratory space located at the Porton Down facility for a term of eight years. The Company has the right to terminate the lease agreements on or after April 30, 2023. It is not likely that the Company will terminate either lease at that time, therefore the entire lease terms are included in the calculation of the lease liabilities. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew.

The Company is also party to several operating leases for office and laboratory space as well as certain lab equipment. Total rent expense was $743,000, $677,000 and $638,000 for the years ended April 30, 2020, 2019 and 2018, respectively and is reflected in general and administrative expenses and research and development expenses as determined by the underlying activities.

Incremental borrowing rate – The Company's lease agreements do not provide an implicit rate. The Company estimated the incremental borrowing rate based on the rate of interest the Company would have to pay to borrow a similar amount on a collateralized basis over a similar term and economic environment.

Lease and non-lease components – The Company has elected the practical expedient which allows non-lease components to be combined with lease components for all existing asset classes and will therefore include any fixed additional rent amounts in its lease payments. Any variable lease payments are excluded from the lease liability and are recognized in the period incurred.

The following table summarizes lease costs included in research and development and general and administrative expense for the year ended April 30, 2020 (in thousands):

	Year Ended April 30, 2020
Operating lease costs	$ 743
Finance lease costs	54
Short-term lease costs	13
Variable lease costs	47
Total lease costs	$ 857

The following table summarizes the maturity of undiscounted payments due under lease liabilities and the present value of those liabilities as of April 30, 2020 (in thousands):

Years ending April 30,	Operating Leases
2021	$ 679
2022	383
2023	239
2024	142
2025	142
Thereafter	439
Total lease payments	2,024
Less: imputed interest	379
Total lease liabilities	1,645
Current lease liabilities	588
Long-term lease liabilities	$ 1,057

Disclosures related to relevant periods prior to adoption of Topic 842:

Future minimum payments under these leases as of April 30, 2019 are as follows (in thousands):

Years ending April 30,	Finance Leases	Operating Leases
2020	$ 54	$ 687
2021	—	474
2022	—	328
2023	—	194
2024 and thereafter	—	495
Total minimum lease payments	$ 54	$ 2,178
Less amounts representing interest	—	
Present Value of minimum payments	54	
Current portion	54	
Long-term portion	$ —	

The following table summarizes the lease term and discount rate as of April 30, 2020:

	April 30, 2020
Weighted-average remaining lease term (years)	
Operating leases	4.8
Weighted-average discount rate	
Operating leases	9.0%

The following table summarizes the cash paid for amounts included in the measurement of lease liabilities for the year ended April 30, 2020 (in thousands):

	April 30, 2020
Cash paid for amounts included in the measurement of operating lease liabilities	$ 708
Cash paid for amounts included in the measurement of finance lease liabilities	$ 54

Note 10. Income Taxes

The components of the Company's loss before income taxes for the years ended April 30, 2020, 2019 and 2018 consisted of the following (in thousands):

	2020	2019	2018
Domestic	$ (6,337)	$ (5,006)	$ (4,020)
Foreign	(22,903)	(15,686)	(11,785)
	$ (29,240)	$ (20,692)	$ (15,805)

For the year ended April 30, 2020, the Company recorded a U.S. Federal income tax benefit of $124,000. For the year ended April 30, 2019, the Company recorded a U.S. Federal income tax expense of $124,000. Prior to fiscal year 2019, the company incurred net losses since inception and has not historically recorded a benefit or expense related to income taxes.

A reconciliation between the effective tax rates and statutory rates for the years ended April 30, is as follows:

	2020	2019	2018
Income tax benefit at U.S. federal statutory rate	21.0%	21.0%	30.4%
Foreign rate differential	(1.6)%	(0.9)%	(4.3)%
Nondeductible expenses - UK R&D credit	(12.1)%	(5.9)%	(16.3)%
Other	(0.5)%	(0.9)%	(4.5)%
Effect of change in tax rates	—	—	(3.6)%
Globl Intangible Low-Taxed Income ("GILTI")	—	(7.6)%	—
Valuation allowance	(6.6)%	(6.3)%	(1.7)%
	0.2%	(0.6)%	—

The tax effect of significant temporary differences representing deferred tax assets and liabilities as of April 30, 2020 and 2019 is as follows (in thousands):

	2020	2019
Net operating loss ("NOL") carryforwards	$ 7,367	$ 7,424
Other	2,162	968
Valuation allowance	(9,529)	(8,392)
Net deferred tax asset	$ —	$ —

Management of the Company has determined it is not more likely than not that the Company will recognize the benefits of net deferred tax assets, the majority of which are NOLs, and has provided a valuation allowance for the full amount of deferred tax assets as of as of April 30, 2020 and 2019, respectively. During the years ended April 30, 2020, 2019, and 2018 the valuation allowance changed by $1.1 million, $1.6 million and $1.0 million, respectively. Realization of deferred tax assets is dependent upon the generation of future taxable income.

As of April 30, 2020, the Company has NOL carryforwards for federal income taxes of $312,000 that begin to expire in 2024 and $1.7 million that can be carried forward indefinitely. The Company also has NOL carryforwards for state income taxes of $5.9 million that begin to expire in 2036 and NOL carryforwards for U.K. income taxes of $37.1 million that do not expire. The ability to utilize the Company's domestic net operating losses is limited due to changes in ownership as defined by Section 382 of the Internal Revenue Code (the "Code"). Under the provisions of Sections 382 and 383 of the Code, a change of control, as defined in the Code, imposes an annual limitation on the amount of the Company's net operating loss and tax credit carryforwards, and other tax attributes that can be used to reduce future tax liabilities. The Company determined that ownership changes occurred as a result of a transaction in November 2016 and a public offering in September 2018. As a result of these ownership changes, it is estimated that the effect of Section 382 will generally limit the amount of the net operating loss carryforwards that are available to offset future taxable income to approximately $5.0 million, annually.

The Company recognizes the financial statement effects of a tax position when it becomes more likely than not, based upon the technical merits, that the position will be sustained upon examination. The Company files U.S. Federal tax returns, as well as certain state returns. The Company also files returns in the United Kingdom. The Company is subject to U.S. Federal, state, and U.K. income tax examinations by authorities for tax years ending after 2015. There are currently no federal, state, or U.K. audits in process. Tax year 2016 and subsequent years contain matters that could be subject to differing interpretations of the applicable tax laws and regulations as it relates to the amount and or timing of income, deductions, and tax credits. Although the outcome of tax audits is always uncertain, management has analyzed the Company's tax positions taken for all open tax years and has concluded that no provision for unrecognized tax benefits from uncertain tax positions is required in the Company's consolidated financial statements for the years ended April 30, 2020 and 2019, respectively.

Note 11. Defined Contribution Plans

Participation in a personal pension plan is available to all U.K. based employees of the Company upon commencement of their employment. Employer contributions are made in accordance with the terms and conditions of the employment contract. Employees may contribute in accordance with the prevailing statutory limitations. Employees of the U.S. parent company are eligible to participate in the Company's 401(k) Plan. The Company matches up to 4% of employee contributions to the Plan. Total employer contributions to both plans for the years ended April 30, 2020, 2019 and 2018 were $314,000, $237,000 and $219,000 respectively.

Note 12. Other Income

As of April 30, 2020 and 2019, the Company had research and development tax credits receivable totaling $16.5 million and $11.3 million, respectively. This tax credit is related to a tax scheme for small and medium enterprises in the United Kingdom as well as an R&D expenditure credit system that allows the Company to file a claim for cash credit in proportion to the Company's R&D expenditure for the year. This amount is included in other income, as it is a refundable credit that does not depend on the Company's ongoing tax status or position. The Company recognized $9.5 million, $7.6 million and $4.4 million related to these programs in the years ended April 30, 2020, 2019 and 2018, respectively. In the year ended April 30, 2020, other income also included $0.3 million of realized gains from the sale of available for sale securities.

Note 13. Unaudited Quarterly Financial Information (in thousands):

Fiscal year 2020	Quarter ended July 31, 2019	Quarter ended October 31, 2019	Quarter ended January 31, 2020	Quarter ended April 30, 2020
Revenue	$ 3,369	$ 3,920	$ 1,577	$ 3,824
Operating expenses	12,933	13,209	14,301	12,781
Net loss	(7,338)	(5,903)	(9,291)	(6,585)
Net loss per share	$ (0.42)	$ (0.33)	$ (0.52)	$ (0.37)

Fiscal year 2019	Quarter ended July 31, 2018	Quarter ended October 31, 2018	Quarter ended January 31, 2019	Quarter ended April 30, 2019
Revenue	$ 3,718	$ 5,592	$ 3,890	$ 2,926
Operating expenses	10,727	10,485	10,550	14,186
Net loss	(5,030)	(3,304)	(3,956)	(8,526)
Net loss per share	$ (0.47)	$ (0.22)	$ (0.23)	$ (0.49)