

**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, 2023

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

(State or other jurisdiction of
incorporation or organization)

**55 Cambridge Parkway
Suite 901 East**

Cambridge, Massachusetts

(Address of principal executive offices)

20-0915291

(I.R.S. Employer
Identification No.)

02142

(Zip Code)

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

Securities registered pursuant to Section 12(g) of the Act

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

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

Non-accelerated filer

Accelerated filer

Smaller reporting company

Emerging growth company

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

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

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

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

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

The aggregate market value of common stock held by non-affiliates of the registrant calculated based on the closing price of \$5.07 of the registrant's common stock as reported on The NASDAQ Global Market on October 31, 2022, the last business day of the registrant's most recently completed second quarter, was \$119,620,059.

The number of shares of Registrant's Common Stock outstanding as of June 28, 2023 was 34,233,643.

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 2023. 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, 2023.

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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, macroeconomic conditions, including rising inflation and interest rates, labor shortages, supply chain issues, and global conflicts such as the war in Ukraine, 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. We apply our insights into the chemistry and biology of proteases to develop orally delivered therapeutics with high selectivity, potency and bioavailability that we believe will make them successful treatments for diseases. We have used these capabilities to develop novel, small molecule plasma kallikrein inhibitors targeting the disease hereditary angioedema (“HAE”). We also are conducting preclinical development on a novel, oral Factor XIIa (“Factor XIIa”) inhibitor program, which we are initially advancing to provide a next generation of HAE therapeutics and which also offers the opportunity for expansion into other high unmet need indications in the future.

HAE is a rare and potentially life-threatening, genetically-driven disease that features episodes of debilitating and often painful swelling in the skin, gastrointestinal tract or airways. Although multiple therapies have been approved for the disease, we believe people living with HAE are in need of alternatives that better meet their objectives for quality of life and ease of disease control. Other than one oral therapy approved for prophylaxis, currently marketed therapies are all administered by injection, which patients find challenging despite their efficacy because they are painful, time consuming to prepare and administer, and difficult to transfer and store. As a result, many attacks are treated too late to prevent significant symptoms, and a large percentage aren’t treated at all, leading to needless suffering. We anticipate that there will be strong interest in safe and effective, orally delivered 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 belief that our therapies could fundamentally transform the manner in which HAE is managed is based upon extensive and continuing research we conduct with patients, physicians and payers. Recently we have conducted research to further understand the process that people living with HAE follow when determining what therapy to use, how they treat their attacks and how often they do so. In our research, which we refer to as the HAE Attack Journey, we have discovered that people living with HAE carry their on-demand treatment only approximately 33% of the time and, for this reason and others, treat only about 50% of attacks. When patients do treat, we believe they tend to delay that treatment excessively for reasons including not having their treatment with them, injection-associated pain, and lack of a private area for treatment. As a result, our data indicate that a significant majority of patients experience attacks that are more severe and last longer than if they treated earlier. Patient surveys have indicated to us, in contrast, that if provided with an oral on-demand therapy, they would expect to carry it 95% of the time, would expect to treat 94% of attacks, and 93% of patients would expect to treat their attacks earlier. This is the reason we believe that an oral on-demand therapy could represent such a significant advance.

We have advanced our candidate sebetrastat into Phase 3 clinical development as a potential oral, on-demand therapy for HAE attacks. In February 2021 we announced data from a Phase 2 efficacy trial in which sebetrastat demonstrated statistically and clinically significant responses across all primary and secondary endpoints. Based upon these data, we completed an end-of-Phase 2 meeting with the United States (“U.S.”) Food and Drug Administration (“FDA”) in the fall of 2021 and initiated the Phase 3 KONFIDENT clinical trial in early 2022 that is intended to support submission of a New Drug Application (“NDA”). KONFIDENT is a double-blind, placebo-controlled, event-driven crossover trial in which approximately 84 patients will treat a total of three attacks: one each with 300 mg sebetrastat, 600 mg sebetrastat, and placebo, given in a randomized sequence. The study includes both adults and adolescents ages 12 and up, and allows patients to be on approved prophylactic regimens as well as on-demand only. All attack locations are eligible for treatment, including laryngeal attacks. The primary endpoint of the study is time to beginning of symptom relief assessed using the PGI-C scale. KONFIDENT is being conducted in approximately 60 sites in 20 countries. In July 2023, we announced that we reached our enrollment target of 114 patients in the study and as a result we expect data from KONFIDENT in the fourth quarter of 2023. If the trial is successful, we anticipate submitting an NDA to the FDA in the first half of 2024.

In August 2022, we initiated KONFIDENT-S, a two-year open-label extension trial assessing the long-term safety and tolerability profile of sebetrastat. In addition, this study is examining the potential use of sebetrastat as short-term prophylaxis in the setting of medical and dental procedures, where HAE attacks are known to be triggered. We also are developing an oral disintegrating tablet (“ODT”) formulation of sebetrastat and have received FDA feedback on our proposed development program to support a supplemental NDA submission, which did not include a recommendation to conduct efficacy trials. We anticipate that the ODT formulation will follow the expected initial launch formulation in the U.S. and European Union (“E.U.”), although it may become the initial launch formulation in other geographies.

Sebetrastat has received Fast Track and Orphan Drug designation from the FDA, and Orphan Drug designation in the E.U. A Pediatric Investigational Plan (“PIP”) has also been approved by the European Medicines Agency (“EMA”) for sebetrastat.

In October 2022, we announced the termination of the Phase 2 KOMplete study for our potential HAE prophylactic treatment KVD824, due to elevations in liver enzymes observed in several patients during the trial. We remain uncertain as to the cause and the potential contribution of KVD824 to these elevations, but we do not anticipate further development of KVD824.

Our oral Factor XIIa inhibitor program targets an enzyme that plays a key role in HAE, as the most upstream mechanism in the biochemical pathway that initiates HAE attacks. For this reason, we believe that inhibition of Factor XIIa will block the underlying causes of HAE attacks, including the uncontrolled generation of both plasma kallikrein and bradykinin which lead to swelling and pain. Clinical studies of an injectable Factor XIIa-inhibitory antibody have demonstrated a high degree of efficacy in preventing HAE attacks, and there are no known safety implications of long-term inhibition of this enzyme. We believe that our program has the potential to be the first orally delivered Factor XIIa inhibitor to enter clinical development, initially for HAE and over time for additional indications that are supported by scientific evidence. Our internal research team has discovered multiple series of low nanomolar potency Factor XIIa inhibitors that are both selective and orally bioavailable, and we continue to progress multiple compounds in IND-enabling studies. Concurrently, we have recently presented preclinical data supporting potential development in HAE as well as diabetic macular edema (“DME”) and thrombosis.

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 oral plasma kallikrein inhibitors for HAE and Factor XIIa inhibitors for HAE and other indications; however, we believe our scientific capabilities also can be applied to other proteases to develop therapies for diseases with high unmet need.
- *Develop multiple HAE product candidates to provide a full set of therapeutic options for patients.* We intend to develop drug candidates for both on-demand and prophylactic use to provide people living with HAE with a complete set of oral options to treat their disease. Our most advanced program for HAE is sebetralstat, for which we are currently conducting the Phase 3 KONFIDENT clinical trial to evaluate the safety and efficacy of sebetralstat as a potential oral, on-demand therapy for treatment of HAE attacks. We are also in the preclinical development stage with Factor XIIa inhibitor candidates as a potential next generation of oral prophylactic treatments that may further enhance treatment options for people living with HAE.
- *Grow our capabilities internally as well as through strategic partnerships.* We intend to retain ownership and control of our pipeline programs to key milestones and in certain markets. 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 to commercialize the products in major markets. For programs that address larger markets or require greater infrastructure or resources, or for markets outside the U.S. and major E.U. countries, we may seek partners 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 and commercialization cycle.

Plasma Kallikrein in HAE

Plasma kallikrein is a serine protease enzyme that is a key mediator of inflammation and edema. The body modulates the downstream inflammatory effects of plasma kallikrein through a circulating inhibitor protein called C1-esterase inhibitor (“C1-INH”). Most patients with HAE have a genetic mutation that leads 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.

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. Untreated attacks can be functionally disabling and commonly take days to fully resolve.

Attacks can occur spontaneously although they often are associated with triggers such as anxiety, stress, minor trauma, surgery, or illnesses. 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 mean number of attacks per month for patients is approximately two. Although life-threatening airway swelling is rare, published research suggests 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, and even most patients on long-term prophylaxis continue to experience breakthrough attacks on some basis.

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. 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.

While HAE most often results from the inheritance of a defective gene from a parent, it is estimated that up to 25% 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, currently referred to as 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 XII, plasminogen or angiopoietin, although in most cases a specific genetic abnormality isn't found. 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. There are currently no therapies specifically approved for normal C1-INH HAE.

Current Treatments and Market Opportunities

There are a number of marketed and development stage therapeutics for HAE, both for prophylaxis as well as on-demand use. Lanadelumab (Takhzyro[®]) 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 labeling approval by the FDA includes a boxed warning limiting its administration to healthcare professionals with appropriate medical support to manage anaphylaxis and HAE, and requiring close monitoring of patients. 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. Berotralstat (ORLADEYO[®]) is an oral prophylactic treatment which was launched in 2021. 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 on-demand agent has the potential to transform treatment for this 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, oral on-demand plasma kallikrein inhibitor therapy. There are no therapies currently approved specifically for normal C1-INH HAE.

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. The first of these product candidates being evaluated in late stage clinical trials is sebetralstat. A positive Phase 2 clinical trial for sebetralstat as a potential on-demand treatment for HAE attacks was completed in February 2021, and we are currently conducting the Phase 3 KONFIDENT clinical trial.

Sebetralstat

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, and treatment guidelines strongly recommend early treatment of attacks. Despite clear evidence that early treatment markedly reduces attack severity and 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 limitations and lower the barrier for treatment for patients. The combination of the rapid uptake of sebetralstat 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.

In February 2021 we announced data from a Phase 2 efficacy trial in which sebetralstat demonstrated statistical and clinically significant responses across all primary and secondary endpoints. KVD900-201 was a double-blind, placebo-controlled, crossover trial investigating the safety and efficacy of a single dose of 600 mg sebetralstat as an on-demand treatment for HAE attacks in patients with Type 1 or Type 2 HAE. The trial met its primary endpoint comparing the time to use of rescue treatment within 12 hours on sebetralstat versus placebo ($p = 0.001$) with rates of use at 12 hours of 15.1% following treatment with sebetralstat versus 30.2% after placebo. The trial also met all secondary endpoints: reduced worsening of attacks ($p < 0.0001$; PGI-S or use of rescue) and reduced time to onset of symptom relief measured using both PGI-C ($p < 0.0001$) and VAS ($p < 0.0001$).

Based upon these data, we completed an end-of-Phase 2 meeting with the FDA in the fall of 2021 and initiated the Phase 3 KONFIDENT clinical trial in early 2022 that is intended to support an NDA submission. KONFIDENT is a double-blind, placebo-controlled, event-driven crossover trial in which approximately 84 patients will treat a total of three attacks: one each with 300 mg sebetralstat, 600 mg sebetralstat, and placebo, given in a randomized sequence. The primary endpoint of the study is time to onset of symptom relief using the PGI-C scale. We agreed with the FDA that this is an appropriate primary endpoint for a registration-directed trial, and in the Phase 2 study, sebetralstat achieved this endpoint in a highly statistically significant manner. KONFIDENT is being conducted in approximately 60 sites in 20 countries. We have reached our target enrollment of 114 patients in the study, and expect data from KONFIDENT in the fourth quarter of 2023. If the trial is successful, we anticipate submitting an NDA in the first half of 2024.

Sebetralstat has received Fast Track and Orphan Drug designation from the FDA and has been granted Orphan Drug designation in the E.U. A PIP has also been approved by the EMA for sebetralstat.

Factor XIIa

Factor XIIa (“FXIIa”) is an enzyme that plays a key role in HAE as the most upstream mediator in the biochemical pathway that initiates HAE attacks. For this reason, we believe that inhibition of Factor XIIa will block the underlying mechanism of HAE attacks, including the uncontrolled generation of both plasma kallikrein and bradykinin which cause swelling and pain. Clinical studies of an injectable Factor XIIa-inhibitory antibody have demonstrated efficacy in preventing HAE attacks, and there are no published safety concerns of long-term inhibition of this enzyme. We believe that our program has the potential to be the first orally delivered Factor XIIa inhibitor to enter clinical development, initially for HAE and over time for additional indications that are supported by scientific evidence.

Our goal is to develop an oral FXIIa inhibitor suitable for once-daily dosing and sustained suppression of kallikrein kinin system activation. Using X-ray structure-enabled drug design, we have identified multiple series of oral FXIIa inhibitors from structurally distinct discovery lineages. These series are designed to interact with different substrate pockets of the active catalytic domain of the FXIIa enzyme, thereby providing a high level of structural diversity in our portfolio of compounds.

We have presented pharmacology data for a FXIIa compound that demonstrates our ability to achieve plasma half-life consistent with once daily dosing to provide near complete inhibition of FXIIa-mediated plasma kallikrein generation and block high molecular weight kininogen cleavage that results in generation of bradykinin. We have also shown that orally administered FXIIa compounds can protect mice from angioedema. These findings that demonstrated the oral pharmacodynamic effects of a Factor XIIa inhibitor were reported at the European Academy of Allergy & Clinical Immunology in 2022. Additional studies have demonstrated that oral administration of Factor XIIa inhibitors can protect mice from arterial thrombosis induced by iron chloride, which further demonstrates target engagement. These results have been presented at the International Society of Thrombosis and Hemostasis in June 2023.

It is our expectation that this portfolio of compounds will provide multiple opportunities for the clinical development of a once-daily administered oral FXIIa inhibitor with efficacy comparable to leading injectable therapies for HAE prophylaxis. In addition, the diversity within our portfolio creates opportunities to identify oral FXIIa inhibitors that fulfill the target profile needed for the treatment of other FXIIa-mediated diseases, including thrombosis and other diseases associated with edema and inflammation.

Competition

In treating HAE, we expect to face competition from several FDA-approved therapeutics for both prophylactic and on-demand usage. These include Takhzyro®, marketed by Takeda Pharmaceuticals Company Limited (“Takeda”) in the U.S. and Europe for the prevention of angioedema attacks in adults and adolescents; Firazyr, marketed by Takeda in the U.S., 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; Ruconest, marketed by Pharming Group for the treatment of acute angioedema attacks in adult patients; and Orladeyo, an oral prophylactic treatment marketed by BioCryst Pharmaceuticals, Inc. Firazyr became available as a generic drug in 2019 and is sold by multiple companies as generic icatibant for acute usage. We are also aware of other companies that are engaged in the clinical development of potential HAE treatments, including Pharvaris GmbH, Intellia Therapeutics, Inc., BioMarin Pharmaceutical Inc., and Ionis Pharmaceuticals, Inc.

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. Our patent portfolio includes patents and patent applications covering plasma kallikrein inhibitors (the “plasma kallikrein portfolio”), and patent applications covering FXIIa inhibitors (the “FXIIa portfolio”).

In the plasma kallikrein portfolio, as of April 30, 2023, we are the owner of, and intend to maintain, 16 U.S. patents expiring between 2034 and 2040, absent any extensions, as well as seven pending U.S. patent applications and one pending U.S. provisional application. Any patents issuing from the foregoing U.S. patent applications, or patents arising from applications claiming priority from the foregoing U.S. provisional applications, are expected to expire between 2034 and 2044, absent any adjustments or extensions. In the plasma kallikrein portfolio, as of April 30, 2023, we are the owner of, and intend to maintain, approximately 140 pending foreign applications and approximately 453 patents in foreign jurisdictions. Any issued patents, or those issuing from these foreign patent applications, are expected to expire between 2034 and 2041, absent any adjustments or extensions. In the plasma kallikrein portfolio, as of April 30, 2023, we also control and intend to maintain two pending international applications that, if issued, are expected to expire between 2042 and 2043, absent any adjustments or extensions.

Sebetralstat is an oral plasma kallikrein inhibitor, and 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. The anticipated expiration dates of these patents, patents arising from those applications, or patents arising from applications claiming priority from provisional applications range from 2035 to 2044, absent any adjustments or extensions. Sebetralstat 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, European patents arising from applications, or European patents arising from applications claiming priority from U.S. provisional applications range from 2035 to 2044 absent any extensions.

In the FXIIa portfolio, as of April 30, 2023, we are the owner of, and intend to maintain, four pending U.S. patent applications, six pending U.S. provisional applications, two pending international applications, and 34 pending foreign applications in multiple jurisdictions. Any patents issuing from the foregoing applications, or patents arising from applications claiming priority from U.S. provisional applications, in the FXIIa portfolio are expected to expire in between 2039 and 2044, absent any adjustments or 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 market or intend to market our products and services under various trademarks, and have obtained or are in the process of obtaining registered trademark protection for those trademarks in the U.S. and certain countries outside the U.S. We consider these trademarks to be valuable because of their contribution to the brand identification of our current and future products and services and for protection against counterfeits.

As of April 30, 2023, we are the owner of, and intend to maintain, trademark registrations for “KALVISTA” in six foreign countries as well as all E.U. member states via an E.U. Trade Mark (a unitary right covering all twenty-seven member states of the E.U.). We also own pending trademark applications and registrations for “KALVISTA” and the K Design in the U.S. and multiple foreign countries.

We also use other forms of protection, such as 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 U.S., at the federal, state and local level, and in other countries and jurisdictions, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the U.S. 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 U.S., pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act (the “FDC 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. Pharmaceutical products such as small molecule drugs and biological products, or biologics used for the prevention, treatment, or cure of a disease or condition of a human being are subject to regulation under the FDC Act. 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 NDAs, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

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

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing 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. 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 meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; and (iii) under protocols detailing the objectives of the trial and the 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 regulations or presents an unacceptable risk to the clinical trial patients. Imposition of a clinical hold may be full or partial. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board (“IRB”) for approval. The IRB will also monitor the clinical trial until completed. 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 patients, the product is tested to assess safety, dosage tolerance, metabolism, pharmacokinetics, pharmacological actions, side effects associated with drug exposure, and to obtain early evidence of a treatment effect if possible. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, determine optimal dose and regimen, and to identify common adverse effects and safety risks. If a drug demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain additional information about clinical effects and confirm 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 safety and efficacy of the drug. In rare instances, a single Phase 3 trial may be sufficient when either (1) the trial is a large, multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible or (2) the single trial is supported by other confirmatory evidence.

In addition, the manufacturer of an investigational drug in a Phase 2 or Phase 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 and distribution of the product may begin in the U.S. The NDA must include the results of all nonclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee. Under an approved NDA, the applicant is also subject to an annual program fee. These fees typically increase annually. An NDA for a drug that has been designated as an orphan drug is not subject to an application fee, unless the NDA includes an indication for other than a rare disease or condition. The FDA has 60 days from its receipt of an NDA to determine whether the application will be filed based on the FDA's determination that it is sufficiently complete to permit substantive review. Once the submission is filed, the FDA begins an in-depth review. The FDA has agreed to certain performance goals to complete the review of NDAs. Most applications are classified as Standard Review products that are reviewed within ten months of the date the FDA files the NDA; most applications classified as Priority Review are reviewed within six months of the date the FDA files the NDA. An NDA can be classified for Priority Review when the FDA determines the drug or biologic 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 reviews may be extended by the FDA for three or more additional months to consider certain late-submitted information or information intended to clarify information already provided in the NDA submission.

The FDA may also refer applications for novel drugs, as well as drugs that present difficult questions of safety or efficacy, to be reviewed by an advisory committee—typically a panel that includes clinicians, statisticians and other experts—for review, evaluation and a recommendation as to whether the NDA should be approved. The FDA is not bound by the recommendation of an advisory committee, but generally follows such recommendations.

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

After the FDA evaluates the NDA and completes any clinical and manufacturing site inspections, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the NDA submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application for approval. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. An approval letter authorizes commercial marketing and distribution of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy (“REMS”) to help ensure that the benefits of the drug outweigh the potential risks to patients. A REMS can include medication guides, communication plans for healthcare professionals, and elements to assure a product's safe use (“ETASU”). An ETASU can include, but is not limited to, special training or certification for prescribing or dispensing the product, dispensing the product only under certain circumstances, special monitoring, and the use of patient-specific registries. The requirement for a REMS can materially affect the potential market and profitability of the product. Moreover, the FDA 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 NDA, including changes in indications, product labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or supplement to an approved NDA, 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 original NDAs.

Orphan Drug Designation

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

Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the drug and its potential orphan disease 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. The first NDA applicant to receive FDA approval for a particular active moiety to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the U.S. for that product in the approved indication. For large molecule drugs, sameness is determined based on the principal molecular structural features of a product.

During the seven-year marketing exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. A product can be considered 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 different drug for the same disease or condition, or the same drug 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

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 a clinical trial are then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of clinical 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 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 with orphan product designation except a product with a new active ingredient that is a molecularly targeted cancer product intended for the treatment of an adult cancer and directed at a molecular target determined by FDA to be substantially relevant to the growth or progression of a pediatric cancer that is subject to an NDA submitted on or after August 18, 2020.

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

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 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 safety summary 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 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 a drug's 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 required regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

The Hatch-Waxman Amendments

Orange Book Listing

Under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch Waxman Amendments, NDA applicants are required to identify to FDA each patent whose claims cover the applicant's drug or approved method of using the drug. Upon approval of a drug, the applicant must update its listing of patents to the NDA in timely fashion and each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book.

Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application ("ANDA"). An ANDA provides for marketing of a drug product that has the same active ingredient(s), strength, route of administration, and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. An approved ANDA product is considered to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved under the ANDA pathway are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug pursuant to each state's laws on drug substitution.

The ANDA applicant is required to certify to the FDA concerning any patents identified for the reference listed drug in the Orange Book. Specifically, the applicant must certify to each patent in one of the following ways: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. For patents listed that claim an approved method of use, under certain circumstances the ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents through a Paragraph IV certification, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA-holder and patentee(s) once the ANDA has been accepted for filing by the FDA (referred to as the "notice letter"). The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice letter. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months from the date the notice letter is received, expiration of the patent, the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed, or a decision in the patent case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired. In some instances, an ANDA applicant may receive approval prior to expiration of certain non-patent exclusivity if the applicant seeks, and FDA permits, the omission of such exclusivity-protected information from the ANDA prescribing information.

Exclusivity

Upon NDA approval of a new chemical entity (“NCE”) which is a drug that contains no active moiety that has been approved by FDA in any other NDA, that drug receives five years of marketing exclusivity during which FDA cannot receive any ANDA seeking approval of a generic version of that drug unless the application contains a Paragraph IV certification, in which case the application may be submitted one year prior to expiration of the NCE exclusivity. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA for a generic version of the drug may be filed before the expiration of the exclusivity period.

Certain changes to an approved drug, such as the approval of a new indication, the approval of a new strength, and the approval of a new condition of use, are associated with a three-year period of exclusivity from the date of approval during which FDA cannot approve an ANDA for a generic drug that includes the change. In some instances, an ANDA applicant may receive approval prior to expiration of the three-year exclusivity if the applicant seeks, and FDA permits, the omission of such exclusivity-protected information from the ANDA package insert.

Patent Term Extension

The Hatch Waxman Amendments permit a patent term extension as compensation for patent term lost during the FDA regulatory review process. Patent term extension, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product’s approval date. After NDA approval, owners of relevant drug patents may apply for the extension. The allowable patent term extension is calculated as half of the drug’s testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval) up to a maximum of five years. The time can be reduced for any time FDA determines that the applicant did not pursue approval with due diligence.

The U.S. Patent and Trademark Office (the “USPTO”) in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. However, the USPTO may not grant an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than requested.

The total patent term after the extension may not exceed 14 years, and only one patent can be extended. The application for the extension must be submitted prior to the expiration of the patent, and for patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the USPTO must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Other U.S. Healthcare Laws and Compliance Requirements

In the U.S., pharmaceutical and biotechnology company activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare & Medicaid Services (“CMS”) other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General and the Office for Civil Rights), 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 some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. 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 Reconciliation Act of 2010 (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 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 covered drugs, devices, biologics 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, certain advance practices nurses and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. The reported data is made available in searchable form on a public website on an annual basis. Failure to submit required information may result in civil monetary penalties.

Commercial distribution of products requires compliance with state laws that require the registration of manufacturers and wholesale distributors of drugs 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. In addition, 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.

Violation of any of the federal and state healthcare laws described above or any other governmental regulations may result in 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, refusal to enter into government contracts, oversight monitoring, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings.

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 U.S. 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 U.S., 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 E.U., 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 U.S. 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.

U.S. Healthcare reform

Healthcare reforms that have been adopted, and that may be adopted in the future, could result in further reductions in coverage and levels of reimbursement for pharmaceutical products, increases in rebates payable under U.S. government rebate programs and additional downward pressure on pharmaceutical product prices.

Recently, healthcare reform initiatives culminated in the enactment of the Inflation Reduction Act (the "IRA"), in August 2022, which will, among other things, permit the Department of Health and Human Service ("HHS") to negotiate the selling price of certain drugs that CMS reimburses under Medicare Part B and Part D, although only high-expenditure single-source drugs that have been approved for at least 7 years can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price. Beginning in January 2023 for Medicare Part B and October 2022 for Medicare Part D, the IRA will also penalize drug manufacturers that increase prices of Medicare Part B and Part D drugs at a rate greater than the rate of inflation. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges.

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 U.S. 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 U.S., 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 U.S. 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 E.U., 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 E.U. 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 E.U., United Kingdom (“U.K.”), and Swiss regulatory systems, we must submit a marketing authorization application (“MAA”). The documentation submitted to the FDA in support of an NDA in the U.S. is almost identical to that required in the E.U., U.K., and Switzerland, with the exception of, among other things, country-specific document requirements. For other countries outside of the E.U., U.K. and Switzerland, such as countries in Eastern Europe, the Middle East, 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.

Human Capital Resources

As of April 30, 2023, we had a total of 118 full-time employees, of whom 53 were located in the U.S., 61 were located in the U.K., 3 were located in Switzerland, and 1 located in Portugal. 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. We believe that our future success largely depends upon our continued ability to attract and retain highly skilled employees. We emphasize a number of measures and objectives in managing our human capital assets, and we provide our employees with competitive salaries and bonuses, opportunities for equity ownership, development programs that enable continued learning and growth and a robust employment package that promotes well-being across all aspects of their lives, including health care, retirement planning and paid time off. In July 2021, the Company adopted an Equity Inducement Plan in order to provide incentives to attract and motivate new employees through the grant of stock options and restricted share units.

Corporate Information

Our principal executive offices are located at 55 Cambridge Parkway, Suite 901 East, 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.

Summary of Risk Factors

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

- We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.
- Our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.
- We will need substantial additional funding. If we are unable to raise capital when needed, we may need to delay, reduce or eliminate our product development programs or commercialization efforts.
- If we 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.
- 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.
- 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.
- 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.
- We may seek orphan drug exclusivity for some of our product candidates, and we may be unsuccessful.
- 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.
- Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.
- 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.
- We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.
- 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.
- 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.

- 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.
- 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.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- We expect to expand our development 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.
- 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.
- Shareholder activism could cause material disruption to our business.
- 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.
- Unstable or unfavorable global market and economic conditions may have adverse consequences on our business, financial condition and stock price.

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

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 several 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 a previous option agreement with Merck 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, and undertaking up to Phase 3 clinical studies of our most advanced product candidates. 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

If we 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;
- complete any clinical trials beyond Phase 2;
- move other product candidates into late-stage 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 sebetralstat 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;

- delay or failure in having subjects complete a trial or return for post-treatment follow-up;
- delay or failure in data collections in connection with a clinical trial;
- clinical sites and investigators deviating from trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial;
- 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;
- 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 or political instability;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; or
- 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 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.

Patient enrollment is affected by many 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;
- 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. In October 2022, we terminated a Phase 2 clinical trial of KVD824, which was being developed as a potential HAE prophylaxis therapy, due to elevated liver enzymes observed in multiple study patients. Although we have not conclusively determined that KVD824 was the cause of, or a significant contributor to, these elevations, we do not anticipate further development of KVD824. Our on-demand HAE program sebetralstat is still in 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 U.S. and by the EMA and similar regulatory authorities outside the U.S. prior to commercialization. The process of obtaining marketing approvals, both in the U.S. 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 and therapeutic indications 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. Securing marketing approval requires the submission of extensive chemistry, manufacturing and 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 usually requires inspection of manufacturing facilities by the regulatory authorities and also audits of the clinical trial sites, data and CROs that have supported KalVista in the clinical development. 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 an 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.

For example, the U.K. formally left the E.U. on January 31, 2020, often referred to as Brexit, and the transition period ended on December 31, 2020. Brexit has caused uncertainty in the current regulatory framework in Europe. For instance, Brexit has resulted in the EMA, moving from the U.K. to the Netherlands. The U.K. has now put in place legislation to cover the approval of new medicinal products in the U.K., including designations such as orphan designation, and a pediatric investigational plan. The requirements are similar to those in the E.U. and in many cases have adopted the same requirements. However, there are still adjustments being made to legislation. Any of these adjustments as a result of Brexit could result in significant delays and additional expense to our business. Any of the foregoing factors could have a material adverse effect on our business, results of operations, or financial condition.

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.

An Orphan Drug Designation by the FDA or EMA or MHRA does not increase the likelihood that our product candidates will receive marketing exclusivity.

Regulatory authorities in some jurisdictions, including the U.S. 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 prevalence of fewer than 200,000 individuals in the U.S.

Generally, if a product with an orphan drug designation in a particular jurisdiction 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 authority in that jurisdiction 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 U.S. and ten years in Europe. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective, the criteria on which the orphan designation was originally issued no longer apply or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

The FDA has granted orphan drug designation for sebetralstat. This designation may not effectively protect sebetralstat (or other drug products for which KalVista seeks Orphan Designation) from competition because the designation does not preclude different drugs from being approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that it 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 sebetralstat 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 sebetralstat 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 U.K., E.U. 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 FDA approval. The regulatory approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U.S., it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We, or our third party collaborators, may not obtain approvals from regulatory authorities outside the U.S. on a timely basis, if at all. Approval in any one jurisdiction does not ensure approval by regulatory authorities in other countries or jurisdictions, and likewise approval by one regulatory authority outside the U.S. does not ensure approval by regulatory authorities in any other countries or jurisdictions including the U.S. 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, E.U., MHRA, Swiss and other regulatory authorities. In the U.S., 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 FDC 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 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 U.K. and E.U. 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 U.K. and E.U.'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 U.S. 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 been the subject of legislative and judicial efforts to modify, repeal or otherwise invalidate all or certain aspects of its provisions. The ACA mandated a substantial number of major changes to the healthcare system that impact our business, and several other pieces of legislation 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 U.S. tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries of the E.U. and the U.K., 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;
- FDA-approved labeling which may include restrictive safety and efficacy data, or may not include aspects of safety and efficacy that we believe are important;
- 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. Our estimates of the potential market opportunities for our products are informed by work that is not definitive and future analyses may lead to estimates that are higher or lower than these estimates than those provided at any given time, with respect to addressable patient populations. If our market opportunity is lower than anticipated, our business may suffer.

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 U.S., 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 U.S., 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 U.S. 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 U.S., the reimbursement for our products may be reduced compared with the U.S. and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third party payors, in the U.S. 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 U.S. 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 2030 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 provides financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended and reduced the 2% Medicare sequester from May 1, 2020 through June 30, 2022, and extended the sequester policy, through 2031, in order to offset the added expense of the 2020 cancellation. Moreover, the American Taxpayer Relief Act of 2012 among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

The IRA, which was enacted in August 2022, will, among other things, allow HHS to negotiate the selling price of certain drugs and biologics that CMS reimburses under Medicare Part B and Part D, although only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price. Beginning in January 2023 for Medicare Part B and October 2022 for Medicare Part D, the IRA will also penalize drug manufacturers that increase prices of Medicare Part B and Part D drugs at a rate greater than the rate of inflation. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. For example, in June 2023, the drug price negotiation program for Medicare Parts B and D was challenged in federal court. It is unclear whether such litigation or other litigation, if brought, will be successful.

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 U.S. may also impact us negatively, such as by limiting the functioning of international regulatory agencies in countries outside the U.S. 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 million in product liability insurance coverage in the aggregate, with a per incident limit of \$10 million 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 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.

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.

Even if we choose to self-manufacture, 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 U.S. 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 U.S., 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.

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. 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;
- 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.

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 U.S., the E.U., and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the U.S. 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 U.S. 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 U.S. 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 U.S. 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 U.S. 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 E.U., the U.S. 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 U.S. 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 U.S. 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 U.S. 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, 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.

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. 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.

Our failure to comply with privacy and data security laws, regulations and standards may cause our business to be materially adversely affected.

We are, and may increasingly become, subject to various laws and regulations, as well as contractual obligations, relating to data privacy and security in the jurisdictions in which we operate. Personal privacy and data security have become significant issues in the U.S., Europe and in many other jurisdictions. The regulatory framework for privacy and security issues worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. We maintain a large quantity of sensitive information, including confidential business and patient health information in connection with our clinical development regarding the patients enrolled in our clinical trials. Any violations of these rules by us could subject us to civil and criminal penalties and adverse publicity and could harm our ability to initiate and complete clinical trials. We cannot provide assurance that current or future legislation will not prevent us from generating or maintaining personal data or that patients will consent to the use of their personal data (as necessary); either of these circumstances may prevent us from undertaking or publishing essential research and development, manufacturing, and commercialization, which could have a material adverse effect on our business, results of operations, financial condition, and prospects.

The myriad international and U.S. privacy and data breach laws are not consistent, and compliance in the event of a widespread data breach is difficult and may be costly. In many jurisdictions, enforcement actions and consequences for noncompliance are also rising. In addition to government regulation, privacy advocates and industry groups may propose new and different self-regulatory standards that either legally or contractually applies to us. Any inability to adequately address privacy and security concerns, even if unfounded, or comply with applicable privacy and data security laws, regulations and policies, could result in additional cost and liability to us, damage our reputation, and adversely affect our business. Additionally, all of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, distract management or divert resources from other initiatives and projects, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Enforcement actions and investigations by regulatory authorities related to data security incidents and privacy violations continue to increase. Any failure or perceived failure by us (or the third parties with whom we have contracted to process such information) to comply with applicable privacy and data security laws, policies or related contractual obligations, or any compromise of security that results in unauthorized access, use or transmission of, personal user information, could result in a variety of claims against us, including governmental enforcement actions and investigations, class action privacy litigation in certain jurisdictions and proceedings by data protection authorities, potentially amounting to significant compensation or damages liabilities, as well as associated costs, diversion of internal resources, and reputational harm. When such events occur, our reputation may be harmed, we may lose current and potential users and the competitive positions of our brand might be diminished, any or all of which could materially adversely affect our business, operating results, and financial condition. In addition, if our practices are not consistent or viewed as not consistent with legal and regulatory requirements, including changes in laws, regulations and standards or new interpretations or applications of existing laws, regulations and standards, we may become subject to audits, inquiries, whistleblower complaints, adverse media coverage, investigations, loss of export privileges, or severe criminal or civil sanctions, all of which may have a material adverse effect on our business, operating results, reputation, and financial condition.

Our business and operations would suffer in the event of system failures, cyberattacks or a deficiency in our cybersecurity.

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. The risk of a security breach or disruption, particularly through cyberattacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity, and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. The costs to us or our CROs or other contractors or consultants we may utilize to mitigate network security problems, bugs, viruses, worms, phishing attempts, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. 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.

In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state privacy and security laws, if applicable, including the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. We would also be exposed to a risk of loss or litigation and potential liability under laws, regulations and contracts that protect the privacy and security of personal information. We would also be exposed to a risk of loss or litigation and potential liability, which could materially adversely affect our business, reputation, results of operations, financial condition and prospects.

We also depend on our information technology infrastructure for communications among our personnel, contractors, consultants and vendors. System failures or outages 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. 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, or changes to treatment recommendations or guidelines applicable to treatment;
- 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 U.S., the U.K. or the E.U.;
- 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 U.S. equity markets, including due to rising inflation and interest rates, labor shortages, supply chain issues, and global conflicts such as the war in Ukraine; 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.

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, 2023. 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.

Shareholder Activism Could Cause Material Disruption to Our Business.

Publicly traded companies have increasingly become subject to campaigns by activist investors advocating corporate actions such as actions related to environment, social and governance ("ESG") matters, financial restructuring, increased borrowing, dividends, share repurchases or even sales of assets or the entire company. Responding to proxy contests and other actions by such activist investors or others in the future could be costly and time-consuming, disrupt our operations and divert the attention of our

board of directors and senior management from the pursuit of our business strategies, which could adversely affect our results of operations and financial condition.

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. For example, we believe we experienced an "ownership change" within the meaning of Section 382 of the Internal Revenue Code of 1986, as amended, in December 2022, and we continue to analyze the impact if any on our ability to utilize NOLs in the future. 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 Act (the "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.

General Risk Factors

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. Challenging or uncertain economic conditions including those related to global epidemics, pandemic, or contagious diseases, geopolitical turmoil, inflation, fluctuation in interest rates and foreign exchange rates, instability in the global banking system, disruptions in supply chains may adversely affect our general business strategy and stock price. In addition, a recession, depression or other sustained adverse market event could materially and adversely affect our business and the value of our common stock.

For example, on March 10, 2023, Silicon Valley Bank (“SVB”) was closed by the California Department of Financial Protection & Innovation and the Federal Deposit Insurance Corporation (the “FDIC”) was named receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. While the FDIC has taken steps to make whole all depositors of SVB, there is no assurance that similar guarantees will be made in the event of further bank closures and continued instability in the global banking system. If other banks and financial institutions enter receivership or become insolvent in the future in response to financial conditions affecting the banking system and financial markets, then our ability to obtain financing may be threatened, which could have a material adverse effect on our business and financial condition. Moreover, events such as the closure of SVB, in addition to other global macroeconomic conditions, may cause further turbulence and uncertainty in the capital markets.

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. There is also 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. In addition, regarding the current conflict in Ukraine, we do not have any clinical trial sites or operations in Ukraine or Russia. However, if the current conflict in the region continues, there is the potential for trial sites in other eastern European countries to slow or stop enrollment, or to be unable to administer our clinical trials.

Changes in tax laws or tax rulings could materially affect our financial position, results of operations and cash flows.

The tax regimes we are subject to or operate under, including income and non-income taxes, are unsettled and may be subject to significant change. Changes in tax laws, regulations, or rulings, or changes in interpretations of existing laws and regulations, could materially affect our financial position and results of operations. For example, the 2017 Tax Cuts and Jobs Act (the “Tax Act”) made broad and complex changes to the U.S. tax code, including changes to U.S. federal tax rates, additional limitations on the deductibility of interest, both positive and negative changes to the utilization of future net operating loss (“NOL”) carryforwards, allowing for the expensing of certain capital expenditures, and putting into effect the migration from a “worldwide” system of taxation to a more territorial system. Future guidance from the IRS with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. The CARES Act has already modified certain provisions of the Tax Act. The IRA, enacted on August 16, 2022, further amended the U.S. tax code, imposing a 15% minimum tax on “adjusted financial statement income” of certain corporations as well as an excise tax on the repurchase or redemption of stock by certain corporations, beginning in the 2023 tax year. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the CARES Act, the IRA or any newly enacted federal tax legislation. The issuance of additional regulatory or accounting guidance related to the Tax Act could materially affect our tax obligations and effective tax rate in the period issued.

As we continue to expand internationally, we will be subject to other jurisdictions around the world with increasingly complex tax laws, the application of which can be uncertain. The amount of taxes we pay in these jurisdictions could increase substantially as a result of changes in the applicable tax principles, including increased tax rates, new tax laws or revised interpretations of existing tax laws and precedents, which could have an adverse impact on our liquidity and results of operations. In addition, the authorities in several jurisdictions could review our tax returns and impose additional tax, interest and penalties, which could have an impact on us and on our results of operations. In addition, many countries in Europe and a number of other countries and organizations, have recently proposed or recommended changes to existing tax laws or have enacted new laws that could significantly increase our tax obligations in the countries where we do or intend to do business or require us to change the manner in which we operate our business.

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 may 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 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 8,300 square feet of office space under a lease agreement that runs through September 2028. We maintain approximately 13,400 square feet of office and research laboratory space in Porton Down, United Kingdom, under a lease agreement that runs through April 2028. We maintain approximately 6,200 square feet of office space in Salt Lake City, Utah that runs through February 2032. We also maintain approximately 500 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 28, 2023, there were 21 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.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. Reserved.

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, 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. We apply our insights into the chemistry and biology of proteases to develop orally delivered, small molecule inhibitors with high selectivity, potency and bioavailability that we believe will make them successful treatments for diseases. We have used these capabilities to develop small molecule plasma kallikrein inhibitors targeting the disease hereditary angioedema (“HAE”). We also are conducting preclinical development of a novel, oral Factor XIIa (“Factor XIIa”) inhibitor program, which initially is being advanced to provide a next generation of HAE therapeutics and which also offers the opportunity for expansion into other high unmet need indications in the future.

Our most advanced program for HAE is sebetralstat, which is being developed as a potential on-demand oral therapy for treatment of HAE attacks. In March 2022 we initiated the KONFIDENT trial, a Phase 3 clinical study to evaluate the safety and efficacy of sebetralstat as a potential on-demand therapy for HAE attacks. In July 2023, we announced that we had reached our targeted enrollment of 114 patients, and data from this study is anticipated in the fourth quarter of 2023. If the trial is successful, we anticipate submitting an NDA to the FDA in the first half of 2024.

In October 2022, we announced the termination of the Phase 2 KOMLETE study for our potential HAE prophylactic treatment KVD824, due to elevations in liver enzymes observed in several patients during the trial. We remain uncertain as to the cause and the potential contribution of KVD824 to these elevations, but we do not anticipate further development of KVD824.

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.

On May 21, 2021, we entered into a Controlled Equity OfferingSM Sales Agreement with Cantor Fitzgerald & Co. (the “Sales Agreement”), which established an at-the-market (“ATM”) offering program pursuant to which we may offer and sell shares of our common stock from time to time. The Sales Agreement provides for the sale of shares of our common stock having an aggregate offering price of up to \$100.0 million. We have conducted no sales through the ATM.

On December 23, 2022, we entered into subscription agreements with institutional investors to sell, in a registered direct offering, an aggregate of 9,484,199 shares of our common stock at a price of \$6.00 per share and pre-funded warrants to purchase up to 182,470 shares of common stock at a price of \$5.999 per pre-funded warrant. The purchase price per share of each pre-funded warrant represents the per share offering price for the common stock, less the \$0.001 per share exercise price of each pre-funded warrant. The net proceeds from the registered direct offering, after deducting estimated expenses, were approximately \$57.7 million.

We have funded operations primarily through the issuance of capital stock. As of April 30, 2023, we had an accumulated deficit of \$343.1 million and hold \$149.4 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

We have not generated any revenue in the current fiscal year. 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 product revenue unless and until we obtain regulatory approval for, and commercialize, one of our current or future product candidates.

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, commercial planning, 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 U.K. government's tax incentive programs set up to encourage research and development in the U.K., realized and unrealized exchange rate gains/losses on cash held in foreign currencies and transactions settled in foreign currencies, and realized gains and losses from sales of marketable securities.

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 tax returns in the U.K. 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 U.S. ("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:

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 2023 and 2022 items and year-to-year comparisons between fiscal years 2023 and 2022. Discussions of fiscal year 2022 items and year-to-year comparisons between fiscal years 2022 and 2021 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, 2022, which was filed with the SEC on July 7, 2022.

Year Ended April 30, 2023 Compared to Year Ended April 30, 2022

The following table sets forth the key components of our results of operations for the years ended April 30, 2023 and 2022:

	Years Ended		Increase (Decrease)
	April 30,		
	2023	2022	
	(in thousands)		
<u>Income</u>			
Revenue	\$ —	\$ —	\$ —
<u>Operating Expenses</u>			
Research and development expenses.....	80,276	70,167	10,109
General and administrative expenses	30,595	26,446	4,149
<u>Other income</u>			
Interest, exchange rate gain and other income	17,964	14,274	3,690

Revenue. No revenue was recognized in the years ended April 30, 2023 or 2022.

Research and Development Expenses. Research and development expenses were \$80.3 million in the year ended April 30, 2023 compared to \$70.2 million in the prior year. The increase of \$10.1 million was primarily due to increases in spending on sebetralstat of \$3.5 million, personnel costs of \$3.5 million, and preclinical activities of \$4.3 million. These increases were offset by a decrease in spending on KVD824 of \$1.2 million. The impact of exchange rates on research and development expenses was a decrease of approximately \$7.7 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		Increase (Decrease)	
	April 30,			
	2023	2022		
	(in thousands)			
Program-specific costs				
Sebetralstat.....	\$ 27,037	\$ 23,493	3,544	15%
KVD824	11,651	12,879	(1,228)	-10%
Unallocated costs				
Personnel	23,452	19,925	3,527	18%
Preclinical activities.....	18,136	13,870	4,266	31%
Total.....	<u>\$ 80,276</u>	<u>\$ 70,167</u>	<u>\$ 10,109</u>	14%

Expenses for the sebetralstat program increased primarily due to activities related to the ongoing Phase 3 KONFIDENT trial. We anticipate that these expenses will remain at or above current levels as this clinical trial progresses.

Expenses for the KVD824 program decreased primarily due to the termination of the Phase 2 KOMLETE clinical trial in October 2022. We anticipate that these expenses will cease in the near term as we do not anticipate any further development of KVD824.

Personnel expenses increased primarily due to higher research and development and medical headcount compared to the prior year. We anticipate that these expenses will continue to increase to support the growth of the ongoing clinical trials and preclinical activities.

Expenses for preclinical activities increased primarily due to additional projects compared to the prior year. We anticipate that these expenses will continue to increase as we continue to progress our oral Factor XIIIa inhibitor program and conduct other preclinical activities

General and Administrative Expenses. General and administrative expenses were \$30.6 million in the year ended April 30, 2023 compared to \$26.4 million in the prior fiscal year. The increase of \$4.2 million was primarily due to increases of \$3.9 million in commercial strategy expenses, \$0.8 million in investor and public relations expenses, and \$0.7 million in insurance and other administrative expenses. These increases were offset by decreases in professional fees of \$0.6 million and employee-related expenses of \$0.6 million 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 \$18.0 million for the year ended April 30, 2023 compared to \$14.3 million in the prior fiscal year. The increase of \$3.7 million was primarily due to an increase of \$0.5 million in income from research and development tax credit, an increase of \$1.1 million in interest income, an increase in foreign currency exchange rate gains of \$1.6 million from transactions denominated in foreign currencies in our U.K. subsidiary, and a decrease in realized loss from available for sale securities of \$0.4 million, compared to the prior year.

Liquidity and Capital Resources

Since inception, we have not generated any revenue from product sales and have incurred losses since inception and cash outflows from operating activities for the years ended April 30, 2023 and 2022. As of April 30, 2023, we had an accumulated deficit of \$343.1 million and cash, cash equivalents and marketable securities totaling \$149.4 million. We have not yet commercialized any of our product candidates, which are in various phases of preclinical and clinical development, and we do not expect to generate revenue from sales of any products for the foreseeable future, and will continue to incur net losses as we continue the research and development efforts on our product candidates, hire additional staff, including clinical, scientific, operational, and financial and management personnel.

Sources of Liquidity

On May 21, 2021, we filed a shelf registration statement on Form S-3 pursuant to which the Company may offer and sell securities having an aggregate public offering price of up to \$300 million. In connection with the filing of the Registration Statement, we also entered into a Controlled Equity Offering Sales Agreement with Cantor Fitzgerald & Co. (the “2021 Sales Agreement”), through which we may offer and sell shares of our common stock under an at-the-market offering program having an aggregate offering of up to \$100.0 million through Cantor Fitzgerald & Co., as our sales agent. We will pay the sales agents a commission of up to 3% of the gross proceeds of sales made through the 2021 Sales Agreement. During the twelve months ended April 30, 2023, we did not offer or sell any shares under the 2021 Sales Agreement.

In December 2022, we entered into subscription agreements with institutional investors to sell, in a registered direct offering, an aggregate of 9,484,199 shares of our common stock at a price of \$6.00 per share and pre-funded warrants to purchase up to 182,470 shares of common stock at a price of \$5.999 per pre-funded warrant (the “Offering”). The net proceeds from the Offering, after deducting estimated expenses, were approximately \$57.7 million. As of April 30, 2023, no pre-funded warrants were exercised.

Cash Flows

The following table shows a summary of the net cash flow activity for the years ended April 30, 2023 and 2022:

	Years Ended April 30,	
	2023	2022
	<i>(in thousands)</i>	
Cash flows used in operating activities	\$ (75,261)	\$ (78,134)
Cash flows provided by investing activities	41,415	57,860
Cash flows provided by financing activities	58,116	1,581
Effect of exchange rate changes on cash	1,236	(1,167)
Net (decrease) increase in cash and cash equivalents	\$ 25,506	\$ (19,860)

Net cash used in operating activities

Net cash used in operating activities was \$75.3 million for the year ended April 30, 2023 and primarily consisted of a net loss of \$92.9 million adjusted for stock-based compensation of \$9.9 million, an increase in the research and development tax credit receivable of \$2.3 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. Net cash used in operating activities was \$78.1 million for the year ended April 30, 2022 and primarily consisted of a net loss of \$82.4 million adjusted for stock-based compensation of \$11.1 million, an increase in the research and development tax credit receivable of \$5.2 million, and other changes in net working capital.

Net cash provided by investing activities

Net cash provided by investing activities was \$41.4 million for the year ended April 30, 2023 and consisted of sales and maturities of marketable securities of \$140.9 million offset by purchases of marketable securities of \$98.3 million and acquisitions of property and equipment of \$1.2 million. Net cash used in investing activities was \$57.9 million for the year ended April 30, 2022 and consisted of sales and maturities of marketable securities of \$195.7 million offset by purchases of marketable securities of \$136.9 million and acquisitions of property and equipment of \$0.9 million.

Net cash provided by financing activities

Net cash provided by financing activities was \$58.1 million for the year ended April 30, 2023 and primarily consisted of the \$57.7 million in net proceeds from the December 2022 registered direct offering of common stock and pre-funded warrants. Net cash provided by financing activities was \$1.6 million for the year ended April 30, 2022 and primarily consisted of the issuance of common stock from equity incentive plans.

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.

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

A description of recently issued accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 2 to our consolidated financial statements.

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

Interest Rate Risk

Because of the short-term nature of the bank deposit arrangements, 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 of securities due to changes in interest rates and other market factors. 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, 2023 was composed of \$56.2 million in cash and cash equivalents which consisted of readily available checking and bank deposit accounts held primarily in both USD and GBP and \$93.1 million of USD denominated marketable securities. As of April 30, 2023, 83% of cash and cash equivalents were held in USD and 17% 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, 2023. 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, 2023 our Chief Executive Officer and Chief Financial Officer have concluded that, as of April 30, 2023, 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, 2023. 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, 2023, 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, 2023. 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, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Jurisdictions That Prevent Inspections

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by the Item is set forth in our 2023 Proxy Statement to be filed with the SEC within 120 days of April 30, 2023, 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 2023 Proxy Statement to be filed with the SEC within 120 days of April 30, 2023, 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 2023 Proxy Statement to be filed with the SEC within 120 days of April 30, 2023, 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, 2023, with respect to the shares of our common stock that may be issued under our existing equity compensation plans.

Plan Category	(a) Number of Securities to be Issued upon Exercise of Outstanding Options, Warrants and Rights	(b) Weighted- average Exercise Price of Outstandin g Options, Warrants and Rights (1)	(c) Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (excluding securities reflected in column (a))
Equity compensation plans approved by stockholders	5,276,758	(2) \$ 15.05	1,506,028 (3)
Equity compensation plans not approved by stockholders	245,659	(4) \$ 14.36	124,396 (5)
Total	5,522,417		1,630,424

- (1) The weighted average exercise price in column (b) includes options only as performance and restricted stock units do not have an exercise price.
- (2) Includes 103,366 shares subject to options issued pursuant to the KalVista Pharmaceuticals Inc. 2015 Incentive Plan, 97,845 shares subject to options issued pursuant to the Enterprise Management Incentives Plan, 3,613,305 shares subject to options issued, 742,242 subject to restricted stock grants, and 720,000 performance stock units issued pursuant to the 2017 Equity Incentive Plan.
- (3) As of April 30, 2023, the number of securities remaining available for issuance includes 531,358 share available for future issuance in the form of options under the 2017 Equity Incentive Plan and 974,670 shares available for future issuance under the 2017 Employee Stock Purchase Plan
- (4) Includes 245,659 shares subject to options issued pursuant to the 2021 Equity Inducement Plan.
- (5) As of April 30, 2023, the number of securities remaining available for issuance includes 124,396 shares available for future issuance under the 2021 Equity Inducement Plan.

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

The information required by the Item is set forth in our 2023 Proxy Statement to be filed with the SEC within 120 days of April 30, 2023, 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 2023 Proxy Statement to be filed with the SEC within 120 days of April 30, 2023, 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.	8-K	001-36830	3.1	June 14, 2023	
4.1	Form of Common Stock Certificate.	S-1/A	333-201278	4.2	January 23, 2015	
4.2	Description of Registrant's Securities.	10-K	001-36830	10.24	July 16, 2019	
4.3	Form of Pre-Funded Warrant.	8-K	001-36830	4.1	December 27, 2022	
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	
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#	Enrollment/Change Form under the 2017 Employee Stock Purchase Plan.	S-8	333-237059	99.4	March 10, 2020	
10.11#	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	

10.12#	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	
10.13#	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	
10.14#	Amended and Restated Executive Employment Agreement by and between Registrant and Edward Feener.	10-K	001-36830	10.21	July 16, 2019	
10.15#	Executive Employment Agreement by and between Registrant and Michael Smith.	10-K	001-36830	10.22	July 16, 2019	
10.16#	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	
10.17#	Executive Employment Agreement by and between Registrant and Dr. Paul K. Audhya, MD.	10-K	001-36830	10.18	July 13, 2021	
10.18	First Amendment of Lease, dated November 20, 2020, to the Office Lease Agreement by and between the Registrant and 55 Cambridge Parkway, LLC, dated May 19, 2017.	10-Q	001-36830	10.1	December 10, 2020	
10.19	Controlled Equity Offering Sales Agreement, dated May 21, 2021, between the Registrant and Cantor Fitzgerald & Co.	S-3	333-256378	1.2	May 21, 2021	
10.20	Subscription Agreement, dated as of December 23, 2022, by and among the Registrant and the purchasers identified on the signature page thereto.	8-K	001-36830	10.1	December 27, 2022	
10.21	Amended and Restated Executive Employment Agreement between the Registrant and Benjamin L. Palleiko, dated June 8, 2023.	8-K	001-36830	10.1	June 14, 2023	
10.22	Amended and Restated 2021 Equity Inducement Plan and forms of agreement.	S-8	333-272777	99.1	June 20, 2023	
21.1	Subsidiaries of the Registrant.	10-K	001-36830	21.1	July 1, 2020	
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
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	Inline XBRL Instance Document - the instance document does not appear in the interactive data file because its XBRL tags are embedded within the inline XBRL document.	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.	X
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document.	X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.	X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)	X

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.

KALVISTA PHARMACEUTICALS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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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, 2023 and 2022, 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, 2023, 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, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended April 30, 2023, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

Critical Audit Matters

Critical audit matters are matters arising from the current-period audit of the financial statements that were communicated or required to be communicated to the audit committee and that (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ Deloitte & Touche LLP
Boston, Massachusetts
July 7, 2023

We have served as the Company's auditor since 2016

KALVISTA PHARMACEUTICALS, INC.
Consolidated Balance Sheets
April 30, 2023 and 2022
(in thousands except share and per share amounts)

	2023	2022
Assets		
Current assets:		
Cash and cash equivalents	\$ 56,238	\$ 30,732
Marketable securities	93,137	135,470
Research and development tax credit receivable	16,568	14,098
Prepaid expenses and other current assets	6,383	13,347
Total current assets	172,326	193,647
Property and equipment, net	2,948	2,178
Right of use assets	7,822	7,862
Other assets	106	193
Total assets	\$ 183,202	\$ 203,880
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 4,817	\$ 3,638
Accrued expenses	9,128	6,961
Lease liability - current portion	1,087	977
Total current liabilities	15,032	11,576
Long-term liabilities:		
Lease liability - net of current portion	7,145	7,211
Total long-term liabilities	7,145	7,211
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Common stock, \$0.001 par value, 100,000,000 authorized		
Shares issued and outstanding: 34,171,138 and 24,550,748 as of April 30, 2023 and 2022, respectively	34	25
Additional paid-in capital	507,133	439,104
Accumulated deficit	(343,082)	(250,175)
Accumulated other comprehensive loss	(3,060)	(3,861)
Total stockholders' equity	161,025	185,093
Total liabilities and stockholders' equity	\$ 183,202	\$ 203,880

See notes to consolidated financial statements.

KALVISTA PHARMACEUTICALS, INC.
Consolidated Statements of Operations and Comprehensive Loss
Years Ended April 30, 2023, 2022 and 2021
(in thousands, except share and per share amounts)

	<u>2023</u>	<u>2022</u>	<u>2021</u>
Revenue.....	\$ —	\$ —	\$ —
Operating expenses:			
Research and development.....	80,276	70,167	41,286
General and administrative.....	30,595	26,446	16,637
Total operating expenses.....	<u>110,871</u>	<u>96,613</u>	<u>57,923</u>
Operating loss.....	(110,871)	(96,613)	(57,923)
Other income:			
Interest income.....	2,232	1,090	903
Foreign currency exchange gain (loss).....	90	(1,537)	847
Other income (expenses), net.....	15,642	14,721	9,929
Total other income.....	<u>17,964</u>	<u>14,274</u>	<u>11,679</u>
Loss before income taxes.....	(92,907)	(82,339)	(46,244)
Income tax (benefit) expense.....	—	—	—
Net loss.....	<u>\$ (92,907)</u>	<u>\$ (82,339)</u>	<u>\$ (46,244)</u>
Other comprehensive income (loss):			
Foreign currency translation (loss) gain.....	(604)	(1,499)	1,076
Unrealized holding (loss) gain on marketable securities.....	1,266	(1,511)	(473)
Reclassification adjustment for realized loss (gain) on available for sale securities included in net loss.....	<u>139</u>	<u>581</u>	<u>(153)</u>
Total other comprehensive (loss) income:	<u>\$ 801</u>	<u>\$ (2,429)</u>	<u>\$ 450</u>
Comprehensive loss.....	<u>\$ (92,106)</u>	<u>\$ (84,768)</u>	<u>\$ (45,794)</u>
Net loss per share, basic and diluted.....	\$ (3.33)	\$ (3.36)	\$ (2.42)
Weighted average common shares outstanding, basic and diluted...	27,890,846	24,473,092	19,094,440

See notes to consolidated financial statements.

KALVISTA PHARMACEUTICALS, INC.
Consolidated Statements of Changes in Stockholders' Equity
Years Ended April 30, 2023, 2022 and 2021
(in thousands, except share and per share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount				
Balance at May 1, 2020	17,845,599	\$ 18	\$ 207,208	\$ (121,592)	\$ (1,882)	\$ 83,752
Issuance of common stock from public offering, net of issuance costs of \$0.2 million	6,181,250	6	208,928	—	—	208,934
Issuance of common shares under an at-the-market sales agreement, net of issuance costs of \$0.1 million	97,332	—	1,648	—	—	1,648
Issuance of common stock from equity incentive plans	298,350	—	1,535	—	—	1,535
Stock-based compensation expense	—	—	7,118	—	—	7,118
Net loss	—	—	—	(46,244)	—	(46,244)
Foreign currency translation (loss) gain ..	—	—	—	—	1,076	1,076
Unrealized holding (loss) gain from marketable securities.....	—	—	—	—	(473)	(473)
Reclassification adjustment for realized loss (gain) on marketable securities included in net loss	—	—	—	—	(153)	(153)
Balance at April 30, 2021	<u>24,422,531</u>	<u>24</u>	<u>426,437</u>	<u>(167,836)</u>	<u>(1,432)</u>	<u>257,193</u>
Issuance of common stock from equity incentive plans	128,217	1	1,581	—	—	1,582
Stock-based compensation expense	—	—	11,086	—	—	11,086
Net loss	—	—	—	(82,339)	—	(82,339)
Foreign currency translation (loss) gain ..	—	—	—	—	(1,499)	(1,499)
Unrealized holding (loss) gain from marketable securities.....	—	—	—	—	(1,511)	(1,511)
Reclassification adjustment for realized loss (gain) on marketable securities included in net loss	—	—	—	—	581	581
Balance at April 30, 2022	<u>24,550,748</u>	<u>25</u>	<u>439,104</u>	<u>(250,175)</u>	<u>(3,861)</u>	<u>185,093</u>
Issuance of common stock from equity incentive plans	62,267	—	449	—	—	449
Release of restricted stock units.....	73,924	—	—	—	—	—
Issuance of common stock, net of issuance costs of \$0.3 million	9,484,199	9	56,573	—	—	56,582
Issuance of pre-funded warrants for the purchase of common stock, net of issuance costs	—	—	1,085	—	—	1,085
Stock-based compensation expense	—	—	9,922	—	—	9,922
Net loss	—	—	—	(92,907)	—	(92,907)
Foreign currency translation (loss) gain ..	—	—	—	—	(604)	(604)
Unrealized holding (loss) gain from marketable securities.....	—	—	—	—	1,266	1,266
Reclassification adjustment for realized loss (gain) on marketable securities included in net loss	—	—	—	—	139	139
Balance at April 30, 2023	<u>34,171,138</u>	<u>\$ 34</u>	<u>\$ 507,133</u>	<u>\$ (343,082)</u>	<u>\$ (3,060)</u>	<u>\$ 161,025</u>

See notes to consolidated financial statements.
KALVISTA PHARMACEUTICALS, INC.
Consolidated Statements of Cash Flows
Years Ended April 30, 2023, 2022 and 2021
(in thousands)

	2023	2022	2021
Cash flows from operating activities:			
Net loss	\$ (92,907)	\$ (82,339)	\$ (46,244)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	718	564	537
Stock-based compensation expense	9,922	11,086	7,118
Realized loss (gain) from sale of marketable securities	139	581	(153)
Non-cash operating lease expense	84	179	114
Amortization of premium on available for sale securities	988	2,565	685
Foreign currency exchange loss (gain)	(1,618)	1,552	(574)
Changes in operating assets and liabilities:			
Research and development tax credit receivable	(2,316)	(5,201)	7,457
Prepaid expenses and other assets	6,690	(9,280)	(244)
Accounts payable	1,107	1,687	150
Accrued expenses	1,932	472	983
Net cash used in operating activities	(75,261)	(78,134)	(30,171)
Cash flows from investing activities:			
Purchases of available for sale securities	(98,246)	(136,920)	(201,210)
Sales and maturities of available for sale securities	140,857	195,711	53,638
Acquisition of property and equipment	(1,196)	(931)	(82)
Net cash provided by (used in) investing activities	41,415	57,860	(147,654)
Cash flows from financing activities:			
Issuance of common stock, net of offering expenses	56,582	—	210,582
Issuance of pre-funded warrants	1,085	—	—
Issuance of common stock from equity incentive plans	449	1,581	1,535
Net cash provided by financing activities	58,116	1,581	212,117
Effect of exchange rate changes on cash and cash equivalents	1,236	(1,167)	511
Net (decrease) increase in cash and cash equivalents	25,506	(19,860)	34,803
Cash and cash equivalents, beginning year	30,732	50,592	15,789
Cash and cash equivalents, end of year	\$ 56,238	\$ 30,732	\$ 50,592
Supplemental disclosures of cash flow information:			
Right of use assets obtained in exchange for operating lease liabilities...	\$ 1,192	\$ 3,185	\$ 4,784
Property and equipment included in accounts payable and accrued expenses	\$ 47	\$ 149	\$ —

See notes to consolidated financial statements.

KALVISTA PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements

Note 1. Description of Business and Basis of Presentation

KalVista Pharmaceuticals, Inc. (together with its subsidiaries, 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 candidate is an inhibitor of plasma kallikrein being developed for hereditary angioedema (“HAE”). 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.

In March 2022 the Company initiated the KONFIDENT trial, a phase 3 clinical study to evaluate the safety and efficacy of sebetralstat as a potential on-demand therapy for acute HAE attacks. In October 2022, the Company announced the termination of the phase 2 KOMLETE study for its potential prophylactic treatment KVD824, due to elevations in liver enzymes observed in patients during the trial. In July 2023, the Company announced that the KONFIDENT trial has reached its targeted enrollment of 114 patients and that data from the trial is expected in the fourth quarter of 2023.

The Company’s headquarters is located in Cambridge, Massachusetts, with additional offices and research activities located in Porton Down, United Kingdom, and Salt Lake City, Utah.

The Company has devoted substantially all of its efforts to research and development, including clinical trials of its product candidate sebetralstat. 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 United States (“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. As of April 30, 2023, the Company had an accumulated deficit of \$343.1 million and cash, cash equivalents and marketable securities totaling \$149.4 million. The Company’s working capital, primarily cash, cash equivalents 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.

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 United Kingdom (“U.K.”) 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.

Recent Accounting Pronouncements: In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which amends the impairment model by requiring entities to use a forward-looking approach on expected losses to estimate credit losses on certain financial instruments, including trade receivables and available-for-sale debt securities. The new guidance is effective for the Company as of May 1, 2023. The adoption of ASU 2016-13 is not expected to have a material impact on the Company’s financial position, results of operations, and cash flows.

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:

<u>Asset Classification</u>	<u>Estimated Useful Life</u>
Machinery and equipment	1-5 Years
Furniture and fixtures	1-5 Years
Computer equipment	3-4 Years
Leasehold improvements	15 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.

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:

	<u>2023</u>	<u>April 30, 2022</u>	<u>2021</u>
Stock options and awards	5,554,951	3,968,559	2,836,598

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.

The weighted average number of common shares used in the basic and diluted net loss per common share calculations includes the weighted-average pre-funded warrants outstanding during the period as they are exercisable at any time for nominal cash consideration.

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 similar instruments or 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, 2023 and 2022:

	<u>Level 1</u>	<u>Level 2</u>	<u>Level 3</u>	<u>Balance at April 30, 2023</u>
Cash equivalents	\$ 31,507	\$ —	\$ —	\$ 31,507
Marketable securities:				
Corporate debt securities.....	—	77,967	—	77,967
U.S. government agency securities	—	15,170	—	15,170
	<u>\$ 31,507</u>	<u>\$ 93,137</u>	<u>\$ —</u>	<u>\$ 124,644</u>

	<u>Level 1</u>	<u>Level 2</u>	<u>Level 3</u>	<u>Balance at April 30, 2022</u>
Cash equivalents	\$ 13,735	\$ —	\$ —	\$ 13,735
Marketable securities:				
Corporate debt securities.....	—	112,005	—	112,005
U.S. government agency securities	—	23,465	—	23,465
	<u>\$ 13,735</u>	<u>\$ 135,470</u>	<u>\$ —</u>	<u>\$ 149,205</u>

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, 2023 and 2022:

	<u>April 30, 2023</u>			
	<u>Amortized Cost</u>	<u>Unrealized Gains</u>	<u>Unrealized Losses</u>	<u>Fair Value</u>
Corporate debt securities	\$ 77,768	\$ 367	\$ (168)	\$ 77,967
Obligations of the U.S. Government and its agencies	15,094	76	—	15,170
Total investments.....	<u>\$ 92,862</u>	<u>\$ 443</u>	<u>\$ (168)</u>	<u>\$ 93,137</u>

	<u>April 30, 2022</u>			
	<u>Amortized Cost</u>	<u>Unrealized Gains</u>	<u>Unrealized Losses</u>	<u>Fair Value</u>
Corporate debt securities.....	\$ 112,997	\$ 2	\$ (994)	\$ 112,005
Obligations of the U.S. Government and its agencies	23,602	—	(137)	23,465
Total investments	<u>\$ 136,599</u>	<u>\$ 2</u>	<u>\$ (1,131)</u>	<u>\$ 135,470</u>

The unrealized losses of the Company's available-for-sale securities above were a result of market interest rate increases. The Company's portfolio is structured to allow its short-term debt securities to mature, if needed, to avoid any material losses related to the rise in interest rates. As of April 30, 2023, if the securities are held to maturity, the change in fair value to be recognized as other comprehensive income (loss) is calculated as immaterial.

The following table summarizes the scheduled maturity for the Company's investments at April 30, 2023:

	April 30,
	2023
Maturing in one year or less	\$ 81,419
Maturing after one year through two years	7,687
Maturing after two years through four years.....	4,031
Total investments	<u>\$ 93,137</u>

Note 4. Prepaid Expenses and Other Current Assets

At April 30, 2023 and 2022, prepaid expenses and other current assets consisted of (in thousands):

	<u>2023</u>	<u>2022</u>
Prepaid clinical expenses	\$ 1,724	\$ 8,404
Other prepaid expenses	2,583	2,234
Interest and other receivables.....	654	888
VAT receivable	1,422	1,821
Total prepaid expenses and other current assets .	<u>\$ 6,383</u>	<u>\$ 13,347</u>

Note 5. Property and Equipment

At April 30, 2023 and 2022, property and equipment consisted of (in thousands):

	<u>2023</u>	<u>2022</u>
Laboratory equipment	\$ 2,404	\$ 2,153
Office equipment	249	148
Furniture & fixtures	398	299
Leasehold improvements.....	2,855	1,997
Total property and equipment at cost	5,906	4,597
Less: Accumulated depreciation.....	(2,958)	(2,419)
Property and equipment, net.....	<u>\$ 2,948</u>	<u>\$ 2,178</u>

For the years ended April 30, 2023 and 2022, depreciation expense was \$0.7 million and \$0.6 million, respectively.

Note 6. Accrued Expenses

At April 30, 2023 and 2022, accrued expenses consisted of (in thousands):

	<u>2023</u>	<u>2022</u>
Accrued research expense	\$ 3,817	\$ 2,011
Accrued compensation	4,207	4,168
Accrued professional fees	906	474
Other accrued expenses	198	308
Total accrued expenses.....	<u>\$ 9,128</u>	<u>\$ 6,961</u>

Note 7. Stockholder's Equity

Direct Offering

On December 23, 2022, the Company entered into subscription agreements with institutional investors to sell, in a registered direct offering, an aggregate of 9,484,199 shares of common stock at a price of \$6.00 per share and pre-funded warrants to purchase up to 182,470 shares of common stock at a price of \$5.999 per pre-funded warrant. The purchase price per share of each pre-funded warrant represents the per share offering price for the common stock, less the \$0.001 per share exercise price of each pre-funded warrant. The net proceeds from the registered direct offering, after deducting \$0.3 million in expenses, were approximately \$57.7 million. The pre-funded warrants do not expire and are exercisable at any time after the issuance date. The Company evaluated the pre-funded warrants for liability or equity classification in accordance with the provisions of ASC Topic 480, *Distinguishing Liabilities from Equity*, and determined that equity treatment was appropriate because the pre-funded warrants did not meet the definition of liability instruments and met the criteria for permanent equity. As of April 30, 2023, no pre-funded warrants were exercised.

Public Offering of Common Stock

On February 16, 2021, the Company completed a public offering of 6,181,250 shares of its common stock at a price of \$36.00 per share, including the underwriters' full exercise of their option to purchase 806,250 additional shares of common stock. The total net proceeds to the Company were \$209.2 million, after deducting underwriting discounts, commissions, and other offering expenses payable by the Company.

ATM Program

On May 21, 2021, the Company filed a shelf registration statement pursuant to which the Company may offer and sell securities having an aggregate public offering price of up to \$300 million. In connection with the filing of the Registration Statement, the Company also entered into a sales agreement with a sales agent, pursuant to which the Company may issue and sell shares of its common stock under an at-the-market (the "ATM") offering program. During the twelve months ended April 30, 2023, the Company did not offer or sell any shares under the sales agreement.

Note 8. Stock-Based Compensation

The Company has four plans that provide for equity-based compensation. Two are legacy plans for which no further grants are to be made. As of April 30, 2023, 531,358 stock awards remain available for grant under the 2017 Equity Incentive Plan ("2017 Plan"). There are 6,178,171 shares of the Company's common stock that are reserved for issuance upon exercise or settlement of stock options or other awards under these four 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.

In July 2021, the Company approved the 2021 Equity Inducement Plan to reserve 350,000 shares of its common stock to be used exclusively for grants of awards as a material inducement to such individuals' entry into employment with the Company within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. As of April 30, 2023, there were 124,396 shares remaining available to be issued under the 2021 Inducement Plan.

In June 2023, the Company amended and restated the 2021 Equity Inducement Plan (the "Amendment and Restated 2021 Equity Inducement Plan") to register 500,000 additional shares of its common stock. See Note 14, Subsequent Events.

The Company also has in place the 2017 Employee Stock Purchase Plan ("ESPP"), under which employees have the option to purchase the Company's common stock at a discount of 15% from the market price during predetermined offering periods each year. There are 974,670 shares available for future issuance under the ESPP as of April 30, 2023.

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. The Company determined the expected volatility by using available historical price information. 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:

	<u>2023</u>	<u>2022</u>	<u>2021</u>
Risk-free interest rate	3.11%	1.08%	0.47%
Expected life of the options	6.25 years	6.25 years	6.25 years
Expected volatility of the underlying stock	92.24%	85.4%	81.7%
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,		
	2023	2022	2021
Research and development.....	\$ 5,384	\$ 5,189	\$ 3,174
General and administrative.....	4,538	5,897	3,944
Total stock-based compensation expense.....	<u>\$ 9,922</u>	<u>\$ 11,086</u>	<u>\$ 7,118</u>

A summary of option activity for the year ended April 30, 2023 is presented below:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding at May 1, 2022.....	3,593,021	\$ 16.10	7.26	\$ 6,430
Options Exercised.....	(16,938)	10.00		
Options Granted.....	608,750	9.24		
Options Cancelled.....	(124,658)	18.93		
Outstanding at April 30, 2023.....	<u>4,060,175</u>	<u>\$ 15.01</u>	<u>6.65</u>	<u>\$ 1,668</u>
Exercisable at April 30, 2023	<u>2,801,769</u>	<u>\$ 14.63</u>	<u>5.99</u>	<u>\$ 1,548</u>
Vested and expected to vest at April 30, 2023	<u>4,060,175</u>	<u>\$ 15.01</u>	<u>6.65</u>	<u>\$ 1,668</u>

The weighted-average grant date fair value of stock options granted during the years ended April 30, 2023, 2022 and 2021 was \$7.14, \$16.98, and \$8.24, 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, 2023, 2022 and 2021 was \$0.3 million, \$0.8 million and \$4.2 million, respectively. The total cash received by the Company as a result of employee stock option exercises during the years ended April 30, 2023, 2022 and 2021 was \$0.2 million, \$1.4 million, and \$1.5 million, respectively.

As of April 30, 2023, there was \$12.3 million of unrecognized compensation expense related to unvested awards, which is expected to be recognized over a weighted-average period of 2.2 years.

Restricted Stock Units

During the fiscal year ended April 30, 2023, the Company granted both executives and employees Restricted Stock Units ("RSUs") from the 2017 Equity Incentive Plan. All RSUs granted are subject to a service condition, and vest over a three or four-year period with equal quarterly vesting.

A summary of activity in connection with our RSUs for the year ended April 30, 2023 is as follows:

	Number of Shares Outstanding	Weighted Average Grant Date Fair Value Per Share
RSU outstanding at April 30, 2022.....	-	-
RSUs awarded.....	817,166	8.00
RSUs released	(73,924)	8.43
RSUs forfeited.....	(1,000)	8.12
RSUs outstanding at April 30, 2023	<u>742,242</u>	<u>7.96</u>

As of April 30, 2023, the unrecognized stock-based compensation cost related to the RSUs was \$5.5 million, which is expected to be recognized over a weighted-average period of 2.82 years

In March 2022, the Company granted 360,000 performance-based restricted stock units (“PSUs”) to five executives under the 2017 Equity Incentive Plan with a grant date fair value of \$15.39. The performance-based metric for the awards is the success of the Company’s Phase 3 clinical trial of the sebetralstat program. Upon successful completion of the performance metric, 100% of the PSUs will vest in full. As of April 30, 2023 the Company has not recognized any compensation expense related to these awards as the achievement of the Performance Metric is not yet deemed to be probable.

In January 2023, the Company granted 360,000 PSUs to five executives under the 2017 Equity Incentive Plan with a grant date fair value of \$6.82. The performance-based metric for the awards is the FDA approval of a New Drug Application for sebetralstat. Upon successful completion of the performance metric, 100% of the PSUs will vest in full. As of April 30, 2023 the Company has not recognized any compensation expense related to these awards as the achievement of the Performance Metric is not yet deemed to be probable.

Note 9. 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 \$30.5 million as of April 30, 2023.

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, 2023 and 2022.

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 for DME, 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 10. Leases

The Company has a lease agreement for approximately 8,300 square feet of space for its headquarters located in Cambridge, Massachusetts that runs through September 2028.

The Company has lease agreements for approximately 13,400 square feet of office and research laboratory space located in Porton Down, United Kingdom that runs through April 2028.

The Company has a lease agreement in Salt Lake City, Utah for approximately 6,200 square feet of office space that commenced in November 2021 that runs through February 2032.

The Company has a lease agreement for approximately 500 square feet of research laboratory space in Cambridge, Massachusetts that commenced in July 2022 with an option to renew annually.

The Company is also party to several operating leases for office and laboratory space as well as certain lab equipment. Total rent expense was \$1.8 million, \$1.7 million and \$0.9 million for the years ended April 30, 2023, 2022 and 2021, 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 years ended April 30, 2023 and 2022 (in thousands):

	<u>2023</u>	<u>2022</u>
Operating lease costs	\$ 1,806	\$ 1,743
Short-term lease costs	13	14
Variable lease costs	174	169
Total lease costs	<u>\$ 1,993</u>	<u>\$ 1,926</u>

The following table summarizes the undiscounted payments due under lease liabilities and the present value of those liabilities as of April 30, 2023 (in thousands):

<u>Years ending April 30,</u>	<u>Operating Leases</u>
2024.....	\$ 1,736
2025.....	1,772
2026.....	1,809
2027.....	1,848
2028.....	1,844
Thereafter	1,537
Total lease payments.....	10,546
Less: imputed interest	2,314
Total lease liabilities	8,232
Current lease liabilities.....	1,087
Long-term lease liabilities.....	<u>\$ 7,145</u>

The following table summarizes the lease term and discount rate as of April 30, 2023 and 2022:

	<u>2023</u>	<u>2022</u>
Weighted-average remaining lease term (years)	6.0	6.9
Weighted-average discount rate	9.0%	9.0%

The following table summarizes the cash paid for amounts included in the measurement of lease liabilities for the years ended April 30, 2023 and 2022 (in thousands):

	<u>2023</u>	<u>2022</u>
Cash paid for amounts included in the measurement of operating lease liabilities	\$ 1,615	\$ 1,287

Note 11. Income Taxes

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

	<u>2023</u>	<u>2022</u>	<u>2021</u>
Domestic	\$ (27,437)	\$ (21,145)	\$ (10,909)
Foreign	(65,470)	(61,194)	(35,335)
	<u>\$ (92,907)</u>	<u>\$ (82,339)</u>	<u>\$ (46,244)</u>

For the years ended April 30, 2023, 2022 and 2021, the Company did not record any U.S. Federal income tax benefit or expense.

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

	<u>2023</u>	<u>2022</u>	<u>2021</u>
Income tax benefit at U.S. federal statutory rate	21.0%	21.0%	21.0%
Foreign rate differential	2.8%	(1.5)%	(1.6)%
Nondeductible expenses - UK R&D credit	(7.7)%	(10.6)%	(8.3)%
Other	(0.3)%	(0.8)%	0.4%
Valuation allowance	(15.8)%	(8.1)%	(11.5)%
	<u>—</u>	<u>—</u>	<u>—</u>

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

	<u>2023</u>	<u>2022</u>
Deferred tax assets:		
Net operating loss ("NOL") carryforwards	\$ 35,790	\$ 23,219
Operating lease liabilities	1,777	1,634
174 Capitalization	3,922	864
Other	5,549	4,072
Subtotal	47,038	29,789
Less: valuation allowance	(45,276)	(28,212)
Deferred tax assets, net of valuation allowance	1,762	1,577
Deferred tax liabilities:		
Operating lease - Right-of-use assets	(1,693)	(1,570)
Other	(69)	(7)
Net deferred tax asset	<u>\$ —</u>	<u>\$ —</u>

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 April 30, 2023 and 2022, respectively. During the years ended April 30, 2023 and 2022 the valuation allowance changed by \$17.0 million. Realization of deferred tax assets is dependent upon the generation of future taxable income.

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 public offerings in December 2005, a transaction in November 2016 and a public offering in September 2018. The offering in September of 2018 resulted in an ownership change as of February 2019. The Company believes an ownership change occurred in December 2022 and continues to analyze the impact if any on future NOL utilization.

As of April 30, 2023, the Company has NOL carryforwards for U.S. federal income taxes of \$6.1 million that expire in 2036 and \$16.1 million that can be carried forward indefinitely. The Company also has NOL carryforwards for state income taxes of \$16.8 million that begin to expire in 2036 and NOL carryforwards for U.K. income taxes of \$120.3 million that do not expire.

The Company anticipates NOL carryforwards to be limited in the future based on the impact of an ownership change in December 2022. The analysis of which will be final upon the filing of the Company's 2022 tax return.

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 tax returns in the U.K. The Company is subject to U.S. Federal, state, and U.K. income tax examinations by authorities for tax years ending after 2018. There are currently no federal, state, or U.K. audits in process. Tax year 2019 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, 2023 and 2022, respectively.

As part of the Tax Cuts and Jobs Act of 2017 (TCJA), beginning with the Company's 2022 tax year, the Company is required to capitalize research and development expenses, as defined under Internal Revenue Code section 174. For expenses that are incurred for research and development in the U.S., the amounts will be amortized over 5 years, and expenses that are incurred for research and experimentation outside the U.S. will be amortized over 15 years. This provision has not had a significant impact to the consolidated financial statements.

Note 12. 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 of the U.S. parent company are eligible to participate in the Company's 401(k) Plan in which employee contributions on a pre-tax basis are supplemented by matching contributions by the Company. Total employer contributions to both plans for the years ended April 30, 2023, 2022 and 2021 were \$0.8 million, \$0.6 million and \$0.4 million respectively.

Note 13. Other Income (Expenses), Net

At April 30, 2023 and 2022, other income and expenses consisted of (in thousands):

	2023	2022
R&D tax credit.....	\$ 15,785	\$ 15,303
Realized (loss) on sale of securities.....	(139)	(581)
Miscellaneous.....	(4)	(1)
Other income (expenses), net.....	<u>\$ 15,642</u>	<u>\$ 14,721</u>

As of April 30, 2023 and 2022 the Company had research and development tax credits receivable totaling \$16.6 million and \$14.1 million, respectively. This tax credit is related to a tax scheme for small and medium enterprises in the U.K. 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 \$15.8 million and \$15.3 million related to these programs in the years ended April 30, 2023 and 2022, respectively.

The Company receives tax credits from the U.K. government based on claims made under the Small Medium Enterprise ("SME") research and development tax relief program. Qualifying expenditures largely relate to research and development activities performed by third parties on the Company's behalf, as well as employment costs for research staff and consumables incurred. The research and development tax credits are recognized when the qualifying expenditure has been incurred and there is reasonable assurance that the reimbursement will be received.

In November 2022, the U.K. government announced changes to the research and development tax credit program. These changes, which include a reduction in tax credit rates for SMEs, were effective on April 1, 2023 and resulted in the credit for the SME R&D regime being reduced from 130% to 86%.

Note 14. Subsequent Events

In June 2023, the Company amended and restated the 2021 Equity Inducement Plan to register 500,000 additional shares of its common stock to be used exclusively for grants of awards as a material inducement to such individuals' entry into employment with the Company within the meaning of Rule 563(c)(4) of the Nasdaq Listing Rules.

In July 2023, the achievement of the performance metric for certain PSUs granted in June 2023 with performance factors based on full enrollment for the KVD900-301 clinical trial was certified by the Compensation Committee of the Company's Board of Directors. 306,667 PSUs were granted to seven executives under the 2017 Equity Incentive Plan with a grant date fair value of \$9.99 and will vest in four quarterly installments beginning in August 2023.

