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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2018

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: **001-37569**

STRONGBRIDGE BIOPHARMA plc
(Exact name of Registrant as specified in its charter)

Ireland	**98-1275166**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

900 Northbrook Drive
Suite 200
Trevose, PA 19053
+1 610-254-9200
(Address of principal executive offices)

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

Title of each class	Name of each exchange on which registered
Ordinary shares, par value $0.01 per share	**The NASDAQ Global Select Market**

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

None
(Title of Class)

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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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

Large Accelerated Filer ☐	Accelerated Filer ☒
Non-Accelerated Filer ☐	Smaller reporting company ☒
	Emerging growth company ☒

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

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

The aggregate market value of the voting and non-voting stock held by non-affiliates of the Registrant, as of June 30, 2018, the last business day of the Registrant's most recently completed second fiscal quarter, was approximately $260,068,140. Solely for purposes of this disclosure, ordinary shares held by executive officers and directors of the Registrant as of such date have been excluded because such persons may be deemed to be affiliates. This determination of executive officers and directors as affiliates is not necessarily a conclusive determination for any other purposes.

54,158,948 ordinary shares were issued and outstanding as of February 20, 2019.

DOCUMENTS INCORPORATED BY REFERENCE: NONE

Strongbridge Biopharma plc
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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS AND MARKET DATA

This Annual Report on Form 10-K ("Annual Report") contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, size of market or patient population, timing and likelihood of success, plans and objectives of management for future operations, and future results of current and anticipated products, are forward-looking statements. These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. The words "anticipate," "assume," "believe," "contemplate," "continue," "could," "estimate," "expect," "goal," "intend," "may," "might," "objective," "plan," "potential," "predict," "project," "positioned," "seek," "should," "target," "will," "would," or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are based on current expectations, estimates, forecasts and projections about our business and the industry in which we operate and management's beliefs and assumptions, are not guarantees of future results, performance or developments and involve known and unknown risks, uncertainties and other factors that may cause our actual results or developments to differ materially from the expectations contained in the forward-looking statements. Such risks and uncertainties include those described throughout this Annual Report and particularly in "Risk Factors" in Part I, Item 1A of this Annual Report. Given these risks and uncertainties, readers are cautioned not to place undue reliance on such forward-looking statements. Readers are urged to carefully review and consider the various disclosures made in this Annual Report and in other documents we file from time to time with the Securities and Exchange Commission (the "SEC") that disclose risks and uncertainties that may affect our business. The forward-looking statements included in this Annual Report do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. In addition, the forward-looking statements in this Annual Report are made as of the date of this filing, and we do not undertake, and expressly disclaims any duty, to update such statements, whether as a result of new information, new developments or otherwise, except to the extent that disclosure may be required by law.

Solely for convenience, the trademarks and trade names in this Annual Report are referred to without the ® and ™ symbols, but absence of such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. The trademarks, trade names and service marks appearing in this Annual Report are the property of their respective owners.

Unless the context requires otherwise, references in this Annual Report to "Strongbridge," "we," "us" and "our" refer to Strongbridge Biopharma plc.

PART I

ITEM 1. BUSINESS

Overview

We are a global, commercial-stage biopharmaceutical company focused on the development and commercialization of therapies for rare diseases with significant unmet needs.

Our first commercial product is Keveyis (dichlorphenamide), the first and only treatment approved by the U.S. Food and Drug Administration (the "FDA") for hyperkalemic, hypokalemic, and related variants of primary periodic paralysis ("PPP"), a group of rare hereditary neuromuscular disorders that cause episodes of muscle weakness or paralysis.

In January 2018, Strongbridge Ireland Ltd., one of our wholly-owned subsidiaries, acquired the U.S. and Canadian rights to Macrilen (macimorelin), the first and only oral drug approved by the FDA for the diagnosis of patients with adult growth hormone deficiency. We launched Macrilen in the United States in July 2018. In December 2018, we sold Strongbridge Ireland Ltd. to Novo Nordisk Healthcare AG ("Novo") for $145 million plus tiered royalties on net sales of Macrilen through 2027. In addition, Strongbridge U.S. Inc, another of our wholly-owned subsidiaries, entered into an agreement with Novo Nordisk Inc., a subsidiary of Novo ("NNI"), pursuant to which NNI will fund the costs of 23 of our field-based employees to provide full-time ongoing services to NNI, including the promotion of Macrilen in the United States, for a period of three years. Novo also purchased 5.2 million of our ordinary shares at a purchase price of $7.00 per share.

We have two clinical-stage product candidates for rare endocrine diseases, Recorlev and veldoreotide. Recorlev (levoketoconazole) is a cortisol synthesis inhibitor currently being studied for the treatment of endogenous Cushing's syndrome. Veldoreotide is a next-generation somatostatin analog being investigated for potential applications in conditions amenable to somatostatin receptor activation, such as acromegaly. Both Recorlev and veldoreotide have received orphan designation from the FDA and the European Medicines Agency ("EMA").

We are building a rare disease, franchise-based business model focused on expansion through a disciplined in-licensing and acquisition strategy. We will continue to identify and evaluate the acquisition of products and product candidates for licensing or acquisition that would be complementary to our existing rare neuromuscular and endocrine franchises or that would form the basis for new rare disease franchises. We believe this approach will enable us to maximize our commercial potential by further leveraging our existing resources and expertise.

Our Franchises

Rare Endocrine Franchise

- *Macrilen (macimorelin), an oral growth hormone secretagogue receptor agonist, is indicated for the diagnosis of AGHD.* In December 2018, we sold our subsidiary that held the U.S. and Canadian marketing rights to Macrilen to Novo Nordisk for $145 million and the right to receive tiered royalties on net sales of Macrilen by Novo through 2027. In addition, Novo will fund the costs of 23 of our field-based employees to provide full-time ongoing services to Novo, including the promotion of Macrilen in the United States, for a period of three years
- *Recorlev (levoketoconazole), a cortisol synthesis inhibitor, is in Phase 3 clinical development for the treatment of endogenous Cushing's syndrome.* Endogenous Cushing's syndrome is a rare endocrine disorder characterized by sustained elevated cortisol levels that most commonly result from a benign tumor of the pituitary gland. We believe that Recorlev, which is the isolated, "left-handed" mirror image, or enantiomer, of ketoconazole, has the potential to become the new standard of care for the drug therapy of endogenous Cushing's syndrome. In August 2018, we announced top-line results from our multinational, pivotal Phase 3 SONICS study evaluating Recorlev for treatment of endogenous Cushing's syndrome. The

open-label, single-arm SONICS study achieved statistical significance of its pre-specified primary endpoint, with 30 percent of patients achieving normalization of mean urinary free cortisol ("UFC") following six months of maintenance treatment with Recorlev without a dose increase during maintenance therapy (one-sided p=.0154, vs the null hypothesis of less than or equal to 20%). Sensitivity analyses as well as secondary and exploratory endpoints of UFC response were supportive of the primary endpoint.

In addition, we have initiated LOGICS, a second Phase 3 clinical trial of Recorlev for the treatment of endogenous Cushing's syndrome. The LOGICS study will supplement the long-term efficacy and safety data from the SONICS trial via a double-blind, placebo-controlled, randomized-withdrawal phase of approximately 8 weeks among 54 patients that follows an open-label titration and maintenance phase of approximately 14 weeks. Top-line data following the randomized-withdrawal phase of LOGICS are expected by the end of 2019.

Upon completion of the clinical development program, we intend to file for marketing authorizations in the United States and elsewhere. Following consultations with the FDA, we have determined that the 505(b)(2) approval pathway, which permits a New Drug Application ("NDA") applicant to rely on data from studies that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference, is the appropriate pathway for a Recorlev NDA. Because NDA approval can rely in part on data already accepted by the FDA or otherwise publicly available, an abbreviated and reduced development program may be possible. We intend to rely on published literature and the FDA's prior findings concerning the safety and/or effectiveness of ketoconazole in our NDA for Recorlev. A similar marketing authorization pathway is available in most of the rest of the world, and we believe that the studies supporting U.S. approval will likewise support approvals to market Recorlev elsewhere, including in the European Union.

- *Veldoreotide modified-release, a novel multi-receptor targeted somatostatin analog ("SSA") that was previously in Phase 2 development as an immediate release formulation.* Based on the differentiated activation pattern of somatostatin receptor subtypes ("SSTs") and the preclinical and clinical profile of immediate-release veldoreotide, we believe that modified-release veldoreotide is a next-generation somatostatin analog with potential applications in conditions amenable to somatostatin receptor activation, such as acromegaly. Veldoreotide has been granted orphan drug designation by the FDA and the EMA for treatment of acromegaly. The lead formulation for veldoreotide modified-release is based upon PLGA microspheres. PLGA is a well-known polymer, which has been widely applied in modified-release formulations due to its biocompatibility, biodegradability, and favorable release kinetics. We have initiated nonclinical studies and are planning clinical studies that seek to determine additional differentiating features of veldoreotide in both endocrine and non-endocrine conditions.

Rare Neuromuscular Franchise

- *Keveyis (dichlorphenamide), an oral carbonic anhydrase inhibitor and the only therapy approved in the United States to treat hyperkalemic, hypokalemic and related variants of PPP.* PPP is a rare genetic, neuromuscular disorder that can cause extreme muscle weakness and/or paralysis; some forms are also commonly associated with myotonia or muscle stiffness. It often interferes with daily activities and, as patients get older, it can lead to permanent muscle weakness. The two most common forms of this disorder are "hyperkalemic" and "hypokalemic" periodic paralysis. Keveyis was approved by the FDA in August 2015 and has orphan drug exclusivity status in the United States through August 7, 2022. From May 2016 to December 2016, Taro Pharmaceuticals Industries Ltd. and its affiliates ("Taro"), supplied Keveyis on a non-commercial basis to patients through a single specialty pharmacy in the United States. We acquired the U.S. marketing rights to Keveyis in December 2016 and we launched Keveyis in the United States in April 2017.

Product Sales

Our product sales in 2018 resulted from sales of Keveyis and Macrilen. In December 2018, we sold our subsidiary that held the U.S. and Canadian marketing rights to Macrilen to Novo. All of our sales were in the United

States. We operate in one operating reporting segment. We recognize net product sales at the time our products are received by our customers (primarily wholesalers and specialty pharmacies). The products are subsequently sold to patients, who are covered by payors that may provide for government-mandated or privately negotiated rebates with respect to the purchase of our products.

Our Strategy

Our goal is to transform the lives of patients by building a leading franchise-based, commercially oriented biopharmaceutical company addressing rare diseases with significant unmet medical needs. We are focused on developing, in-licensing, acquiring and eventually commercializing products and product candidates that target rare diseases across various therapeutic areas.

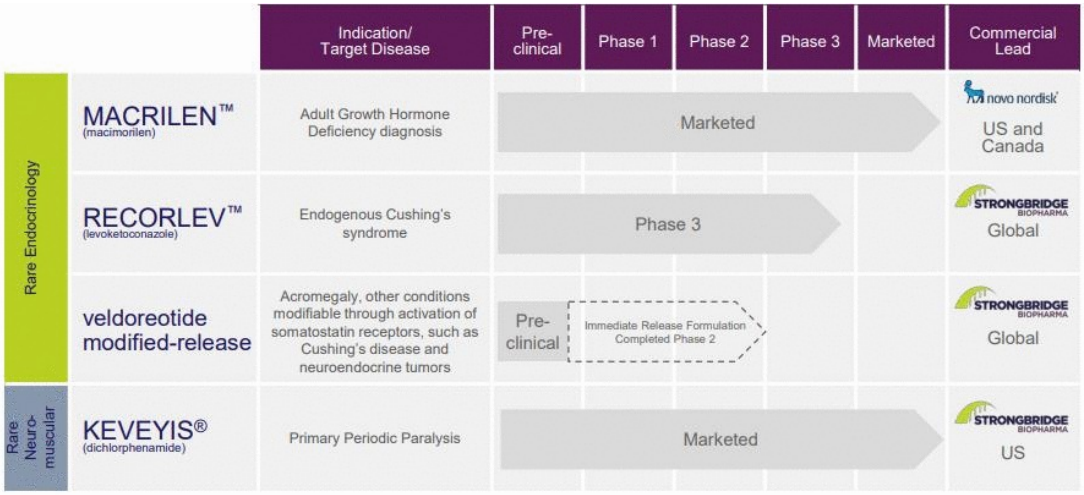
To achieve our goal, we are pursuing the following strategies:

- ***Focus on rare diseases, including development of Recorlev.*** We are selling or developing treatments for rare diseases, initially PPP and endogenous Cushing's syndrome. Rare diseases typically have a high unmet need for innovative treatment options. Drug development for the treatment of rare diseases often requires smaller clinical trials than for common diseases. Product candidates focused on rare diseases also often qualify for orphan drug designation, which in the United States provides for seven years of market exclusivity and in the European Union provides for 10 years of market exclusivity after regulatory approval to market has been granted.
- ***Independently commercialize Keveyis and other products in the United States and the European Union, while providing commercial services to Novo in order to generate additional revenue.*** We launched Keveyis in the United States in April 2017 and marketed Macrilen in the United States from July to December 2018, when we sold our subsidiary that held the U.S. and Canadian marketing rights to Novo. Our other rare disease product candidates, if approved, may be marketed in the United States, the European Union, and, selectively, in other key global markets. Given the relatively small prescriber bases for Keveyis and our two product candidates, we believe we can use a relatively small, focused field-based team to effectively promote and support our products and patients. We have established sales, marketing, market access and patient service capabilities in the United States to market Keveyis and we will continue to promote Macrilen on behalf of Novo pursuant to our agreement with them for a three-year period. We believe that some of the activities involved in our commercialization activities related to Keveyis and Macrilen will provide synergies to our commercialization of Recorlev if successful. We believe that our ability to execute on this strategy is enhanced by the significant prior commercial experience of key members of our management team. Prior to joining our company, members of our management team were involved in the launch or commercialization of over 20 pharmaceutical products.
- ***Provide Commercial Services to Novo Nordisk for the promotion of Macrilen***. As part of the transaction in December 2018, in which we sold our U.S. and Canada marketing rights to Novo Nordisk, we will receive tiered royalties on sales of Macrilen through 2027. In addition, we entered into a services agreement with Novo pursuant to which Novo will fund the costs of 23 of our field-based employees to provide full-time ongoing services to Novo, including the promotion of Macrilen in the United States, for a period of three years.
- ***Expand our portfolio through a disciplined in-licensing and acquisition strategy.*** We plan to source new product candidates by in-licensing or acquiring them. Our management team seeks to mitigate the potential risks of this strategy by adhering to our disciplined criteria of focusing on in-licensing or acquisition of products that are already commercially available or that have human clinical data that we believe suggest a relatively high probability of success for development and an attractive potential return on investment. As a result of our management team's experience in sourcing, selecting, in-licensing, and acquiring products and product candidates, we were successful in acquiring the U.S. rights to Keveyis and the U.S. and Canadian rights to Macrilen, as well as augmenting our rare endocrine franchise by adding veldoreotide to our product pipeline.

- ***Utilize a franchise model built on rare disease therapeutic areas.*** We intend to build our company by in-licensing and acquiring products and product candidates that target rare diseases in therapeutically aligned franchises with significant commercial opportunity. We believe that complementary products and product candidates will allow us to significantly leverage our expertise as well as our development and commercial infrastructure.
- ***Expand indications of products and product candidates within our franchises.*** In addition to identifying products and product candidates that can form the basis of new rare disease franchises, we also intend to leverage opportunities to develop potential products and product candidates for additional indications within their respective therapeutic franchises. We believe that this approach will enable us to maximize our commercial potential by further leveraging our existing resources and expertise.

Our Product Candidate Pipeline

The following table illustrates our product candidates by stage:



Our Rare Endocrine Franchise

Macrilen

In January of 2018, Strongbridge Ireland Ltd., one of our wholly-owned subsidiaries, acquired the U.S. and Canadian rights to Macrilen (macimorelin), the first and only oral drug approved by the FDA for the diagnosis of patients with adult growth hormone deficiency. We launched Macrilen in the United States in July 2018.

In December 2018, we sold Strongbridge Ireland Ltd. to Novo Nordisk ("Novo") for $145 million plus tiered royalties on net sales of Macrilen through 2027. Between January 1, 2019 and December 31, 2021, Novo will pay to us 12% of annual net sales of Macrilen in the United States. Between January 1, 2022 and December 31, 2027, Novo will pay to us (i) 4% of any portion of annual net sales in the United States up to $100 million and (ii) 8% of any portion of annual net sales in the United States greater than $100 million. The royalty payments are subject to certain conditions and reductions, including if Macrilen is no longer covered by a valid claim of a patent in the United States or Novo or its affiliates no longer hold exclusive marketing rights granted by the FDA. In addition, we entered into a services agreement with Novo pursuant to which Novo will fund the costs of 23 of our field-based employees to provide full-time ongoing services to Novo, including the promotion of Macrilen in the United States, for a period of three years. We will also be entitled to a performance fee of up to $1.5 million per contract year if certain conditions are met by our field-

based employees under the services arrangement, which conditions will be determined and measured by a joint committee comprised of members from Novo and from Strongbridge, with a majority of members from Novo.

Recorlev

Overview

Recorlev (levoketoconazole) is a cortisol synthesis inhibitor that we are developing for the treatment of endogenous Cushing's syndrome. The active pharmaceutical ingredient in Recorlev, levoketoconazole, exerts its therapeutic effect by blocking the synthesis of cortisol in the adrenal glands, leading to the reduction and, ideally, the normalization of blood cortisol. Recorlev has been granted orphan drug designation by the FDA and the EMA and is being developed using a dose regimen of twice daily oral administration.

Ketoconazole, although not approved for such use in the United States, is the most frequently prescribed drug therapy for endogenous Cushing's syndrome. It is used to reduce blood cortisol and ameliorate comorbidities associated with Cushing's syndrome. Molecules of ketoconazole form as mirror images, referred to as enantiomers. Manufactured ketoconazole consists of two enantiomers, 2R,4S-ketoconazole and 2S,4R-ketoconazole, that are found in equal amounts, and is therefore referred to as a racemate. Recorlev is a pure form of one (2S,4R-ketoconazole) of the two enantiomers of ketoconazole. Single-enantiomer drugs, like Recorlev, may offer safety and efficacy advantages over racemates because one of the enantiomers in a racemate can have safety issues or be less effective in the treatment of the disorder or disease. The more therapeutically favorable enantiomer may be known as the eutomer. We believe that levoketoconazole is the eutomer of ketoconazole with respect to cortisol synthesis inhibition and treatment of endogenous Cushing's syndrome.

Recorlev inhibits the cortisol synthesis pathway at several points. Based on recent top-line interim results from the SONICS study, we believe that Recorlev can have a beneficial impact on hypercortisolism, the hallmark of endogenous Cushing's syndrome, as well as benefits related to several comorbidities of endogenous Cushing's syndrome, including those associated with cardiovascular disease risk, such as diabetes, weight gain and elevation in LDL-cholesterol. In addition, we believe that Recorlev may offer an advantageous safety profile in a representative population with endogenous Cushing's syndrome. We believe that Recorlev has the potential to become a new standard of care for chronic drug therapy of endogenous Cushing's syndrome due to its demonstrated clinical properties.

Overview of Endogenous Cushing's Syndrome

There are two variants of Cushing's syndrome: exogenous, which is caused by factors outside the body (e.g., corticosteroid or cortisol-like medications) and endogenous, which is caused by factors within the body. The signs and symptoms may be the same in both forms. The more common form is exogenous Cushing's syndrome, which is often found in people taking cortisol-like medications for long periods of time or for shorter periods of time using very potent forms. Cortisol-like medications are often used to treat inflammatory disorders such as asthma and rheumatoid arthritis. Unlike endogenous Cushing's syndrome, exogenous Cushing's syndrome may be alleviated by withdrawing the inciting medication.

Endogenous Cushing's syndrome is a rare endocrine disorder characterized by sustained elevated blood cortisol. Cortisol is a hormone produced in the adrenal gland and is naturally secreted as an end-product of the activity of the hypothalamic-pituitary-adrenal axis. Corticotropin-releasing-hormone ("CRH") is secreted from the hypothalamus and stimulates the secretion and release of adrenocorticotropin ("ACTH") from the pituitary gland, which in turn stimulates cortisol (and other hormone) secretion from the adrenal gland. Cortisol itself exerts negative feedback control on both CRH in the hypothalamus and ACTH in the pituitary gland, thereby reducing CRH and ACTH secretion, keeping cortisol levels in a normal range.

The most common form of endogenous Cushing's syndrome is called Cushing's disease, which is typically caused by a benign pituitary tumor that secretes ACTH autonomously. Cushing's disease represents approximately 70% to 80% of patients with endogenous Cushing's syndrome. Other causes of endogenous ACTH-dependent Cushing's syndrome include extrapituitary tumors producing ACTH, known as ectopic ACTH, or less often CRH (ectopic CRH).

The source of ectopic ACTH/CRH secretion is most often small-cell carcinoma of the lung or bronchial carcinoid tumors but neuroendocrine tumors found in many different organs can also be sources. In a smaller number of cases, approximately 20%, endogenous Cushing's syndrome is ACTH-independent, meaning that it does not arise through tumor secretion of ACTH but rather results from excess secretion of cortisol itself in the adrenal gland by adrenocortical tumors, either benign or malignant, or by non-malignant enlargement of the adrenal glands called hyperplasia.

In patients with endogenous Cushing's syndrome, the normal feedback mechanisms of the hypothalamic-pituitary-adrenal axis are disrupted as a result of a tumor autonomously secreting ACTH, CRH or cortisol. This causes chronic exposure to high circulating cortisol levels that give rise to the clinical state of Cushing's syndrome. The most common signs and symptoms of the syndrome include: weight gain, especially in the upper body with a rounded face ("moon face") and extra fat on the upper back and above the collarbones; high blood sugar or diabetes mellitus; high blood pressure or hypertension; thin bones or osteoporosis; muscle loss or sarcopenia; thin, fragile skin that bruises easily; purple-red stretch marks called striae, usually over the abdomen and under the arms; depression and difficulty thinking clearly; too much facial hair, or hirsutism, usually noticed only in women; irregular or absent menstrual periods and infertility; reduced sex drive or libido; and in children, poor height growth.

An estimated 25,000 patients in the United States and 40,000 patients in Europe are diagnosed with endogenous Cushing's syndrome. When first diagnosed, patients are most commonly adults aged 20 to 50 and five times more often women than men. However, endogenous Cushing's syndrome is believed to be underdiagnosed due to lack of disease recognition, which often leads to a delay in diagnosis of six years on average. Endogenous Cushing's syndrome patients are believed to have a mortality risk two to three times that of the age-and-gender-matched general population, with cardiovascular disease, venous thrombosis and infections being the primary causes of death.

Current Treatment Landscape and Limitations on Current Treatment Options

Treatment of endogenous Cushing's syndrome varies depending on the cause of the disease. For patients with Cushing's disease, initial treatment is almost always the attempted surgical removal of the pituitary tumor. In anticipation of surgery and when surgery is not effective or not feasible, drug or radiation therapy, or both, is used to suppress excessive cortisol production and the accompanying clinical symptoms.

A typical approach to drug therapy is to inhibit cortisol synthesis through the oral administration of an inhibitor of enzymes that regulate adrenal cortisol synthesis. Ketoconazole acts in this way and is the most widely used drug therapy for endogenous Cushing's syndrome in the United States. Although approved in the European Union for this indication, ketoconazole is not approved for this indication by the FDA and is therefore prescribed "off-label". The percentage of endogenous Cushing's syndrome patients treated with ketoconazole monotherapy who achieve normalized levels of cortisol, assessed by measuring UFC has been reported from retrospective, uncontrolled studies, with varying definitions of normalization, to be between 33% and 100%. Data from a recent retrospective study of 200 patients in 14 French centers solely treated with ketoconazole for endogenous Cushing's syndrome between 1995 and 2012 suggested that ketoconazole controlled cortisol in approximately 50% of patients and likewise improved clinical symptoms. Also, beneficial effects of oral ketoconazole on clinical symptoms and signs that drive the morbidity and mortality of endogenous Cushing's syndrome have been reported including reduction in high blood pressure, improvement of diabetes, and normalization of hypokalemia, or low potassium blood levels. However, some patients treated with ketoconazole experience tolerability issues and, in some cases, liver injury (also known as hepatotoxicity). As a result of the hepatotoxicity risk, the FDA has issued a boxed warning to prescribers in the labeling describing the use of ketoconazole to treat fungal infections, the only approved indication for ketoconazole in the United States. The FDA has also cautioned that safety and effectiveness have not been established for off-label use of ketoconazole in Cushing's syndrome. Although elevations in liver enzymes associated with ketoconazole are generally mild to moderate and reversible upon cessation of drug, in rare cases, severe hepatotoxicity may occur (estimated as one in every 10,000 to 15,000 patients). In extremely rare cases, ketoconazole-related liver injury may be irreversible and result in death or require liver transplantation. In July 2013, the Committee for Medicinal Products for Human Use ("CHMP") recommended that ketoconazole be withdrawn for use as an antifungal agent in the European Union. The EMA adopted the CHMP recommendation in August 2013, and the recommendation was subsequently confirmed by the European Commission. In September 2014, HRA Pharma received a recommendation of approval from the EMA for ketoconazole

for the treatment of endogenous Cushing's syndrome, based on the well-established use of ketoconazole in medical practice as well as documentation from retrospective studies in the literature.

An alternative medical approach to treating Cushing's syndrome targets pituitary tumors that produce ACTH (i.e., in Cushing's disease). Among Cushing's disease patients, the dopamine agonist cabergoline, which is not approved for use to treat Cushing's disease in the United States, has been shown to achieve normalization of UFC levels, gold-standard evidence of disease control, in about 30% of patients. The SSA pasireotide, which is marketed as Signifor® and Signifor LAR for the treatment of Cushing's disease in the United States, has shown normalization of UFC levels with stable dosing of the immediate-release formulation in 15% of patients at a dosage of 600 µg twice-daily and in 26% of patients at a dosage of 900 µg twice-daily over a 6-month period. Certain SSAs, including Signifor, are known to have undesirable side effects on glucose metabolism. Forty percent of patients with Cushing's disease treated with Signifor in its Phase 3 clinical trial reported the occurrence of hyperglycemia-related adverse events, and in the cohort receiving Signifor 900 µg twice-daily, glycated hemoglobin ("HbA1c") increased from 5.8% at baseline to 7.3% at Month 6.

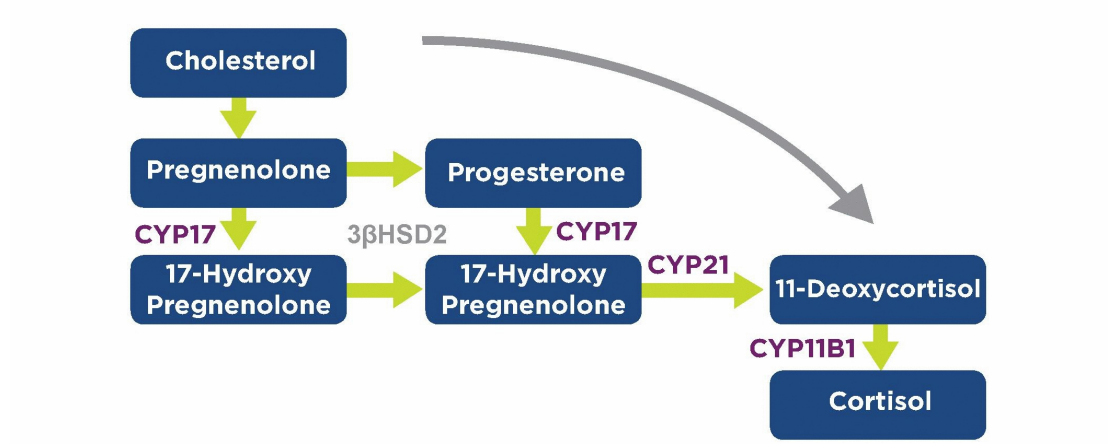
Another alternative drug therapy, Korlym, or mifepristone, works by inhibiting the action of cortisol at the cortisol-receptor level but does not lower blood cortisol levels, which actually tend to increase during therapy. As a result of this mechanism of action, it is not possible to monitor response (i.e., effectiveness and safety) to Korlym by measuring UFC or cortisol levels (from blood or saliva), which are the standard ways clinicians monitor disease progression and response to treatment. As a result, Korlym is usually titrated and monitored through use of clinical signs and symptoms improvements (e.g., blood sugar reductions). Korlym has been approved in the United States to control hyperglycemia secondary to hypercortisolism in patients with endogenous Cushing's syndrome who also have diabetes mellitus. About one-third of patients with endogenous Cushing syndrome have diabetes. Korlym is contraindicated in pregnant women and in women with a history of unexplained vaginal bleeding, as its side effects include termination of pregnancy, endometrial thickening and vaginal bleeding. It is also frequently associated with hypokalemia.

We believe that the efficacy and usage limitations and safety concerns associated with currently available drug therapies for endogenous Cushing's syndrome are an important reason why a significant unmet medical need exists among endogenous Cushing's syndrome patients with persistent or recurrent disease post-surgery. In a survey we commissioned in 2014 of 89 U.S. physicians treating patients with Cushing's syndrome, when asked, "Of your patients on medication to manage cortisol levels, what percentage are well controlled?", the physicians estimated that only approximately 37% of such patients were well controlled. A recent multicenter study of 230 Cushing's disease patients followed for up to 27.5 years and treated with any modality (i.e., surgery, radiation or drugs) found that only 49% had documented biochemical control. We believe that our potential addressable market for Recorlev includes diagnosed endogenous Cushing's syndrome patients that at any time are eligible for drug therapy, including patients anticipating surgery, for whom surgery or radiation is not feasible, is contraindicated or has been unsuccessful. This unmet need may also be impacted by what we believe to be the current lack of disease awareness among physicians and patients, resulting in a relatively low rate of diagnosis.

Our Solution—Recorlev

We believe that Recorlev has the potential to become a new standard of care for the drug therapy of endogenous Cushing's syndrome because it may provide a favorable efficacy, safety and tolerability profile compared to current drug therapies, including ketoconazole. Based on interim results of the SONICS study, Recorlev effectively reduces UFC, in contrast to Korlym, and demonstrates anti-hyperglycemic effects, in contrast to Signifor. In addition, we believe Recorlev may have an improved safety profile compared with that of ketoconazole.

Recorlev, like ketoconazole, is a cortisol synthesis inhibitor that inhibits the cortisol synthesis pathway at multiple points. The following graphic illustrates the cortisol synthesis pathway:



Preclinical and pharmacokinetic data provide evidence that the presumed efficacy of ketoconazole to treat hypercortisolism is due to the ability of levoketoconazole to inhibit adrenal cortisol synthesis. This conclusion is inferred from evidence that the antipode of levoketoconazole (dextroketoconazole) is a far less potent inhibitor of cortisol synthesis *in vitro*. Furthermore, the relatively greater potency of levoketoconazole to inhibit cortisol (and androgen) synthesis implies that, all else being equal, a lower dose of levoketoconazole could result in the same or better efficacy as a higher dose of ketoconazole, thus potentially reducing the risk of toxicity, such as liver toxicity, if such toxicity is contributed approximately equally by each enantiomer of ketoconazole. These conclusions are based on the following:

- In *in vitro* studies, Recorlev was found to have markedly higher potency than ketoconazole and its mirror-image enantiomer, 2R,4S-ketoconazole, in inhibiting the key enzymes in cortisol synthesis (CYP11B1, CYP17, and CYP21). The inhibitory potency *in vitro* of levoketoconazole on these enzymes is approximately twice that of ketoconazole, precisely the ratio that would be expected if levoketoconazole accounted for essentially all of the *in vitro* potency. Combined with the pharmacokinetic profile of the enantiomers (below), these data suggest that essentially all *in vivo* cortisol inhibition observed following administration of ketoconazole can be ascribed to the single 2S,4R enantiomer (levoketoconazole, the active ingredient of Recorlev).
- The pharmacokinetics of the enantiomers also suggest a potentially larger therapeutic index of Recorlev relative to ketoconazole. The two enantiomers found within ketoconazole are present in equal amounts, but in a Phase 1 clinical study in healthy subjects, it was observed that administration of ketoconazole resulted in integrated blood concentrations (i.e., exposure) of the single enantiomer, 2S,4R-ketoconazole (i.e., Recorlev) that exceeded those of the other enantiomer, 2R,4S-ketoconazole, by approximately three times. This observation suggests either that (i) 2R,4S-ketoconazole is extracted by the liver to a greater extent than the other single enantiomer, 2S,4R-ketoconazole (i.e., Recorlev), and may therefore contribute more than Recorlev to the observed liver toxicity of ketoconazole or (ii) 2S,4R-ketoconazole is preferentially absorbed. Even if the liver-clearance of the enantiomers is not different, the higher blood levels of 2S,4R-ketoconazole upon dosing with racemate suggest that a lower amount of drug administration of the single 2S,4R enantiomer (levoketoconazole) may result in equivalent efficacy to a higher amount of drug administration of ketoconazole, assuming that 2S,4R-ketoconazole accounts for essentially all of the *in vivo* cortisol inhibition of the racemate (ketoconazole—see above).
- Compared with ketoconazole, it was observed in *in vitro* studies that Recorlev is less potent than the other enantiomer (i.e., its antipode, 2R,4S-ketoconazole) in inhibiting the activity of CYP7A. CYP7A is the first

and rate-limiting enzyme for production of bile acids in the liver. While a role of CYP7A in liver injury is not established, this finding suggests a possible differential effect of the ketoconazole enantiomers on metabolic and detoxifying enzymes in the liver contributing to reduced hepatotoxicity potential of Recorlev.

- Preliminary evidence from studies performed *in vitro* using primary human hepatocytes suggests that at relevant pharmacological concentrations there are distinct differences between ketoconazole enantiomers in their propensity to perturb metabolic functions of the cells that favor levoketoconazole over its antipode (2R,4S-ketoconazole) or ketoconazole. Such differences are believed to be relevant clinically as they suggest differences in the potency of these compounds to induce metabolic abnormalities that are believed to be responsible for a condition known as oxidative stress (an imbalance between oxidizing free radicals and the molecules that neutralize them, known as antioxidants). It is believed that oxidative stress may be an early event in the pathogenesis of liver injury from many different drugs, including ketoconazole.

Previously, levoketoconazole (then called DIO-902) was studied clinically for the treatment of type 2 diabetes. DiObex, our licensee from 2004 to 2008, initiated three clinical trials to investigate the use of levoketoconazole for treatment of type 2 diabetes and two clinical drug-drug interaction studies in healthy volunteers. Results from these studies established the clinical pharmacology profile of levoketoconazole, contributed to an understanding of its potential efficacy in type 2 diabetes and established preliminary clinical safety and tolerability profiles.

Thirty-seven patients with Type 2 Diabetes Mellitus ("T2DM") were enrolled in a Phase 1/2a double-blind, placebo-controlled, parallel-group study and administered levoketoconazole at 200, 400, or 600 mg once daily (QD), ketoconazole 400 mg QD, or placebo, for 14 days (Study DIO-501). A total of 21 patients with T2DM received levoketoconazole. Levels of LDL-cholesterol were significantly decreased in patients treated with levoketoconazole. Non-significant trends suggestive of improvement in glycemic control and reduction in cortisol secretion relative to placebo were observed.

Administration of levoketoconazole in patients with T2DM was safe and well tolerated. Headache and nausea were the most frequently reported adverse events ("AE"), some of which were considered drug-related. No clinically significant changes in hematology, blood chemistry, and urinalysis were noted in any treatment group. No treatment-related changes in markers of liver injury (LFTs) were reported. Plasma area under the concentration-time curves (AUCs) and maximum concentration (Cmax) increased in a non-proportional manner over the dose range of 200 mg to 400 mg; clearance was decreased at 600 mg QD.

Two Phase 2b studies (one main study plus an open-label extension) designed to evaluate the efficacy of levoketoconazole in combination with atorvastatin in patients with T2DM were voluntarily terminated early due to the perceived high regulatory and commercial hurdles for the approval and use of levoketoconazole in T2DM at the time of development in 2008, given the emerging benefits and risks profile observed. Study DIO-502 was a 4-month, double-blind, randomized, placebo-controlled, eight-arm dose-ranging trial of levoketoconazole (150 mg to 450 mg QD) with concomitant administration of metformin and either atorvastatin 10 mg or matching placebo for atorvastatin 10 mg. Study DIO-503 was an open-label, follow-on extension to Study DIO-502 to evaluate safety, tolerability, and pharmacodynamics after 24 weeks of dosing with levoketoconazole in combination with metformin and atorvastatin or placebo in patients with T2DM. At the time of study terminations, of 133 patients enrolled in the combined studies, 129 were treated, and 97 received at least one dose of levoketoconazole. A total of 47 patients received treatment with levoketoconazole between one and three months duration, while 38 patients exceeded three months of dosing. The frequency of AEs reported was generally similar across treatment arms. Diarrhea was the most frequently reported AE overall with administration of levoketoconazole. No SAEs were reported in the terminated studies.

A safety signal of elevated serum transaminases was identified in the DIO-502 and DIO-503 studies. Three of 129 randomized and treated patients were discontinued prematurely from the studies as required by the safety monitoring plan for elevated LFTs. All three was receiving levoketoconazole and atorvastatin study therapies at the time of their adverse events. Among these three patients, LFTs returned to normal after study drug was discontinued. Three other patients had modest elevations in LFT levels that led to elective premature study withdrawal (i.e. not dictated by the safety monitoring plan). The LFT levels in these three patients also returned to normal after study drug was discontinued.

Four additional patients required close monitoring of LFTs following an observed LFT abnormality, per protocol, and had resolution of their LFT abnormalities while receiving study drug. A detailed analysis of the liver transaminase elevations in this study showed that there was no correlation between the dose of levoketoconazole and abnormal liver transaminases. A safety signal consistent with drug-induced QTc prolongation was also observed in one of the drug-drug interaction studies.

Owing to the known risks of liver injury and QTc prolongation with ketoconazole and the observed safety signals in the Phase 2 program in type 2 diabetes, suspected liver injury and QTc prolongation (including related cardiac adverse events) were pre-defined as adverse events of special interest ("AESIs") in the Phase 3 Cushing's syndrome studies.

Clinical and Preclinical Development of Recorlev in Cushing's Syndrome

In the United States, Recorlev is considered a new molecular entity. Upon completion of the clinical development program for Cushing's Syndrome, we intend to file for marketing authorizations in the United States and elsewhere. In the United States, an NDA, which is a prerequisite to marketing authorization, can be submitted under one of a number of approval paths defined in the Federal Food, Drug, and Cosmetic Act. Following consultations with the FDA, we determined that the 505(b)(2) approval pathway, which permits an NDA applicant to rely on data from studies that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference, is the appropriate pathway for a Recorlev NDA. Because a 505(b)(2) NDA approval can rely in part on data already accepted by the FDA or otherwise publicly available, an abbreviated and reduced development program may be possible. In the case of Recorlev, we intend to rely in our NDA on published literature and the FDA's prior findings concerning the safety and/or effectiveness of ketoconazole. A similar marketing authorization path is available in most of the rest of the world, and we anticipate that the studies supporting U.S. approval will likewise support approvals to market Recorlev elsewhere, including in the European Union. The FDA has acknowledged that no additional preclinical investigations will be required for Recorlev prior to an NDA filing. The EMA's CHMP has requested a study of reproductive toxicity that may be completed prior to filing for marketing authorization in Europe, pending further discussions.

In August 2018, we announced top-line results from the pre-planned interim analysis of our multinational, pivotal Phase 3 SONICS study evaluating Recorlev for treatment of endogenous Cushing's syndrome. The open-label, single-arm, maintenance-of-benefit SONICS study achieved statistical significance of its pre-specified primary endpoint, with 30 percent of patients achieving normalization of mean UFC following six months of maintenance treatment with Recorlev without a dose increase (one-sided p=.0154 vs. the null hypothesis of less than or equal to 20%). Sensitivity analyses as well as secondary and exploratory endpoints of UFC response were supportive of the primary endpoint.

We have also initiated LOGICS, a second Phase 3 clinical trial of Recorlev for the treatment of endogenous Cushing's syndrome. The LOGICS study will supplement the long-term efficacy and safety data from the SONICS trial via a double-blind, placebo-controlled, randomized-withdrawal phase of approximately 8 weeks among 54 patients that follows an open-label titration and maintenance phase of approximately 14 weeks. Top-line data following the randomized-withdrawal phase of LOGICS are expected by the end of 2019.

We believe that if SONICS has (1) demonstrated consistent and significant clinical benefit by meeting the primary endpoint of the trial, specifically the responder rate measured as normalization of UFC levels at the 6-month time point without need for dose increase during the 6-month maintenance phase and (2) show consistent improvement of objectively quantifiable biomarkers of endogenous Cushing's syndrome comorbidities, such as blood glucose, blood lipids, blood pressure or weight, and improvement of other clinical signs and symptoms of endogenous Cushing's syndrome, then it would be regarded by regulators as adequate proof of efficacy in this rare disease with a high unmet medical need. Therefore, we consider LOGICS as a mechanism for providing independent evidence of efficacy of Recorlev in a second, placebo controlled and blinded trial rather than serving as sole or primary evidence of efficacy for Recorlev in endogenous Cushing's syndrome. Furthermore, if successful, LOGICS has the potential to provide adequate evidence of efficacy durability beyond one year of therapy in the subset of patients who were previously enrolled in SONICS. Finally, we believe that the combination of SONICS and LOGICS will provide an adequate demonstration of the long-term safety and tolerability of Recorlev in patients with endogenous Cushing's syndrome. In total over 130

unique patients with this condition will have been treated with Recorlev during SONICS and LOGICS, and some patients will have been treated with Recorlev for at least 3 years at the time of first NDA submission.

In 2018, we initiated a long-term, open-label extension study with Recorlev ("OPTICS") to capture longer-term safety, tolerability and efficacy data from patients who complete either SONICS or LOGICS and who choose to continue therapy with Recorlev. OPTICS will continue to accrue data for a minimum of three years, with a plan to allow patients to continue participating in the study until it has become available for purchase in their own country. We expect that we might be required by the FDA and the EMA to collect additional safety data post-approval.

Phase 3 Clinical Trials

SONICS Phase 3 Clinical Trial

We enrolled 94 patients in our SONICS Phase 3 clinical trial in the United States, Canada, the European Union and the Middle East. This clinical trial was conducted pursuant to a U.S. IND for Recorlev for the treatment of endogenous Cushing's syndrome that took effect in May 2013. The last patient visit occurred in November 2018.

Following a screening phase, SONICS has three distinct treatment phases. During the dose titration (DT) phase, patients start at 150 mg twice daily dosing (300 mg total daily dose) and titrate in 150 mg increments up to a maximum 600 mg twice daily dosing (1,200 mg total daily dose). Following the dose titration phase, once the therapeutic dose has been reached, patients enter the maintenance ("M") phase, during which the dose is fixed and cannot be changed other than for safety reasons, including loss of efficacy. At the end of the six-month M phase, UFC levels are measured and the UFC responder rate, which is the primary endpoint of the clinical trial, is determined. Patients who have completed the M phase may enter the extended evaluation phase, which we expect will provide additional safety and efficacy data. Throughout the entire clinical trial, various measurements for safety and efficacy are taken.

- The primary endpoint of the clinical trial is the proportion of patients with UFC response to Recorlev, defined as a reduction in mean 24-hour UFC levels to levels that are equal to or less than the upper level of normal range following six months of treatment in the M phase without a dose increase (during the M phase).
- Key secondary endpoints include the number of patients with at least a 50% decrease in UFC levels, changes in blood sugar, blood pressure, cholesterol and weight compared to baseline, effects on clinical signs and symptoms of Cushing's syndrome, quality of life measures obtained from the Cushing's syndrome quality of life questionnaire and the severity of depression obtained from the Beck's Depression Inventory II.

The clinical trial is also designed to investigate the pharmacokinetics of Recorlev in patients with endogenous Cushing's syndrome.

Below is a diagram of the SONICS clinical trial design:

Several elements of the SONICS clinical trial design were informed by the clinical development pathway of currently approved drug therapies in the United States and the European Union. Additionally, we incorporated advice from the CHMP and FDA into the design of the clinical trial. The FDA recommended use of a concurrent control group in SONICS. However, SONICS utilizes an open-label, single-arm design because use of a placebo control in a long-term, parallel-arm monotherapy design was considered unethical or infeasible to enroll, depending on the specific country or clinical trial site under consideration. Studies lacking a concurrent control group are more likely to be subject to unanticipated variability in study results that can potentially lead to flawed conclusions because they do not allow for discrimination of patient outcomes. As a result, even if we achieve the clinical trial's endpoints, the FDA or other regulatory authorities could view our study results as potentially biased. We have attempted to control for bias introduction in SONICS via the use of strict evidence of active disease at baseline based on objective measures, an objectively measured primary endpoint with repeated longitudinal assessments and implementation of a strict data restriction plan that severely limits exposure to efficacy data at the Sponsor.

In August 2018, we announced top-line results from our SONICS study evaluating Recorlev for treatment of endogenous Cushing's syndrome. Approximately 90 patients were planned to be enrolled, and 94 patients were actually enrolled. Of the 94 patients, 77 completed the DT phase and 61 completed the M phase.

The primary objective of normalized mean UFC (mUFC) without an increase in the therapeutic dose over the preceding six months was achieved among 30% of all enrolled patients at the final visit of the 6-month M phase. Statistical significance of the primary endpoint analyzed using the intent-to-treat population was achieved, having excluded an mUFC normalization rate at the 6-month time point of 20% or lower (1-sided $p = 0.0154$; 2-sided $p = 0.031$. Sensitivity analyses and secondary and exploratory analyses of mUFC response were all supportive of and suggested greater efficacy of levoketoconazole than the primary endpoint analysis, indicative of a conservative primary analysis method.

Evidence of clinical benefit from levoketoconazole was further demonstrated by improvements in several pre-defined, key secondary endpoints of cardiovascular risk (i.e. cardiometabolic comorbidities of CS) in the maintenance-completer study population including highly statistically significant (maintaining overall type 1 error at 5%) and clinically meaningful decreases from baseline in mean fasting glucose, hemoglobin A1C, total and low-density lipoprotein-cholesterol and body weight.

Safety and tolerability findings throughout the DT and M phases indicate that levoketoconazole was generally well tolerated, with a discontinuation rate due to adverse events of 13% and no new safety signals observed relative to the prior experience with the drug in type 2 diabetes. Fourteen of 94 patients (15%) reported one or more serious adverse events (SAE), and in 4 patients an SAE was deemed drug-related by investigators (1 case of elevated liver function tests, 2 cases of prolonged QTc, and 1 case of adrenal insufficiency). One patient death not considered drug-related (colon cancer; preferred terms of adenocarcinoma of colon and metastases to liver), was reported during the M phase.

Liver-related adverse events were considered AESIs in SONICS and are of particular interest in light of serious hepatotoxicity reported rarely among users of ketoconazole. Seven (7.4%) patients were reported as having an AESI related to the liver, and five of the seven discontinued study drug permanently at the time of the event; the other two resumed study drug after interruption, although one of the two later discontinued. Transaminases were measured routinely at least every other week during dose titration and at least monthly during the M phase. At the baseline visit, 96% of patients enrolled had alanine aminotransferase (ALT) within the normal reference range. During treatment ALT did not exceed 20x ULN in any patient, and no Hy's Law cases were reported. Three (3.2%) patients were recorded with a post-baseline ALT value greater than 5x ULN and an additional seven (7.4%) of patients had at least 1 ALT value greater than 3x ULN at any time after baseline. Most ALT elevations occurred during dose titration, and all elevations over 3x ULN occurred by Month 2 of the M phase. The aspartate aminotransferase values measured in these cases moved in the same direction as ALT but were less elevated. No patient had a total bilirubin level >1.5x ULN at any time. There was no obvious dose relationship among the cases, and each case was fully reversible upon drug interruption/discontinuation without clinical sequelae. It is not yet known if such events are predictable within an individual, but routine monitoring effectively identified elevated transaminase cases when they were mild and usually asymptomatic.

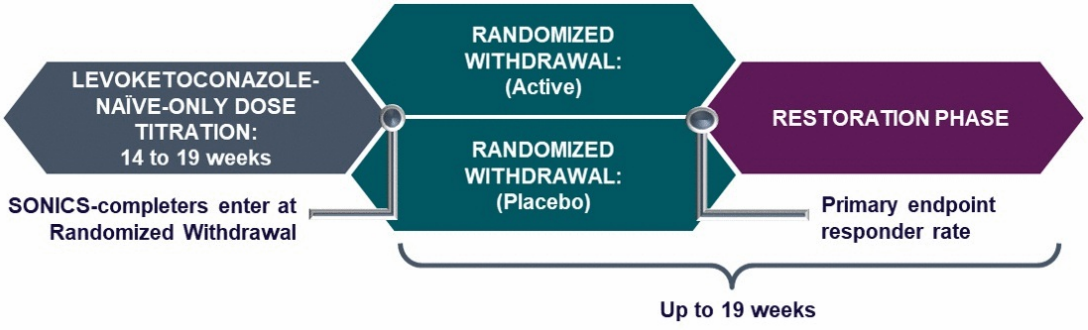
ECGs with centrally over-read QTc were monitored routinely during the study at the same intervals as LFT monitoring. Five (5.3%) patients were reported as having a QT/cardiac-related AESI; in every case the patient was asymptomatic. There were no discontinuations due to QTc prolongation. No arrhythmias were reported. In each case of prolonged QTc, study drug was resumed after temporary interruption. A total of nine (10%) patients had at least one QTc value representing an increase of more than 60 milliseconds from baseline, and two (2.1%) patients had a QTc interval above the pre-defined mandatory drug-interruption threshold of 500 milliseconds. Routine ECG monitoring effectively identified patients with QTc prolongation without any clinical sequelae. Therefore, we believe QTc prolongation safety issues can be appropriately managed with product labeling.

LOGICS Phase 3 Clinical Trial

Rather than alter the design of SONICS to facilitate regulatory authority requests for a concurrent control group with which to compare the efficacy and safety of Recorlev, we initiated LOGICS, a second Phase 3 pivotal study. LOGICS will include a concurrent comparison of Recorlev to matching placebo using a randomized, double-blind withdrawal design that we believe will be both feasible to enroll and ethical to conduct everywhere that SONICS is being conducted. LOGICS will randomize approximately 54 patients.

Following a screening phase, LOGICS has three distinct treatment phases for patients who did not participate in SONICS and two distinct phases for most of those who did participate in SONICS. The first phase, which is only intended for patients new to levoketoconazole or for those who require re-establishment of a therapeutic dose, is dose titration and maintenance. During the dose titration and maintenance phase, patients start at 150 mg twice daily dosing (300 mg total daily dose) and titrate in 150 mg increments up to a maximum 600 mg twice daily dosing (1,200 mg total daily dose) and remain at their individualized therapeutic dose. The total duration of this phase is up to 19 weeks. SONICS-completers who are currently receiving a stable therapeutic dose skip dose titration and maintenance and proceed directly to the second phase, where they are joined by those who progressed through the first phase. The second phase is randomized-withdrawal, during which patients are randomly assigned to either continue active treatment with levoketoconazole or be switched to a matching placebo using the same tablet number. The primary efficacy endpoint comes at the end of the randomized-withdrawal period, which lasts no more than 9.5 weeks for each patient (and may end sooner if a "rescue" is needed). The primary endpoint is the proportion of patients with a loss of established UFC response in the placebo group compared with the proportion in the levoketoconazole group. The final phase of LOGICS is the restoration phase, during which all patients once again receive active therapy; however, in order to conceal the therapy in the randomized-withdrawal phase, it was necessary to blind the therapy during restoration using twice the number of tablets (one active and one placebo). Throughout the entire clinical trial, various measurements for safety and efficacy are taken.

Below is a diagram of the LOGICS clinical trial design:



Veldoreotide Modified-Release —a Novel Somatostatin Analogue

Overview

In June 2015, we acquired veldoreotide, a novel multi-receptor targeted SSA that was previously in Phase 2 development as an immediate-release formulation and has the potential as a next-generation somatostatin analog to provide a new and differentiated treatment option for patients with conditions amenable to somatostatin receptor activation, such as acromegaly. We acquired veldoreotide as part of our strategy to build our rare endocrine franchise. At the time of acquisition, veldoreotide was in Phase 2 clinical development as a treatment for acromegaly in its original, immediate-release formulation. Acromegaly is a rare endocrine disorder that most commonly results from a benign tumor of the pituitary gland, leading to excess production of growth hormone and IGF-1. The treatment goal is the normalization of growth hormone and IGF-1, which is the main cause of the detrimental clinical signs and symptoms of acromegaly.

SSAs are peptides that are administered as deep subcutaneous or intramuscular injections, typically as long-acting formulations for monthly injections. They are the most commonly used drug therapy for the treatment of acromegaly and work by binding to specific subtypes of SSTs that are expressed by the tumor. Binding of SSAs to these SSTs leads to the beneficial inhibition of growth hormone secretion but can also result in the unwanted inhibition of secretion of other endocrine hormones such as insulin and glucagon in the pancreas. Like other SSAs, veldoreotide is a peptide that we are developing for injection. In contrast to approved SSAs, veldoreotide activates a different subset of SSTs. Like the marketed SSAs, it binds and activates signaling via SST2 and SST5. However, in contrast to the approved SSAs, which primarily target one or the other of SST2 or SST5, veldoreotide binds and activates SST2 and SST5 approximately with equal potency. Veldoreotide also has a high affinity for SST4, a receptor believed to be important to modulating pain signals in the peripheral nervous system. Veldoreotide does not bind to SST3 or the mu-opiate receptor at pharmacological concentrations. *In vitro* data suggest that a higher proportion of human adenomas are a target for growth hormone inhibition by veldoreotide as compared to octreotide, which is referred to as a single receptor targeted SSA that binds and activates predominantly via SST2, potentially resulting in an increased responder rate. Nonclinical data indicate that postprandial insulin secretion and gallbladder motility are both less inhibited by veldoreotide as compared with octreotide.

Based on the differentiated activation pattern of veldoreotide upon binding to SST subtypes, we believe that veldoreotide may offer an improved efficacy and safety profile relative to existing drug therapies for acromegaly and other conditions that are modifiable through activation of somatostatin receptors. In the three clinical studies of immediate-release veldoreotide completed outside the United States in healthy volunteers veldoreotide was able to suppress stimulated growth hormone levels to a similar extent as octreotide, and, when compared with immediate-release subcutaneous octreotide, there was less blunting of insulin in response to a mixed meal or oral glucose load. In two studies of patients with acromegaly, veldoreotide caused a similar degree of suppression of elevated serum growth hormone as octreotide. Veldoreotide has been granted orphan drug designation for the treatment of acromegaly by the FDA and the EMA.

We have formulated veldoreotide as a modified-release, long-acting product using PLGA microsphere technology. Preliminary nonclinical studies suggest that an injection volume suitable for subcutaneous administration may be feasible for once-weekly dosing in humans. Depending on the results of ongoing exploratory nonclinical studies, we may elect to pursue a development pathway for veldoreotide modified-release that includes a therapeutic use outside of acromegaly or endocrinology in general. Regardless of indication(s) to be pursued, further development will require preclinical safety (toxicology) studies as well as manufacturing scale-up before the newly formulated product can enter clinical testing. We anticipate that such preclinical studies, once begun, will take at least 18 months to complete.

Completed Clinical Trials

Five clinical trials of veldoreotide have been performed to date: three in healthy male volunteers and two in patients with acromegaly, all of which employed an immediate-release, short-acting formulation injected subcutaneously. At the time the clinical trials described below were conducted, veldoreotide was named DG3173. These

trials were conducted by Aspireo Pharmaceuticals Ltd., other than DG3173-I-001, which was conducted by Develogen AG.

The Phase 1 clinical trials involved 122 healthy subjects and the Phase 2 clinical trial involved 28 patients with acromegaly. No SAEs were observed, and mostly mild adverse events typical for SSAs such as injection site reactions and gastrointestinal side effects were reported. There was no evidence that veldoreotide adversely affects the liver, kidneys or other organ systems, including the cardiovascular system. Data from the multiple ascending dose clinical trial in healthy subjects (Study I 002) showed inhibition of growth hormone comparable to octreotide, but no or less inhibition of insulin secretion and less effect on glucose levels. The single ascending dose trial in patients with acromegaly (Study II 01) and the continuous infusion study in patients with acromegaly (Study II 02) confirmed that veldoreotide also suppresses excessively produced growth hormone to a similar maximal extent as octreotide.

We believe the preliminary clinical findings from these trials corroborate the profile of veldoreotide observed in nonclinical studies, which suggested inhibition of growth hormone secretion without detrimental effects on post-meal insulin or glucose metabolism. These preliminary findings contrast favorably with the well-described insulin and glucose perturbations caused by octreotide, lanreotide and pasireotide, and we intend to conduct additional clinical trials to evaluate the clinical profile of veldoreotide and possibly its differentiation from existing SSAs. We believe veldoreotide potentially could confer distinct therapeutic advantages relative to currently approved SSAs as a treatment for somatostatin-responsive conditions.

The following table summarizes the completed clinical trials with immediate-release veldoreotide.

Clinical Trial Number	Clinical Trial Descriptions	Patients Enrolled	Year and Status	Location	Dose
DG3173-II-02	Phase 2 Trial of the Effect of Subcutaneous Infusions of Three Doses of Veldoreotide on Growth Hormone Levels in Untreated Acromegaly Patients	8	2013/2014 Completed. Bioanalytical report issued.	Ukraine	920-5520 µg continuous infusion over 23 hours
DG3173-II-01	Phase 2 Trial of the Effect of Single Ascending Doses of Veldoreotide and 300 µg of Octreotide on Human Growth Hormone Levels in Untreated Acromegaly Patients	20	2012 Completed. Study report issued.	Ukraine	300-1800 µg QD
DG3173-I-003	Phase 1 Placebo-Controlled, Trial to Assess the Pharmacodynamic Effect on Glucose Metabolism of Single Doses of Veldoreotide, Octreotide and Placebo in Healthy Male Patients	8	2013 Completed. Study report issued.	Switzerland	300-1800 µg QD
DG3173-I-002	Phase 1 Trial to Compare the Safety and Pharmacologic Activity of Repeated Doses of Veldoreotide and Veldoreotide Plus Octreotide with Octreotide and Placebo and Establish Their Pharmacokinetic Interaction in Healthy Male Patients	42	2012/2013 Completed. Study report issued.	Switzerland	100-1800 µg TID
DG3173-I-001	Phase 1 Double-Blind, Placebo-Controlled Trial to Investigate Safety, Tolerability and Pharmacokinetics of Single Escalating Dosing of Veldoreotide in Healthy Male Patients	72	2008 Completed. Study report issued.	Germany	10-2000 µg QD

Our Rare Neuromuscular Franchise

In December 2016, we acquired the U.S. marketing rights to Keveyis (dichlorphenamide) from Taro Pharmaceuticals North America, Inc., a subsidiary of Taro Pharmaceutical Industries Ltd. Keveyis is the first and only therapy approved in the United States to treat hyperkalemic, hypokalemic and related variants of PPP, a group of rare hereditary disorders that cause episodes of muscle weakness or paralysis.

Overview of PPP and Keveyis

PPP is a rare, genetic, neuromuscular disorder related to a defect in muscle ion channels with multiple variants and subtypes. The disease is characterized by episodes of muscle weakness and paralysis. It often interferes with daily activities and, as patients get older, it can lead to permanent muscle weakness. PPP may be localized (“focal”) or more widespread (“generalized”), and it often goes underdiagnosed and/or undertreated. Types of periodic paralysis are differentiated by criteria including underlying genetic mutations and changes in blood potassium during an episode. The two most common forms of PPP are hypokalemic, when episodes can be induced by low blood levels of potassium, and

hyperkalemic, when episodes are associated with elevated levels of blood potassium. We believe, based on our market research, that there are approximately 4,000 to 5,000 patients in the United States diagnosed with PPP.

Keveyis is an oral carbonic anhydrase inhibitor that was approved by the FDA in the United States in August 2015 to treat hyperkalemic, hypokalemic and related variants of PPP. The exact mechanism(s) through which oral carbonic anhydrase inhibitors, and Keveyis in particular, decrease the frequency and severity of periodic paralysis attacks is unknown. However, it is believed that their effects are mediated both locally (i.e., in muscle) and systemically. It is not known whether their effects are disease-modifying. Keveyis has received orphan drug exclusivity status in the United States through August 7, 2022.

Following FDA approval in August 2015, Keveyis was marketed by Taro. In May 2016, Taro announced the cessation of their commercial sales and related promotional activities for Keveyis. Taro supplied Keveyis to patients on a non-commercial basis through a single specialty pharmacy in the United States from May 2016 until our acquisition of the U.S. marketing rights to Keveyis in December 2016. We continued to supply Keveyis to patients on a non-commercial basis until launching Keveyis in April 2017. After acquiring the U.S. marketing rights for Keveyis, we established sales, marketing, market access and patient service capabilities.

Because a large percentage of the people who suffer from PPP remain undiagnosed or inadequately treated, we developed programs to educate the medical community and patients about this illness. In addition, we established a field-based force of medical science liaisons. We use a single, specialty pharmacy to provide reimbursement, clinical and distribution support for Keveyis and to develop cost-sharing and patient assistance programs to support qualified, commercially insured patients, federal- and state-insured patients, and uninsured or under-insured patients. We also donate money to independent charitable foundations dedicated to this cause. Our ultimate goal is to ensure that no PPP patient is denied access to Keveyis for financial reasons.

Clinical Development of Keveyis

The efficacy of KEVEYIS was evaluated in two clinical studies, Study 1 and Study 2.

Study 1

Study 1 was a 9-week, double blind, randomized, placebo-controlled, multi-center study. Study 1 consisted of two substudies: a substudy in patients with hypokalemic periodic paralysis (n=44), and a substudy in patients with hyperkalemic periodic paralysis (n=21). The primary efficacy endpoint in both substudies was the average number of self-reported attacks of muscle weakness per week over the final 8 weeks of the trial. Withdrawal from the study for acute severe worsening was also assessed as an endpoint.

In Study 1, the tested dose of Keveyis was 50 mg b.i.d. for treatment-naïve patients. Patients already receiving dichlorphenamide prior to the study continued on the same dose if randomized to Keveyis during the study. In patients taking acetazolamide prior to the study, the daily dose of Keveyis was set at 20% of the daily acetazolamide dose. Dose reduction for tolerability was permitted.

In the hypokalemic periodic paralysis substudy, median age of patients was 45 years and 73% of patients were male. Patients treated with Keveyis (n=24) had 2.2 fewer attacks per week than patients (n=20) treated with placebo (p=0.02). None of the patients randomized to Keveyis reached the endpoint of acute worsening, vs. five patients randomized to placebo. The mean dose of Keveyis at Week 9 was 94 mg/day.

In the hyperkalemic periodic paralysis substudy, median age of patients was 43 years and 43% of patients were male. During the double-blind treatment period, patients treated with Keveyis (n=12) had 3.9 fewer attacks per week than patients treated with placebo (n=9) (p=0.08). None of the patients randomized to Keveyis reached the endpoint of acute worsening, vs. two patients randomized to placebo. The mean dose of Keveyis at Week 9 was 82 mg/day.

Study 2

Study 2 was a 35-week, double blind, placebo-controlled, randomized, multi-center, two-period crossover study. Study 2 also consisted of two substudies: a substudy in patients with hypokalemic periodic paralysis (n=42), and a substudy in patients with hyperkalemic periodic paralysis (n=31), including patients with Paramyotonia Congenita (together termed potassium-sensitive periodic paralysis or PSPP). The primary endpoint in the hypokalemic periodic paralysis substudy was the incidence of acute intolerable worsening (based on attack frequency or severity) necessitating withdrawal. The primary endpoint in the hyperkalemic periodic paralysis substudy was the average number of self-reported attacks of muscle weakness per week. Dosing was determined similarly to Study 1.

In the hypokalemic periodic paralysis substudy, mean age of patients was 38 years and 79% of patients were male. Acute intolerable worsening was observed in 2 patients on Keveyis vs. 11 patients on placebo (p=0.02). The mean dose of Keveyis at the end of the study was 96 mg/day.

In the hyperkalemic periodic paralysis substudy, mean age of patients was 37 years and 58% of patients were male. Patients treated had 2.3 fewer attacks per week on Keveyis than on placebo (p=0.006). The mean dose of Keveyis at the end of the study was 73 mg/day.

Commercialization Strategy

Our existing commercial infrastructure is limited. After acquiring the U.S. marketing rights for Keveyis in December 2016, we established sales, marketing, market access and patient service capabilities. We believe, based on our market research, that there are approximately 4,000 to 5,000 patients in the United States diagnosed with PPP and we believe that we can address the market by targeting physicians who are managing patients with PPP, including neuromuscular specialists, general neurologists and primary care physicians.

During 2018, we expanded our commercial infrastructure to support the product launch of Macrilen. In December 2018, we sold our subsidiary that help the U.S. and Canadian marketing rights to Macrilen to Novo. However, as noted elsewhere in this Annual Report, in connection with this transaction, we entered into a services agreement with Novo pursuant to which Novo will fund the costs of 23 of our field-based employees to provide full-time ongoing services to Novo, including the promotion of Macrilen in the United States, for a period of three years.

Given the current stage of product development of our product candidates, we do not have a commercialization infrastructure for those product candidates, although we do plan to leverage our current commercial infrastructure when possible. As with Keveyis and Macrilen, we intend to independently commercialize our rare disease-focused product candidates, if approved, in the United States, the European Union and other key global markets. We believe that we can address the markets of our current product candidates by targeting endocrinologists that are focused on the diagnosis and treatment of rare pituitary disorders primarily stemming from benign tumors.

Our commercial strategy for our product candidates, if approved, will encompass promoting their unique benefits, as well as a concerted effort to raise awareness about the underlying disease among the physician/patient community with the goal of increasing the rate of diagnosis when the symptoms may otherwise be overlooked. We believe the combination of our commercial efforts and our product candidate profiles will facilitate our ability to successfully penetrate our target markets.

Manufacturing

We do not have internal manufacturing capabilities and intend to continue to rely on third parties to produce Keveyis and our product candidates.

We have a supply agreement with Taro to produce Keveyis. We are obligated to purchase certain annual minimum amounts of product totaling approximately $29 million over a six-year period from Taro. The supply agreement may extend beyond the orphan exclusivity period unless terminated by either party pursuant to the terms of

the agreement. If the supply agreement is terminated by Taro at the conclusion of the orphan exclusivity period, we have the right to manufacture the product on our own or have the product manufactured by a third party on our behalf.

The manufacturing, packaging and distribution of Recorlev drug product for clinical trials following Good Manufacturing Practices ("GMPs"), is currently outsourced under contracts to experienced contract manufacturers. We expect to enter into similar arrangements for veldoreotide.

Intellectual Property of our Products and Product Candidates

We actively seek to protect the intellectual property and proprietary technology that we believe is important to our business, including seeking, maintaining, enforcing and defending patent rights for our products, product candidates and methods of treatment, whether developed internally or licensed from third parties. Our success will depend on our ability to obtain and maintain patent and other protection (including exclusivity through orphan drug designation) for our products, product candidates and methods of treatment, preserve the confidentiality of any know-how and operate without infringing the valid and enforceable patents and proprietary rights of third parties.

Our policy is to seek to protect our proprietary position generally by filing patent applications initially at the USPTO. After this initial phase, patent applications claiming priority to the initial application are filed in various countries, including the United States, Europe and Canada. In each case, we determine the strategy and territories required after discussion with our patent professionals with the goal of obtaining relevant coverage in territories that are commercially important to us and our product candidates. We will additionally rely on orphan drug designation exclusivity and patent term extensions when available. We also rely on trade secrets and know-how relating to our underlying product technologies. Prior to making any decision on filing any patent application, we consider with our patent professionals whether patent protection is the most sensible strategy for protecting the invention concerned or whether the invention should be maintained as confidential.

We own or license 55 granted patents, of which five are U.S. issued patents. We also own or license 15 pending patent applications, of which eight are U.S. patent applications.

We maintain trademark registrations and/or trademark applications for "Strongbridge Biopharma" and "Recorlev" in key geographies that include the United States, Australia, Brazil, China, Europe, Israel, India, Japan, Mexico, and Canada, among others. We also maintain trademark registrations and/or trademark applications for various additional potential trademarks for potential use if we determine not to utilize Recorlev as the branded pharmaceutical name for our levoketoconazole product candidate, once approved.

Recorlev

We own 45 issued patents related to our product candidate, Recorlev. Issued claims in these patents are directed to methods of treatment of various diseases or conditions associated with elevated cortisol levels or activity using Recorlev. The patents have been granted in major territories including the U.S., Europe, China and Japan and expire in 2026 and 2027. We have three pending U.S. patent applications directed to methods of treating a disease or condition associated with elevated cortisol levels or activity, including Cushing's syndrome, with Recorlev. We also have an issued patent in the United States directed to reducing C-reactive protein levels and systemic inflammation through administration of a once-daily dose of Recorlev that expires in 2030. In addition to any patent exclusivity, we intend to rely on orphan drug designation exclusivity for Recorlev.

Veldoreotide

We own nine issued patents related to our product candidate, veldoreotide. One of the patents is issued in the United States with claims covering an extended-release formulation and a method of manufacturing the formulation. This patent expires in 2037. We have filed eight patent applications that include substantially similar proposed claims in other countries including China, Japan, Canada and various countries in Europe. In addition to any patent exclusivity, we intend to rely on orphan drug designation exclusivity for veldoreotide.

Keveyis

We acquired U.S. marketing rights to Keveyis in late 2016. We are not aware of any issued patents related to Keveyis. We have filed four patent applications in the United States related to Keveyis. Although we intend to rely primarily on orphan drug designation exclusivity for Keveyis, we also expect to continue to prosecute such patent applications and explore additional life cycle management opportunities for Keveyis.

Laws and Regulations Regarding Patent Terms

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional application. In the United States, a patent term may be shortened if a patent is terminally disclaimed over another patent or as a result of delays in a patent prosecution by the patentee. A patent's term may be lengthened by a patent term adjustment, which compensates a patentee for administrative delays by the USPTO in granting a patent. The patent term of a European patent is 20 years from its effective filing date, which, unlike in the U.S., is not subject to patent term adjustments in the same way as U.S. patents.

The term of a patent that covers an FDA-approved drug or biologic may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act") permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug or biologic is under regulatory review. Patent extensions cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved drug, for example Supplementary Protection Certificates. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We anticipate that some of our issued patents may be eligible for patent term extensions, but such extensions may not be available and, therefore, any commercial monopoly may be restricted.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our scientific knowledge, technology, and development experience provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing products and new products that may become available in the future. Many of our competitors, alone or with their strategic partners, have greater experience than we do in conducting preclinical studies and clinical trials, and obtaining FDA, EMA and other regulatory approvals, and have substantially greater financial, technical and other resources than we do, such as larger research and development, clinical, marketing and manufacturing organizations. As a result, these companies may obtain regulatory approval for competing products more rapidly than we are able and may be more effective in selling and marketing their products. Companies that complete clinical trials, obtain required regulatory authority approvals and commence commercial sale of their drugs before their competitors may achieve a significant competitive advantage, and our commercial opportunity could be reduced or eliminated if 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. Drugs resulting from our research and development efforts or from our joint efforts with collaboration partners therefore may not be commercially competitive with our competitors' existing products or products under development.

We are aware of several companies focused on developing or marketing therapies for rare neuromuscular and endocrine disorders. For our product candidates, the main competitors include:

- **Recorlev:** A number of therapies are currently approved and in various stages of development for endogenous Cushing's syndrome. Currently, there are no therapies broadly marketed for the treatment of

endogenous Cushing's syndrome patients in the United States. Two therapies have limited indications in Cushing's syndrome that is not due to adrenal carcinoma. Korlym (mifepristone) is a cortisol receptor blocker indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery. Signifor (pasireotide) and Signifor LAR are marketed by Novartis in the United States and are indicated for the treatment of adult patients with Cushing's disease (a subset of Cushing's syndrome) for whom pituitary surgery is not an option or has not been curative.

Ketoconazole, metyrapone and mitotane are marketed by HRA Pharma in certain European countries. Osilodrostat (LCI699), an 11β-HSD2 inhibitor, is currently in Phase 3 clinical development by Novartis in Cushing's disease. Corcept Therapeutics is developing relacorilant (CORT125134), a selective glucocorticoid receptor antagonist, currently in Phase 3 for Cushing's syndrome. Millendo Therapeutics is developing nevanimibe hydrochloride (ATR-101), a selective acyl-CoA:cholesterol acyltransferase 1 (ACAT) inhibitor, currently in Phase 2. Cedars-Sinai is developing seliciclib (R-roscovitine) for Cushing's disease, in Phase 2.

- **Veldoreotide:** A number of acromegaly therapies are currently approved and in various stages of development. There are currently three approved SSA therapies for acromegaly in the United States: Sandostatin LAR (octreotide) marketed by Novartis; Signifor LAR (pasireotide) marketed by Novartis; and Somatuline Depot (lanreotide) marketed by Ipsen. There is one growth hormone receptor antagonist, Somavert (pegvisomant), marketed by Pfizer. Chiasma had filed an NDA in the United States for RG-3806 (Mycapssa®), an oral octreotide formulation in 2015, and received a Complete Response Letter wherein FDA stated that it did not believe the company's application had provided substantial evidence of efficacy to warrant approval, and advised Chiasma that it would need to conduct another clinical trial in order to overcome this deficiency. Additional therapies (owner) are in Phase 2 clinical development for acromegaly: CRN-00808 an oral SSA (Crinetics); IONIS-GHR-LRx, an antisense inhibitor of the GH receptor (Ionis); CAM-2029, octreotide long-acting (Camurus); ITF-2984 (Italfarmaco); atesidorsen (ATL-1103), an antisense inhibitor of GH receptor (Antisense Therapeutics).
- **Keveyis:** Acetazolamide, an oral carbonic anhydrase inhibitor, is used frequently off-label for the prophylactic and sometimes acute treatment of PPP. Potassium supplements are indicated for use in hypokalemic periodic paralysis in the United States and are frequently used either chronically or for emergency treatment of episodes in that form of PPP. Several other types of drugs have been reported to have benefits for chronic or acute use in one or more than one PPP variant, including potassium-sparing diuretics, beta receptor agonists, mexelitine and other sodium channel blockers, and others. We are not aware of drugs currently in development for prophylactic chronic treatment of PPP. A Phase 2 clinical study of bumetanide, a loop diuretic, is underway in England for acute treatment of paralytic attacks.

Government Regulation

Product Approval Process

The safety, clinical testing, manufacturing, quality, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are subject to extensive regulation by governmental authorities in the United States and other countries. The FDA under the Federal Food, Drug, and Cosmetic Act regulates pharmaceutical products in the United States. The steps required before a drug may be approved for marketing in the United States generally include:

- the completion of preclinical laboratory tests and animal tests conducted under Good Laboratory Practices, ("GLPs"), and other applicable regulations;
- the submission to the FDA of an IND application for human clinical testing, which must be reviewed by the FDA and become effective before human clinical trials commence;

- the successful performance of adequate and well-controlled human clinical trials conducted in accordance with current Good Clinical Practices ("cGCP") to establish the safety and efficacy of the product candidate for each proposed indication;
- analysis of clinical trial data and preparation of submission to the FDA of an NDA;
- the submission to the FDA of an NDA;
- the FDA's acceptance of the NDA;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the product is made to assess compliance with current Good Manufacturing Practices ("cGMPs") to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of FDA inspections of clinical trial sites and GLP toxicology studies; and
- the FDA's review and approval of an NDA prior to any commercial marketing or sale of the drug in the United States.

The testing and approval process requires substantial time, effort, and financial resources, and the receipt and timing of any approval is uncertain.

Preclinical studies include laboratory evaluations of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. The results of the preclinical studies, together with manufacturing information, analytical data and a proposed clinical trial protocol, are submitted to the FDA as part of the IND, which must become effective before clinical trials may be commenced. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the conduct of the clinical trials as outlined in the IND prior to that time and places the IND on clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. A clinical hold may occur at any time during the life of an IND, due to safety concerns or non-compliance, and may affect one or more specific studies or all studies conducted under the IND.

Clinical trials involve the administration of the product candidates to healthy volunteers or patients with the disease to be treated under the supervision of a qualified principal investigator. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board ("IRB"), either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution. Progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors must also report to the FDA serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigation brochure, or any findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

Clinical trials are typically conducted in three sequential phases prior to approval, but the phases may overlap. These phases generally include the following:

- Phase 1. Phase 1 clinical trials represent the initial introduction of a product candidate into human subjects, frequently healthy volunteers. In Phase 1, the product candidate is usually tested for safety, including adverse effects, dosage tolerance, absorption, distribution, metabolism, excretion and pharmacodynamics.
- Phase 2. Phase 2 clinical trials usually involve studies in a limited patient population to (1) evaluate the efficacy of the product candidate for specific indications, (2) determine dosage tolerance and optimal dosage, and (3) identify possible adverse effects and safety risks.

- Phase 3. Phase 3 clinical trials are conducted to further demonstrate clinical efficacy, optimal dosage and safety within an expanded patient population at geographically dispersed clinical trial sites, and to provide sufficient data for the statistically valid evidence of safety and efficacy.

Phase 4 clinical trials are conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations, or when otherwise requested by the FDA in the form of post-market requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in withdrawal of approval.

Clinical trials are inherently uncertain and any phase may not be successfully completed. A clinical trial may be suspended or terminated by the FDA, IRB or sponsor at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides ongoing oversight and safety reviews to determine whether or not a clinical trial may move forward at designated checkpoints based on access to certain data from the clinical trial. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

Sponsors have the opportunity to meet with the FDA at certain points during the development of a new drug to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. These meetings may be held prior to the submission of an IND, at the end of Phase 2 and/or before an NDA is submitted. Meetings may be requested at other times as well.

The results of preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information on the manufacture, composition and quality of the product, proposed labeling and other relevant information are submitted to the FDA in the form of an NDA requesting approval to market the product. The NDA must be accompanied by a significant user fee payment. The FDA has substantial discretion in the approval process and may refuse to accept any application, for example if the NDA is not sufficiently complete, or decide that the data is insufficient for approval and require additional preclinical, clinical or other studies.

In addition, under the Pediatric Research Equity Act ("PREA"), an NDA or supplement to an NDA 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 product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan drug designation has been granted. However, if only one indication for a product has orphan drug designation, a pediatric assessment may still be required for any applications to market that same product for the non-orphan indication(s).

Once the NDA submission has been submitted, the FDA has 60 days after submission of the NDA to conduct an initial review to determine whether it is sufficient to accept for filing. NDAs receive either a standard or priority review. Under the Prescription Drug User Fee Act, the FDA sets a goal date by which it plans to complete its review. For a standard review, this is typically 10 months from the date of submission of the NDA application. The review process is often extended by FDA requests for additional information or clarification. Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with cGMPs and may also inspect clinical trial sites for integrity of data supporting safety and efficacy. The FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data. The FDA is not bound by the recommendations of an advisory committee, but generally follows such recommendations in making its decisions. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. The FDA may require post-marketing testing and surveillance to monitor safety or efficacy of a product.

After the FDA evaluates the NDA and conducts inspections of manufacturing facilities where the drug product and/or its API will be produced, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter generally outlines the deficiencies in the NDA submission and may require substantial additional

clinical testing, such as an additional pivotal Phase 3 clinical trial(s), clinical data, and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

The FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy ("REMS"), plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

Orphan Drug Designation

Under the Orphan Drug Act of 1983, the FDA may grant orphan drug designation to a drug or biological product intended to treat an orphan disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as demonstrating clinical superiority to the product with orphan exclusivity. The designation of such drug also entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug product designated as an orphan product receives regulatory approval for an indication broader than that for which it is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union has similar but not identical benefits in that jurisdiction.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product distribution, advertising and promotion, and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval and may require additional clinical trials and NDA submissions. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use.

Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained, or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, but are not limited to:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Moreover, the federal Drug Supply Chain Security Act imposes obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this new federal legislation, manufacturers are required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. Further, this legislation requires manufacturers to comply with detailed drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Other Healthcare Laws

In addition to FDA restrictions on the marketing of pharmaceutical products, federal and state healthcare laws restrict certain business practices in the biopharmaceutical industry. These laws include, but are not limited to, anti-kickback, false claims, data privacy and security, and transparency statutes and regulations.

The federal Anti-Kickback Statute prohibits, among other things, 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, arranging for, ordering or recommending any good, facility, item or service for which payment is made, in whole or in part, under Medicare, Medicaid or any other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and our future practices may not in all cases meet all of the criteria for a statutory exception or safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations 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 regulatory safe harbor does not make the conduct *per se* illegal under the federal 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. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare program covered business, the statute has been violated. Additionally, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "PPACA"), amended the intent requirement under the Anti-Kickback Statute and criminal healthcare fraud statutes (discussed below) such that a person or entity no longer needs to have actual knowledge of the statute or the specific intent to violate it in order to have committed a violation. In addition, PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below). Due to the breadth of these federal and state anti-kickback laws, and the potential for additional legal or regulatory change in this area, it is possible that our current and future sales and marketing practices and/or our future relationships with physicians might be challenged under these laws, which could cause harm to us.

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.

The federal false claims laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to 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. Recently, several 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 non-covered, uses.

The Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, including private third-party payors, and knowingly and willfully falsifying, concealing or covering up 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.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes 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, and newly empowered state attorneys general with the authority to enforce HIPAA. In January 2013, the Office for Civil Rights of the U.S. Department of Health and Human Services issued the Final Omnibus Rule under HIPAA pursuant to HITECH that makes significant changes to the privacy, security, and breach notification requirements and penalties. The Final Omnibus Rule, which generally took effect in September 2013, enhances certain privacy and security protections, and strengthens the government's ability to enforce HIPAA. The Final Omnibus Rule also enhanced requirements for both covered entities and business associates regarding notification of breaches of unsecured protected health information. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways. These state laws may not have the same effect and often are not preempted by HIPAA, thus complicating compliance efforts.

Additionally, PPACA also included the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. Failure to comply with required reporting requirements could subject applicable manufacturers and others to substantial civil money penalties.

Also, many states have similar healthcare 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. Certain states require pharmaceutical companies to implement a comprehensive compliance program that includes a limit or outright ban on expenditures for, or payments to, individual medical or health professionals and/or require pharmaceutical companies to track and report gifts and other payments made to physicians and other healthcare providers.

Because we commercialize products that are reimbursed under federal and other governmental healthcare programs, we have developed a comprehensive compliance program that establishes internal controls to facilitate adherence to the rules and healthcare program requirements. Although compliance programs and adherence thereto may mitigate the risk of violation of and subsequent investigation and prosecution for violations of the above laws, the risks cannot be entirely eliminated. If our operations are found to be in violation of any of the health care laws or regulations described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings and/or the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we are subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Pharmaceutical Coverage, Pricing and Reimbursement

In both domestic and foreign markets, our sales depend in part on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our commercial products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of the products. Sales of these products therefore depend substantially, both domestically and abroad, on the extent to which the costs of these products are paid by third-party payors. These third-party payors are increasingly focused on containing healthcare costs by challenging the price and examining the cost-effectiveness of medical products and services.

In addition, significant uncertainty exists as to the coverage and reimbursement status of newly approved healthcare product candidates. The market for our product candidates for which we may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. Furthermore, third-party payor reimbursement to providers for our product candidates may be subject to a bundled payment that also includes the procedure administering our products. To the extent there is no separate payment for our product candidates, there may be further uncertainty as to the adequacy of reimbursement amounts. Because each third-party payor individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time consuming, costly and sometimes unpredictable process. We may be required to provide scientific and clinical support for the use of any product to each third-party payor separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness and/or medical necessity of our products. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. We cannot be certain that our product candidates will be considered cost-effective or medically necessary. Because coverage and reimbursement determinations are made on a payor-by-payor basis, obtaining acceptable coverage and reimbursement from one payor does not guarantee the Company will obtain similar acceptable coverage or reimbursement from another payor. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. If we are unable to obtain coverage of, and adequate reimbursement and payment levels for, our product candidates from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition and future success.

Furthermore, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

Healthcare Reform

In the United States and foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future business and operations if and when we begin to directly commercialize our products.

In particular, there have been and continue to be a number of initiatives at the U.S. federal and state level that seek to reduce healthcare costs. Initiatives to reduce the federal deficit and to reform healthcare delivery are increasing cost-containment efforts. We anticipate that Congress, state legislatures and the private sector will continue to review and assess alternative controls on healthcare spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, the creation of large insurance purchasing groups, price controls on pharmaceuticals and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit or eliminate our spending on development projects and affect our ultimate profitability.

In March 2010, PPACA was signed into law. PPACA has substantially changed the way healthcare is financed by both governmental and private insurers. PPACA, among other things: established an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs; revised the methodology by which rebates owed by manufacturers for covered outpatient drugs under the Medicaid Drug Rebate Program are calculated;

increased the statutory minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; extended the Medicaid Drug Rebate Program to prescriptions of individuals enrolled in Medicaid managed care organizations; required manufacturers to offer 50% point-of-sale discounts on negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and implemented payment system reforms including a national pilot program on payment bundling to encourage hospitals, physicians and other providers to improve the coordination, quality and efficiency of certain healthcare services through bundled payment models. For years the U.S. Congress has been assessing new legislation designed to repeal and replace core sections of the PPACA. On December 22, 2017, for instance, the President signed into law the Tax Cuts and Jobs Act of 2017 (the "Tax Act"), which repealed the "individual mandate" of the PPACA. The repeal of the individual mandate is expected to cause millions fewer Americans to be insured in 2027 and premiums in insurance markets may rise. The Trump Administration has also taken executive actions to undermine or delay implementation of the PPACA. In January 2017, the President signed an Executive Order directing applicable federal agencies to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices.

Members of the United States Congress and the Trump administration have expressed an intent to pass legislation or adopt executive orders to fundamentally change or repeal parts of the PPACA.

Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of PPACA or otherwise circumvent some of the requirements for health insurance mandated by PPACA. These actions include directing applicable federal agencies to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, an Executive Order was signed terminating the cost sharing subsidies that reimburse insurers under the PPACA. Several state Attorneys Generals filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. Further, on June 14, 2018 the United States Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12.0 billion in PPACA risk corridor payments to third-party payors. The effects of this gap in reimbursement on third-party payors, the viability of the PPACA marketplace, providers, and our business, are not yet known.

Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under PPACA have been signed into law. On December 22, 2017, for instance, the President signed into law the Tax Cuts and Jobs Act of 2017 (the "Tax Act"), which repealed the "individual mandate" of the PPACA. The repeal of the individual mandate is expected to cause millions fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, on December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of PPACA, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of PPACA are invalid as well. While this judge, as well as the Trump Administration and CMS, have stated that the ruling will have no immediate effect, it is unclear how this judicial decision, subsequent appeals, and other efforts to repeal and replace PPACA will impact PPACA and our business.

In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the PPACA for plans sold through such marketplaces. The Bipartisan Budget Act of 2018, or the BBA, among other things, amends the PPACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In July 2018, the CMS published a final rule permitting further collections and payments to and from certain PPACA qualified health plans and health insurance issuers under the PPACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. Moreover, CMS issued a final rule in 2018 that will give states

greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the PPACA for plans sold through such marketplaces. Further, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed and enacted federal and state legislation, designed to, among other things, bring more transparency to product pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, the Trump Administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients.

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

In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit the prices we will be able to charge for our product candidates, or the amounts of reimbursement available for our product candidates. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, measures to reduce costs of the Medicaid program, and some states are considering implementing measures that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payor or policy actions, which may include cost containment and healthcare reform measures. Such policy actions could have a material adverse impact on our profitability.

Segment and Geographical Information

Information on our total revenues by product attributed to customers who represented at least 10% of our total revenues in each of 2018 and 2017, is included in Note 14 to our consolidated financial statements.

The following table represents total long-lived assets by location (in thousands):

	December 31, 2018	December 31, 2017
United States	$ 294	$ 15
Total long-lived assets (1)	$ 294	$ 15

(1) Long-lived assets consist of property and equipment.

Employees

As of December 31, 2018, we had 106 full-time employees, working in the United States or Ireland. Of these full-time employees, 29 were engaged in research and development, 61 were engaged in commercial activities including sales, marketing and market access, and 16 were engaged in other general and administrative activities.

Corporate Information

Strongbridge Biopharma plc, an Irish public limited company, was established on May 26, 2015 under the name Cortendo plc.

Our principal office in Ireland is located at Suite 206, Fitzwilliam Hall, Fitzwilliam Place, Dublin 2, D02 T292, Ireland. Our principal executive office is located at 900 Northbrook Drive, Suite 200, Trevose, Pennsylvania, 19053, USA, and our telephone number is +1 610-254-9200

Our website is *www.strongbridgebio.com*. The information on, or that can be accessed through, our website is not part of and should not be incorporated by reference into this Annual Report.

Available Information

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, beneficial ownership reports on Forms 3, 4 and 5 and proxy statements, as well as all amendments to those reports are available free of charge through our investor relations website at *strongbridgebio.com*, as soon as reasonably practicable after such reports are electronically filed with, or furnished to, the Securities and Exchange Commission ("SEC"). The information found on our website is not part of this or any other report that we file with or furnish to the SEC. Our SEC filings are also available to the public over the Internet at the SEC's website at www.sec.gov.

ITEM 1A. RISK FACTORS

Certain factors may have a material adverse effect on our business, financial condition and results of operations. You should carefully consider the risks and uncertainties described below, in addition to other information contained in this Annual Report, including our consolidated financial statements and related notes. Our business, financial condition or results of operations could be materially and adversely affected if any of these risks occurs and, as a result, the market price of our ordinary shares could decline and you could lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may have similar adverse effects on us.

Risks Related to Our Business, Industry and Operations

We have generated only limited revenues from product sales to date, we have a history of net losses and negative cash flows, and we may never achieve or maintain profitability.

Until we acquired the U.S. marketing rights to Keveyis, in December 2016, we were a development-stage biopharmaceutical company. We have a limited operating history and have not yet demonstrated an ability to obtain regulatory approval for, or manufacture and commercialize a product candidate.

Since inception, we have incurred significant operating losses. We have devoted substantially all of our financial resources to identifying, in-licensing, acquiring and developing our product candidates, conducting clinical trials, commercializing Keveyis, which we launched in April 2017, and Macrilen, our second commercial product, which we launched in July 2018 and subsequently sold the rights to in December 2018, and providing general and administrative support for these operations.

To date, we have financed our operations primarily through private placements of equity securities, the proceeds from our initial public offering of ordinary shares in the United States in October 2015 and subsequent follow-on public offerings, our at-the-market facility, and debt financings.

Our ability to achieve and maintain profitability in the future will depend on our ability to obtain regulatory approval for our product candidates and to generate sufficient revenues from product sales.

Our future revenue will be dependent, in part, upon the size of the markets in the territories for which our products receive regulatory approval, the accepted prices for our products, the ability to obtain coverage and adequate reimbursement, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from our products.

Furthermore, we anticipate that our expenses will continue to increase as we:

- continue to grow our sales, marketing and distribution infrastructure;
- continue research and nonclinical and clinical development of our product candidates, including advancing our programs from preclinical development into clinical trials and increasing the number and size of our current clinical trials and preclinical studies;
- make up-front, milestone or other payments under any asset acquisition, supply, or license arrangements;
- seek to identify, assess, in-license, acquire and develop additional product candidates;
- change or add manufacturers or suppliers;
- seek regulatory approvals for our product candidates that successfully complete clinical trials;
- seek to maintain, protect and expand our intellectual property portfolio;
- seek to attract and retain skilled personnel;
- create additional infrastructure to support our operations as a U.S. listed company and our product development and commercialization efforts; and
- experience any delays or encounter issues with any of the above, including, but not limited to, failed preclinical studies or clinical trials, complex results, safety issues or other regulatory challenges that may require either longer follow-up of existing preclinical studies or clinical trials or limitation of additional preclinical studies or clinical trials in order to pursue regulatory approval.

The net losses we incur before achieving profitability may fluctuate significantly from quarter-to-quarter and year-to-year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. Moreover, if we incur substantial losses, we could be liquidated, and the value of our shares might be significantly reduced or the shares might be of no value.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to successfully execute on our business strategy would decrease the value of our company and could impair our ability to raise capital, expand our business or continue our operations. A decline in the value of our company could cause you to lose all or part of your investment.

We will receive significant funding from Novo Nordisk through 2021 to subsidize the cost of 23 of our field-based employees, and we have committed that these employees will be fully dedicated during this time to the provide services to Novo, including to promote Macrilen in the United States. As a result, we will be dependent on our relationship with Novo and any setback that may occur with respect to Macrilen sales by Novo and/or its breach of our underlying agreements with them could impair our operating results.

In December 2018, we sold our subsidiary that held the U.S. and Canadian marketing rights to Macrilen to Novo. As consideration for the sale, we received an upfront payment from Novo plus the right to receive tiered royalties on net sales of Macrilen through 2027. In addition, we entered into a services agreement with Novo pursuant to which it will fund, for a period of three years (subject to our right to terminate the arrangement upon six months' notice), the costs of 23 of our field-based employees to provide full-time ongoing services to Novo, including the promotion of Macrilen in the United States. We will also be entitled to a performance fee of up to $1.5 million per contract year if certain conditions are met by our field-based employees under the services arrangement, which conditions will be determined and measured by a joint committee comprised of members from Novo and from Strongbridge, with a majority of members from Novo.

The royalties we are entitled to receive from Novo will depend, in part, on the amount and timing of resources dedicated to the marketing and distribution of Macrilen by Novo. Although we will have the ability to contribute to the overall success of Macrilen, the commercial success of Macrilen will ultimately be determined and controlled by Novo and royalty revenues to us will be negatively impacted if sales of Macrilen by Novo are limited for any reason, including if Novo is unable to market Macrilen effectively as a result of competitive, manufacturing, regulatory or other issues. Furthermore, the royalty payments we receive for Macrilen sales will be determined by Novo based on reported sales. Novo's calculation of royalty payments will be subject to and dependent upon the adequacy and accuracy of its sales and accounting functions. Errors may occur from time to time in these calculations. Although we have the right to audit the calculations and sales data for royalty payments, we will rely in the first instance on Novo to accurately report sales and calculate and pay applicable royalties. If we do exercise our audit rights, such audits may occur many months following our recognition of the royalty revenue errors, may require us to adjust our royalty revenues in later periods and may require us to incur significant expenses. Further, Novo may be uncooperative or have insufficient records, which may complicate and delay the audit process.

Our field-based employees are required under the services agreement to devote all of their time, under the direction of Novo, to the promotion of Novo's growth hormone products, including Macrilen. As a result, we will not be entitled to the services of these employees during the term of the services agreement. In addition, the reimbursement by Novo to us for the costs of our field-based employees is dependent on the satisfaction of our obligations under the services agreement and Novo's fulfillment of its related contractual obligations. We are generally required to maintain the services of the full 23-person team and to use commercially reasonable efforts to ensure that these field-based employees perform the services set forth in a commercial plan to be developed from time to time by Novo. The agreement contains customary provisions regarding events of termination and indemnification, and we are generally obligated to indemnify Novo for the actions of our employees, subject to limitations in the event they are acting at the direction of Novo.

Finally, our right to receive any portion of the annual performance fee will be contingent on a number of factors including the establishment of reasonable performance criteria for our field-based employees (in light of the fact that a majority of the joint committee will be affiliated with Novo), our field-based employees' ability to achieve the annual performance goals established by the joint committee, and the determination and calculation of any performance fees that are owed to us under the services arrangement and our ability to validate and/or challenge such determination and calculation if necessary.

We are highly dependent on our key personnel, including our chief executive officer and chief medical officer, as well as our ability to recruit, retain and motivate additional qualified personnel.

We are highly dependent on Matthew Pauls, our President and Chief Executive Officer, and Dr. Fredric Cohen, our Chief Medical Officer, as well as certain other executive officers. Some members of our management team, including Mr. Pauls, have only been our employees since August 2014. As a result, they have limited experience working for us and working together as a team. Any member of management or employee can terminate his or her relationship with us at any time. Although we have included non-compete provisions in their respective employment or consulting agreements, as the case may be, such arrangements might not be sufficient for the purpose of preventing such key personnel from entering into agreements with any of our competitors. The inability to recruit and retain qualified personnel, or the loss of Mr. Pauls, Dr. Cohen or certain other executive officers, could result in competitive harm as we could experience delays in reaching our in-licensing, acquisition, development and commercialization objectives.

We also depend substantially on highly qualified managerial, sales and technical personnel who are difficult to hire and retain. There is currently a shortage of skilled personnel in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical studies or clinical trials may make it more challenging to recruit and retain qualified personnel. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will be critical to our success.

If we are unable to effectively build, train and equip our sales force, our ability to successfully commercialize Keveyis, and any other products we acquire or for which we receive regulatory approval, and to market and promote Macrilen on behalf of Novo will be harmed.

Prior to our launch of Keveyis in April 2017, we had no experience commercializing products on our own. In order to successfully commercialize Keveyis, and any other products we acquire or for which we receive regulatory approval, and to market and promote Macrilen on behalf of Novo, we must continue to build our sales, marketing, distribution, managerial and other non-technical capabilities. The continued development of our commercial organization will be expensive and time-consuming, and our resources may be limited compared to some of our competitors.

We have expended significant time and resources to train our sales force to be effective in their sales efforts for Keveyis and Macrilen. However, we are likely to experience turnover of the sales representatives that we have hired or will hire, requiring us to train new sales representatives.

If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate physicians and other potential customers about the benefits of Keveyis, Macrilen and any other products we acquire or for which we receive regulatory approval, and their proper administration and label indication, as well as any associated patient access programs, our efforts to successfully commercialize products could be put in jeopardy, which could have a material adverse effect on our financial condition, share price and operations.

We are expanding our organization and may experience difficulties in managing this growth, which could disrupt our operations.

As our development, commercialization, in-licensing, and acquisition plans and strategies develop, and as we continue to commercialize Keveyis, promote Macrilen, and advance the clinical and preclinical development of our product candidates, we expect to experience growth in the number of our employees and the scope of our operations, particularly in the areas of managerial, operational, sales, marketing, financial, legal and other resources. 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. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. Due to our limited financial resources, we may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Any such growth could require significant capital expenditures and may divert financial resources from other projects, such as the in-licensing, acquisition and development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to compete effectively will depend, in part, on our ability to effectively manage any future growth.

Future revenues from product sales and/or royalties may be lower than expected.

Efforts to educate the medical community and third-party payors on the benefits of Keveyis and Macrilen and any other product candidates for which we receive regulatory approval may require significant resources and may not be successful. If the products we promote do not achieve an adequate level of market acceptance, we may not generate significant revenues from product sales and/or royalties or any profits from operations. The degree of market acceptance of Keveyis and Macrilen and any product candidates for which we receive regulatory approval will depend on a variety of factors, including, but not limited to:

- whether clinicians and potential patients perceive the products or product candidates to have better efficacy, safety and tolerability profile, and ease of use compared with alternative therapies;
- the timing of market introduction;

- the number and quality of current and future competing products;
- our ability to provide acceptable evidence of safety and efficacy;
- the prevalence and severity of any side effects;
- relative convenience and ease of administration;
- cost-effectiveness;
- patient diagnostics and screening infrastructure in each market;
- marketing and distribution support; and
- availability of coverage, reimbursement and adequate payment from health maintenance organizations and other third-party payors, both public and private.

In addition, the potential market opportunity for any pharmaceutical product is difficult to estimate precisely. Our estimates of the potential market opportunity for Keveyis, Macrilen and our two product candidates are predicated on several key assumptions such as industry knowledge and publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions may be inaccurate. If any of our assumptions proves to be inaccurate, then the actual market for these products and product candidates, if approved, could be smaller than our estimates of the potential market opportunity. If the actual markets for these products and product candidates, if approved, are smaller than we expect, or if they fail to achieve an adequate level of acceptance by physicians, health care payors and patients, the revenue we recognize from product sales and/or royalties may be limited and we may be unable to achieve or maintain profitability. Further, given the limited number of treating physicians, if we are unable to convince a significant number of such physicians of the value of these products, we may be unable to achieve a sufficient market share to make our products profitable.

We operate in a highly competitive and rapidly changing industry, which may result in competitors discovering, developing or commercializing competing products before or more successfully than we do, or our entering a market in which a competitor has commercialized an established competing product, and we may not be successful in competing with them.

The development and commercialization of pharmaceutical products is highly competitive and subject to significant and rapid technological change. Our success is highly dependent upon our ability to in-license, acquire, develop and obtain regulatory approval for new and innovative drug products on a cost-effective basis and to market them successfully. In doing so, we face and will continue to face intense competition from a variety of businesses, including large, fully integrated, well-established pharmaceutical companies who already possess a large share of the market, specialty pharmaceutical companies and biopharmaceutical companies, academic institutions, government agencies and other private and public research institutions in Europe, the United States and other jurisdictions. In addition, for so long as we are entitled to receive royalties from Novo from their Macrilen sales, our success will depend in part on Novo's ability to compete in this challenging environment.

We anticipate this competition to increase in the future as new companies enter the neuromuscular, endocrinology and rare diseases markets. In addition, the health care industry is characterized by rapid technological change, and new product introductions or other technological advancements could make some or all of our products obsolete.

The highly competitive nature of and rapid technological changes in the biotechnology and pharmaceutical industries could render our products and product candidates and/or Macrilen, obsolete or non-competitive. Our competitors may, among other things:

- have similar or better product candidates or technologies;
- possess greater financial and human resources as well as supporting clinical data;

- develop and commercialize products that are safer, more effective, less expensive, or more convenient or easier to administer;
- obtain regulatory approval more quickly;
- establish superior proprietary positions;
- have access to greater manufacturing capacity;
- seek patent protection that competes with our product candidates;
- implement more effective approaches to sales and marketing; or
- enter into more advantageous collaborative arrangements for research, development, manufacturing and marketing of products.

Additional competitors could enter the market with generic versions of our products or Macrilen, which may result in a decline in sales of affected products.

Under the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application ("ANDA"), seeking approval of a generic copy of an approved innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA under section 505(b)(2) that references the FDA's prior approval of the innovator product. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. Hatch-Waxman also provides for certain periods of regulatory exclusivity, which preclude FDA approval, or, in some circumstances, FDA filing and reviewing, of an ANDA or 505(b)(2) NDA. These include, subject to certain exceptions, the period during which an FDA-approved drug is subject to orphan drug exclusivity.

We intend to rely on orphan drug exclusivity in the marketing and sale of Recorlev. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the "Orange Book." If there are patents listed in the Orange Book, a 505(j) or 505(b)(2) applicant that seeks to market its product via an ANDA before expiration of the patents must include in the ANDA what is known as a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, final approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if Recorlev or any of our other product candidates is approved, competitors could file ANDAs for generic versions of our product candidates, or 505(b)(2) NDAs that reference our product candidates, respectively. If there are patents listed for our product candidates in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict whether any patents issuing from our pending patent applications will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any patents that are granted and listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected product and our ability to generate revenue could be compromised. In addition, for so long as we are entitled to receive royalties from Novo Nordisk, any challenges faced in maintaining the proprietary patent protection associated with Macrilen that have a negative impact on Novo's product sales will have a negative effect on us.

The Orphan Drug designation for our products and product candidates may not prevent competition from companies that develop other compounds for the treatment of the same condition. These companies may have significantly more resources than we do. Competition from them could limit our revenue from the commercialization of our products and/or product candidates, if approved.

Although Keveyis and our two product candidates have received Orphan Drug designation in the United States, and in the case of Recorlev and veldoreotide in Europe, we cannot be assured that we will realize the potential benefits of the designation. Even after an orphan drug is approved for its orphan indication, the FDA or EMA can subsequently approve a different drug for the same condition if it concludes that the later drug is safer, more effective or makes a major contribution to patient care. Upon expiration of the orphan drug exclusivity period, we may be subject to competition from manufacturers offering a generic form of Keveyis or our other product candidates, if approved, at a lower price, in which case our business could be harmed. Similarly, for so long as we are entitled to receive royalties from Novo from Macrilen sales, our business will be negatively impacted by any competitor who is able to offer a generic form of Macrilen at a lower price.

For example, Corcept's Korlym has an Orphan Drug designation in the United States and is approved for the control of hyperglycemia secondary to hypercortisolism in patients with endogenous Cushing's syndrome who have type 2 diabetes or glucose intolerance and have failed surgery or are not candidates for surgery. In 2012 Novartis received approval in both the United States and the European Union (EU) to market its somatostatin analogue Signifor for adult patients with Cushing's disease (a subset of Cushing's syndrome that accounts for approximately 70 percent of all Cushing's syndrome patients) for whom pituitary surgery is not an option or has not been curative.

We expect that we will need additional funding before we can expect to complete the development of our two product candidates.

We are currently advancing two product candidates through clinical development, Recorlev (levoketoconazole) and veldoreotide. Development of product candidates is expensive, and we expect our research and development expenses to increase in connection with our ongoing activities, particularly as we continue our ongoing trials and initiate new nonclinical studies and clinical trials of Recorlev, veldoreotide and any other product candidates we may seek to develop. We expect that we will require additional capital to commercialize Recorlev and to obtain regulatory approval for and commercialize veldoreotide. Our future funding requirements will depend on many factors, including, but not limited to:

- the amount of revenue that we receive from Keveyis sales and Macrilen royalties;
- the cost of expanding our sales, marketing, distribution and administrative capabilities;
- the scope, rate of progress, results and cost of our clinical trials, nonclinical testing, and other related activities;
- the cost of formulation, process development, manufacturing of clinical supplies, and establishing commercial supplies of our product candidates and any other product candidates that we may develop, in-license or acquire;
- the number and characteristics of product candidates that we pursue, including any additional product candidates we may in-license or acquire;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates;
- the cost, timing and outcomes of regulatory approvals;

- the terms and timing of any collaborative, licensing and other arrangements that we may establish, including any required milestone and royalty payments thereunder; and
- the emergence of competing technologies and their achieving commercial success before we do or other adverse market developments.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may compromise our ability to develop and commercialize our product candidates, if approved. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our ordinary shares to decline.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product or product candidate that is approved, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired.

Raising additional capital may cause dilution to our shareholders, restrict our operations, or require us to relinquish rights to our intellectual property or future revenue streams.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of product revenue, royalty income, equity offerings, debt financings, grants, and license and development agreements in connection with any collaborations. We do not have any committed external source of funds. In the event we seek additional funds, we may raise additional capital through the sale of equity or convertible debt securities. In such an event, the ownership interests of our current shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that would adversely affect their rights as shareholders. Debt financing, if available, could result in increased fixed payment obligations and may involve agreements that include restrictive covenants, such as limitations on our ability to incur additional debt, make capital expenditures, acquire, sell or license intellectual property rights or declare dividends, and other operating restrictions that could hurt our ability to conduct our business.

Further, if we raise additional funds through collaborations, strategic alliances, or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property or future revenue streams. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We have no manufacturing capabilities and currently depend on one supplier to manufacture Keveyis. We also depend on a limited number of other suppliers to manufacture our product candidates for use in clinical trials. If these suppliers are unable or unwilling to continue manufacturing for us and we are unable to contract quickly with alternative sources our business will be harmed.

Taro produces all of our requirements for Keveyis. We rely on other third-parties to manufacture our product candidates for use in clinical trials. If any of these vendors is unable or unwilling to meet our future requirements, we may not be able to manufacture our products in a timely manner. Our current arrangements with these manufacturers are terminable by such manufacturers, subject to certain notice provisions.

We may not be successful in executing our research programs or business development efforts.

Research programs and business development efforts to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our research programs, business development efforts or licensing

attempts may fail to yield additional complementary or successful product candidates for clinical development and commercialization for a number of reasons, including, but not limited to, the following:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates with a high probability of success for development progression;
- we may not be able or willing to assemble sufficient resources or expertise to in-license, acquire or discover additional product candidates;
- we may not be able to agree to acceptable terms with the licensor or owner of any product candidates we seek to in-license or acquire;
- our product candidates may not succeed in preclinical studies or clinical trials;
- we may not succeed in formulation or process development;
- our product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive regulatory approval;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates that we develop may be covered by third parties' patents or other exclusive rights;
- product candidates that we develop may not allow us to leverage our expertise and our development and commercial infrastructure as currently expected;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors.

If any of these events occurs, we may not be successful in executing our growth strategy or our growth strategy may not deliver the anticipated results.

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

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

If we acquire other businesses or in-license or acquire other product candidates and are unable to integrate them successfully, our financial performance could suffer.

If we are presented with appropriate opportunities, we may acquire other businesses or product candidates. The integration of new businesses and/or product candidates may produce unforeseen operating difficulties and expenditures, and may absorb significant management attention that would otherwise be directed to the ongoing development of our business. Also, in any future in-licensing or acquisition transactions, we may issue shares of stock that would result in

dilution to existing shareholders, incur debt, assume contingent liabilities or create additional expenses related to amortizing intangible assets, any of which might harm our financial results and cause our stock price to decline. Any financing we might need for future transactions may be available to us only on terms that restrict our business or impose costs that reduce our net income.

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

Our computer systems, as well as those of our clinical research organizations ("CROs"), and other contractors and consultants, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, including hurricanes, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of preclinical study or clinical trial data from completed, ongoing or planned preclinical studies or clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Risks Related to Our Clinical Trials, Government Regulation and Legal Proceedings

Clinical trials are very expensive, time consuming and difficult to design and implement, and involve uncertain outcomes. Furthermore, results of earlier preclinical studies and clinical trials may not be predictive of results of future preclinical studies or clinical trials.

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and earlier clinical trials may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials.

In some instances, there can be significant variability in safety or efficacy results between earlier and later stages of clinical trials of the same product candidate. These discrepancies may be due to a number of factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the administration regimen and other clinical trial protocols, and the rate of dropout among clinical trial participants.

In the case of our two product candidates, Recorlev and veldoreotide, results from our Phase 3 clinical trials may differ from earlier results due to the larger number of patients, clinical trial sites and additional countries involved in our Phase 3 clinical trials. Furthermore, different countries have different standards of care and different levels of access to care for patients, which in part drives the heterogeneity of the patient populations that enroll in our studies. In August 2018, we announced statistically significant positive top-line results from our SONICS Phase 3 clinical trial for Recorlev. However, there can be no assurances that the final results will be positive.

In addition, because we were not involved in and had no control over the preclinical and clinical development of veldoreotide prior to our acquisition of this product candidate in June 2015, we are dependent on the prior research and development of veldoreotide having been conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, the accuracy of reported results of all clinical trials conducted prior to our acquisition, and the correct interpretation of collected data from these clinical trials. If any of these assumptions prove to be incorrect, we could experience increased costs and delays in the development of veldoreotide, which could hurt our ability to generate future revenues from this product candidate.

We may experience delays in our ongoing or future preclinical studies or clinical trials, and we do not know whether future preclinical studies or clinical trials will begin on time, need to be redesigned, enroll an adequate number

of subjects or patients on time or be completed on schedule, if at all. Clinical trials may be delayed, suspended or terminated for a variety of reasons, including delay or failure to:

- obtain authorization from regulators or IRBs to commence a clinical trial at a prospective clinical trial site;
- reach agreements on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- recruit and enroll a sufficient number of patients in clinical trials to ensure adequate statistical power to detect statistically significant treatment effects;
- address any noncompliance with regulatory requirements or safety concerns that arise during the course of a clinical trial;
- have patients complete clinical trials or return for post-treatment follow-up;
- have CROs or other third parties comply with regulatory requirements, adhere to the trial protocol or meet contractual obligations in a timely manner or at all;
- identify a sufficient number of clinical trial sites and initiate them within the planned timelines; and
- manufacture sufficient quantities of the product candidate to complete clinical trials.

We may find it difficult to enroll patients in our clinical trials given the limited number of patients who have the diseases for the treatment of which our product candidates are being studied. Difficulty in enrolling patients in our clinical trials could delay or prevent clinical trials of our product candidates.

Successful and timely completion of clinical trials will require that we enroll a sufficient number of patient candidates. Clinical trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. Patient enrollment depends on many factors, including the size and nature of the patient population, eligibility criteria for the clinical trial, the proximity of patients to clinical sites, the design of the clinical protocol, the availability of competing clinical trials, the availability of new drugs approved for the indication the clinical trial is investigating, and clinicians' and patients' perceptions as to the safety and potential advantages of the product candidate being studied in relation to other available therapies.

Because we are focused on addressing rare diseases, there are limited patient pools from which to draw in order to complete our clinical trials in a timely and cost-effective manner. Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process, and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that may lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

The regulatory approval process of the FDA, EMA or any comparable foreign regulatory agency may be lengthy, time consuming and unpredictable.

We cannot be certain that any of our product candidates will be successful in clinical trials or receive regulatory approval. The FDA, EMA and other comparable foreign regulatory agencies have substantial discretion in the approval process and in determining when or whether regulatory approval will be obtained for any of our product candidates. Even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA, EMA or any comparable foreign regulatory agency. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain regulatory approval for the product candidates.

Furthermore, while certain of our employees have prior experience with submitting marketing applications to the FDA, EMA and comparable foreign regulatory agencies, we, as a company, have not submitted such applications for our product candidates. Applications for any of our product candidates could fail to receive regulatory approval for many reasons, including, but not limited to, the following:

- the FDA, EMA or any comparable foreign regulatory agency may disagree with the design or implementation of our clinical trials or our interpretation of data from nonclinical trials or clinical trials;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which we seek approval, including reliance on foreign clinical data;
- the data collected from clinical trials of our product candidates may not be sufficient to support a finding that has statistical significance or clinical meaningfulness or support the submission of a NDA or other submission, or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA, EMA or any comparable foreign regulatory agency that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA, EMA or any comparable foreign regulatory agency may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA or any comparable foreign regulatory agency may significantly change in a manner rendering our clinical data insufficient for approval.

In communications we had with the FDA, they recommended use of a concurrent control group in our SONICS Phase 3 clinical trial. However, SONICS utilizes an open-label, single-arm design because use of a placebo control in a parallel-arm monotherapy design was considered unethical or infeasible to enroll, depending on the specific country or clinical trial site under consideration. Studies lacking an active control group are more likely to be subject to unanticipated variability in study results that can potentially lead to flawed conclusions because they do not allow for discrimination of patient outcomes. In August 2018, we announced statistically significant positive top-line results from our SONICS Phase 3 clinical trial. However, even if we achieve the clinical trial's endpoints for this clinical trial, the FDA or other regulatory authorities could view our study results as potentially biased due to our lack of an active control group.

Our LOGICS study, which is a second Phase 3 clinical trial of Recorlev for the treatment of endogenous Cushing's syndrome, will supplement the long-term efficacy and safety data from the ongoing SONICS trial via a randomized, double-blind, placebo-controlled design that will randomize approximately 54 patients, in an attempt to address our lack of an active control group in our SONICS trial. There can be no assurances, however, that the FDA or other regulatory authorities will view the LOGICS study results as sufficient.

Upon completion of the clinical development program for Recorlev, we intend to file for marketing authorizations in the United States and elsewhere. Following consultations with the FDA, we have determined that the 505(b)(2) approval pathway, which permits an NDA applicant to rely on data from studies that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference, is the appropriate pathway for a Recorlev NDA. We intend to rely on published literature and the FDA's prior findings concerning the safety and/or effectiveness of ketoconazole in our NDA for Recorlev and on similar processes in other jurisdictions. There can be no assurances, however, that the 505(b)(2) approval pathway in the United States, or similar approval pathways outside of the United States, will be available for Recorlev or that the FDA or other regulatory authorities will approve Recorlev through an application based on such pathways.

We generally plan to seek regulatory approval to commercialize our product candidates in the United States, the European Union and other key global markets. To obtain regulatory approval in other countries, we must comply with regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing and distribution of our product candidates. Even if we are successful in

obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. Failure to obtain marketing authorization for our product candidates in any jurisdiction will result in our being unable to market and sell such products. Similarly, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

Any of our current or future product candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain regulatory approval. This could delay or eliminate any potential product revenue by delaying or terminating the potential commercialization of our product candidates.

Physicians may accept Keveyis and/or Macrilen slowly or may never accept them, which would adversely affect our financial results.

Physicians will prescribe Keveyis only if they determine, based on experience, clinical data, side effect profiles and other factors, that it is preferable to other treatments, even if those products are not approved for PPP. Because PPP is rare, most physicians are inexperienced in the care of patients with the illness and it may be difficult to persuade them to prescribe Keveyis. Other factors that may affect the commercial success of Keveyis include:

- the preference of some physicians for more familiar, long-standing, off-label treatments for PPP, such as acetazolamide;
- long-term persistency and compliance with therapy;
- competition from alternative therapies, such as potassium supplements, diuretics, beta receptor agonists, mexiletine and other sodium channel blockers;
- the cost-effectiveness of Keveyis and the availability of third-party insurance coverage and reimbursement; and
- the product labeling required by the FDA.

Physicians will prescribe Macrilen only if they determine, based on experience, clinical data, side effect profiles and other factors, that it is preferable to other diagnostic methods, even if those methods are not approved for diagnosing AGHD. Because AGHD is rare, most physicians are inexperienced in the diagnosis of patients with the illness and it may be difficult to persuade them to prescribe Macrilen. Other factors that may affect the commercial success of Macrilen include:

- the preference of some physicians to utilize Arginine, an injectable product that is the only other FDA-approved product indicated for use in diagnosing AGHD, or one of several other products that are used off-label to diagnose AGHD, of which the two most frequently prescribed products are the injectables glucagon and insulin;
- the cost-effectiveness of Macrilen and the availability of third-party insurance coverage and reimbursement; and
- the product labeling required by the FDA.

The failure of Keveyis and Macrilen to achieve commercial success could prevent us from generating sufficient product sales and royalties to fully fund our commercial and development activities.

If serious adverse, undesirable or unacceptable side effects are identified during the development of our product candidates or following regulatory approval, we may be required to take actions that could significantly harm our business, financial condition, and results of operations.

If any of our product candidates are found to be associated with serious adverse, undesirable or unacceptable side effects, we may need to abandon their development or limit development to certain uses or sub-populations in which

such side effects are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially show promise in preclinical or early stage testing have later been found to cause side effects that have restricted their use and prevented further development of the compound for larger indications.

In our clinical trials of Recorlev to date, adverse events have included headache, nausea, back pain, dizziness, diarrhea and liver enzyme elevations. For veldoreotide, which is given by subcutaneous injections, adverse events have included injection site reaction such as swelling, itching and pain. Headache and gastrointestinal effects such as nausea and diarrhea have also been observed for veldoreotide. These adverse events can be dose-dependent and may increase in frequency and severity if we increase the dose to increase efficacy. Occurrence of serious treatment-related side effects could impede clinical trial enrollment, require us to halt the clinical trial, and prevent receipt of regulatory approval from the FDA, EMA or any comparable foreign regulatory agency. They could also adversely affect physician or patient acceptance of our product candidates.

Discovery of previously unknown problems, or increased focus on a known problem, with an approved product may result in restrictions on its permissible uses, including withdrawal of the medicine from the market. Currently, ketoconazole is required to include a "black box" warning on its label for use as an antifungal related to liver toxicity in the United States. Manufactured ketoconazole consists of two enantiomers, 2R,4S-ketoconazole and 2S,4R-ketoconazole, that are found in equal amounts, and is therefore referred to as a racemate mixture. Recorlev is a single-enantiomer drug, a pure form of one of the two enantiomers (2S,4R-ketoconazole) of ketoconazole. If Recorlev is required to include a similar "black box" warning on its label, it may limit our ability to commercialize the product, if approved.

Additionally, if we or others identify undesirable side effects caused by Keveyis or any other products candidates for which we receive regulatory approval, a number of potentially significant negative consequences could result, including, but not limited to:

- withdrawal by regulatory authorities of approvals of such product;
- seizure of the product by regulatory authorities;
- recall of the product;
- restrictions on the marketing of the product;
- requirement by regulatory authorities of additional warnings on the label, such as a black box warning;
- requirement that we create a medication guide outlining the risks of such side effects for distribution to patients;
- commitment to expensive additional safety studies prior to launch as a prerequisite of approval by regulatory authorities of such product;
- commitment to expensive post-marketing studies as a prerequisite of approval by regulatory authorities of such product;
- initiation of legal action against us claiming to hold us liable for harm caused to patients; and
- harm to our reputation and resulting harm to physician or patient acceptance of our products.

Any of these events could negatively impact the commercial prospects of the affected product and could significantly harm our business, financial condition, and results of operations. In addition, for so long as we are entitled to receive royalties from Novo from their Macrilen sales, our operations will be negatively impacted by any adverse side effects found to be associated with Macrilen.

We may become exposed to costly and damaging product liability claims, either in connection with the sale of our approved products or when testing our product candidates in the clinic, and our product liability insurance may not cover all damages from such claims.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing, and use of pharmaceutical products. The current and future use of product candidates by us in clinical trials, and the sale of any approved products, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products, and/or other third parties we have agreed to indemnify. Any claims against us, regardless of their merit, could be difficult and costly to defend, and could compromise the market acceptance of our products or any prospects for commercialization of our product candidates, if approved.

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. Physicians and patients may not comply with product instructions or may ignore warnings regarding potential adverse effects and patients who should not use our products. If any of our products or product candidates were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities.

We have limited product liability insurance that offers coverage we believe to be appropriate for a company such as ours. We intend to extend our product liability insurance coverage to any product candidate for which we obtain marketing approval. However, this insurance may be prohibitively expensive or may not fully cover our potential liabilities. Our inability to obtain adequate insurance coverage at an acceptable cost could prevent or inhibit the commercialization of our products or result in meaningful underinsured or uninsured liability. Defending a lawsuit could be costly and significantly divert management's attention from conducting our business. If we were sued successfully, our liability be substantial.

Our ability to successfully commercialize Keveyis and any other product candidates for which we receive regulatory approval will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage and reimbursement levels and pricing policies.

Our ability to successfully commercialize Keveyis and any other product candidates for which we receive regulatory approval will depend, in part, on the extent to which coverage and reimbursement for these products will be available from government and health administration authorities, private health insurers and other third-party payors. To manage healthcare costs, many governments and third-party payors increasingly scrutinize the pricing of new therapies and require greater levels of evidence of favorable clinical outcomes and cost-effectiveness before extending coverage and adequate reimbursement to such new technologies. In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (the “Medicare Modernization Act”) changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly under a new Part D and introduced a new reimbursement methodology based on average sale prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost-reduction initiatives and other provisions of this legislation could decrease the coverage and reimbursement that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors. In light of such challenges to prices and increasing levels of evidence of the benefits and clinical outcomes of new technologies, we cannot be sure that coverage will be available for these products, and, if available, that the reimbursement rates will be adequate. If adequate levels of coverage and reimbursement for these products is unavailable, our ability to generate revenue from product sales and/or royalties will be compromised.

Because each third-party payor individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time consuming, costly and sometimes unpredictable process. We may be required to provide scientific and clinical support, medical necessity or both for the use of a product to each third-party payor separately with no assurance that approval would be obtained, and we may need to conduct expensive

pharmacoeconomic studies in order to demonstrate the cost-effectiveness, medical necessity or both of a product. This process could delay the market acceptance of our products and could have a negative effect on our future revenues and operating results.

Third-party payors may deny coverage and reimbursement status altogether of a given drug product, or cover the product, but may also establish prices at levels that are too low to enable us to realize an appropriate return on our investment in product development. Because the rules and regulations regarding coverage and reimbursement change frequently, in some cases on short notice, even when there is favorable coverage and reimbursement, future changes may occur that adversely impact such favorable coverage and reimbursement status. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States.

The unavailability or inadequacy of third-party coverage and reimbursement could negatively affect the market acceptance of Keveyis and any product candidates for which we receive regulatory approval and the future revenues we may expect to receive from these products. Similarly, for so long as we are entitled to receive royalties from Novo from their Macrilen sales, any difficulties Novo experiences with respect to third-party coverage and reimbursement could negatively impact our operations.

In addition, we are unable to predict what additional legislation or regulation relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future, or what effect such legislation or regulation would have on our business.

We will be subject to ongoing obligations and continued regulatory requirements, which may result in significant additional expense.

Keveyis and any of our product candidates that receive regulatory approval will remain subject to continued regulatory review. Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA, the EMA or any comparable foreign regulatory authority approves any of our product candidates, we will be subject to ongoing regulatory obligations and oversight by regulatory authorities, including with respect to the manufacturing processes, labeling, packing, distribution, storage and adverse event reporting, advertising and marketing, and recordkeeping and, potentially, other post-marketing obligations, all of which may result in significant expense and limit our ability to commercialize such products. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and cGCPs for any clinical trials that we conduct post-regulatory approval. Our three Phase 3 clinical trials of Recorlev are collecting safety data for over approximately 130 patients, and we currently expect that we will be required by the FDA and the EMA to collect additional safety data post-approval.

In addition, approved products, manufacturers and manufacturers' facilities are subject to continual review and periodic inspections. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product;
- withdrawal of the product from the market, or voluntary or mandatory product recalls;

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- restrictions on the marketing or manufacturing of the product;

- withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, disgorgement of profits or revenues, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us;
- suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

If any of these events occurs, our ability to sell such product may be impaired, and we may incur substantial additional expense to comply with regulatory requirements. The policies of the FDA, the EMA or any comparable foreign regulatory agency may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any regulatory approval that we may have obtained, which would compromise our ability to achieve or sustain profitability.

Although we have obtained orphan drug designation for Keveyis and our product candidates from the FDA and EMA, orphan drug designation may not ensure that we will enjoy market exclusivity in a particular market, and if we fail to obtain or maintain orphan drug exclusivity for Keveyis or our product candidates, we may be subject to earlier competition and our potential revenue will be reduced.

Under the Orphan Drug Act of 1983, the FDA may designate a product as an orphan drug if it is intended to treat an orphan disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the United States, orphan drug designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan drug designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the European Union, orphan drug designation entitles a party to financial incentives such as a reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Keveyis has been granted orphan drug designation for the treatment of hyperkalemic, hypokalemic, and related variants of PPP in the United States. Recorlev has been granted orphan drug designation for the treatment of endogenous Cushing's syndrome in the United States and Europe. Veldoreotide has been granted orphan drug designation for the treatment of acromegaly in the United States and Europe.

Even though we have obtained orphan drug designation for our two product candidates, we may not be the first to obtain regulatory approval for any particular orphan indication due to the uncertainties associated with developing biopharmaceutical products. For example, ketoconazole was granted orphan drug exclusivity in Europe and is now being

marketed for the treatment of endogenous Cushing's syndrome. Therefore, Recorlev will need to show significant benefit compared to ketoconazole in order to be marketed in Europe prior to the expiration of the ketoconazole orphan drug exclusivity, in 2024. Further, the exclusivity associated with orphan drug designation may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition, and even the same active ingredient may be approved if it is formulated in such a way as to offer a demonstrated clinical advantage over Recorlev. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We and our collaborators and contract manufacturers are subject to significant regulation with respect to the manufacturing of pharmaceutical products. The manufacturing facilities on which we rely may not continue to meet regulatory requirements or may not be able to meet supply demands.

All entities involved in the preparation of pharmaceutical products for clinical trials or commercial sale, including our existing contract manufacturers for our products and product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures, including record keeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We, our collaborators or our contract manufacturers must supply all necessary documentation in support of an NDA or foreign equivalent on a timely basis and must adhere to GLP and cGMP regulations enforced by the FDA and other regulatory agencies through their facilities inspection program. Some of our contract manufacturers have never produced a commercially-approved pharmaceutical product and therefore have not obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our collaborators and third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products.

In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our collaborators and third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility.

If we, our collaborators or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or another applicable regulatory authority could impose regulatory sanctions including, among other things, refusal to approve a pending application our product candidates, withdrawal of an approval or suspension of production, fines, injunctions, civil penalties, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could harm our business.

Additionally, if the supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through an NDA supplement or equivalent foreign regulatory filing, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us to incur higher costs and could cause the delay or termination of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

We rely on third parties to conduct our nonclinical and clinical trials and if these third parties perform in an unsatisfactory manner, our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third-party CROs to conduct and monitor and manage data for our ongoing nonclinical and clinical programs, and may not currently have all of the necessary contractual relationships in place to do so. Once we have established contractual relationships with such third-party CROs, we will have only limited control over their actual performance of these activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory, environmental and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs and other vendors are required to comply with current cGMP, cGCP, and GLP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Union and any comparable foreign regulatory agency for all of our product candidates in nonclinical and clinical development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, trial sites and other contractors. If we or any of our CROs or vendors fail to comply with applicable regulations, the data generated in our nonclinical and clinical trials may be deemed unreliable and the FDA, EMA or any comparable foreign regulatory agency may require us to perform additional nonclinical and clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that all of our clinical trials comply with cGCP regulations. In addition, our clinical trials must be conducted with products produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Our business involves the controlled use of hazardous materials, chemicals, biologicals and radioactive compounds. Substantially all such use is outsourced to third-party CRO manufacturers and clinical sites. Although we believe that our third-party CROs' safety procedures for handling and disposing of such materials comply with industry standards, there will always be a risk of accidental contamination or injury. By law, radioactive materials may only be disposed of at certain approved facilities. If liable for an accident, or if it suffers an extended facility shutdown, we or our CROs could incur significant costs, damages or penalties.

Our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing nonclinical and clinical programs. If our CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Our CROs may also generate higher costs than anticipated. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs terminates, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. If we are able to replace a CRO, switching or adding additional CROs involves additional cost and requires management time and focus and there is a natural transition period when a new CRO commences work. As a result, delays could occur, which could hurt our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future.

Enacted and future legislation may increase the difficulty and cost for us to obtain regulatory approval of, and commercialize our, product candidates and may affect the prices we may set.

In the United States and the European Union, there have been a number of legislative, regulatory and proposed changes regarding the healthcare system. These changes could prevent or delay regulatory approval of our product candidates, restrict or regulate post-approval activities, and affect our ability to sell profitably any products for which we obtain regulatory approval and begin to commercialize.

As a result of legislative proposals and the trend toward managed health care in the United States, third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs. In the United States, the Medicare Modernization Act changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly under a new Part D and introduced a new reimbursement methodology based on average sale prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost-reduction initiatives and other provisions of this legislation could decrease the coverage and reimbursement that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow the Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act ("PPACA"), as amended by the Health Care and Education Reconciliation Act, a sweeping law intended, among other things, to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry, and impose additional health policy reforms. PPACA, among other things: increased the statutory minimum Medicaid rebates a manufacturer must pay under the Medicaid Drug Rebate Program; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; and established a new Medicare Part D coverage gap discount program in which manufacturers must provide 50% point-of-sale discounts on negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer's outpatient drugs to be covered under Part D and implemented payment system reforms, including a national pilot program on payment bundling to encourage hospitals, physicians and other providers to improve the coordination, quality and efficiency of certain healthcare services through bundled payment models. Further, the PPACA imposed a significant annual nondeductible fee on entities that manufacture or import specified branded prescription drug products and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs. We expect that additional healthcare reform measures will likely be adopted in the future, any of which may increase our regulatory burdens and operating costs and limit the amounts that federal, state and foreign governments will reimburse for healthcare products and services, which could result in reduced demand for our products, if approved, or additional pricing pressures.

Moreover, other legislative changes have also been proposed and adopted in the United States since PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021 was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013 and will stay in effect through 2024 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other health care funding, which could compromise the ability of patients and third-party payors to purchase our product candidates.

There is no assurance that the PPACA, as currently enacted or as amended in the future, will not adversely affect our business and financial results, and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

In the European Union, proposed new clinical trial regulations will centralize clinical trial approval, which eliminates redundancy, but in some cases this may extend timelines for clinical trial approvals due to potentially longer wait times. Proposals to require specific consents for use of data in research, among other measures, may increase the costs and timelines for our product development efforts. Austerity measures in certain European nations may also affect the prices we are able to seek if our products are approved, as discussed below.

Both in the United States and in the European Union, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We do not know whether additional legislative changes will be enacted, whether the regulations, guidance or interpretations will be changed, or what the impact of such changes on the regulatory approvals of our product candidates, if any, may be.

Pricing for pharmaceutical products has come under increasing scrutiny by governments, legislative bodies and enforcement agencies. These activities may result in actions that have the effect of reducing our revenue or harming our business or reputation.

Pharmaceutical product pricing is subject to enhanced government and public scrutiny and calls for reform. There has recently been intense publicity regarding the pricing of pharmaceutical products generally, including publicity and pressure resulting from the prices charged for new products as well as price increases for older products that the government and public deem excessive. We may experience downward pricing pressure on the price of our products due to social or political pressure to lower the cost of drugs, which could reduce our revenue and future profitability. Many companies in our industry have received governmental requests for documents and information relating to drug pricing and patient support programs. On December 19, 2017, we received letters from the offices of U. S. Senators Amy Klobuchar, Susan Collins and Tammy Baldwin, and Senator Claire McCaskill, Ranking member of Homeland Security and Governmental Affairs Committee, that request information relating to the marketing and sales of Keveyis. The letters request information principally relating to the pricing of Keveyis, among other things. We are cooperating with these voluntary requests for information. We could incur significant expense and experience reputational harm as a result of these or other similar future inquiries, as well as reduced market acceptance and demand for our products, which could harm our ability to market our products in the future. These factors could also result in changes in our product pricing and distribution strategies, reduced demand for our products and/or reduced reimbursement of products, including by federal health care programs such as Medicare and Medicaid and state health care programs.

In addition, federal and state governments may adopt policies affecting drug pricing and contracting practices outside of the context of federal programs such as Medicare and Medicaid, which may adversely affect our business. For example, several states have adopted laws that require drug manufacturers to provide advance notice of certain price increase and to report information relating to those price increases.

The Trump Administration and the U.S. Congress have indicated an interest in taking measures pertaining to drug pricing, including potential proposals relating to Medicare price negotiations, and importation of drugs from other countries. On May 11, 2018, the Trump Administration, through the Department of Health and Human Services, requested comments on a "Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs," which outlines proposals and policy considerations intended to improve competition; lower patient out-of-pocket costs; enhance negotiation; and provide incentives for lower manufacturer list prices. At this time, it is unclear whether any of these proposals will be pursued and how they would impact our products or our future product candidates. Notably, some of these and other proposals will require authorization through additional legislation to become effective, but others to not, and the U.S. Congress and the Trump Administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs.

Our relationships with customers, consultants and payors are subject to applicable fraud and abuse, privacy and security, transparency and other healthcare laws and regulations, which, if violated, could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and/or diminished profits and future earnings.

Healthcare providers, physicians and others play a primary role in the recommendation and prescription of any products for which we may in the future obtain regulatory approval and commercialize. Our current and future arrangements with third-party payors, consultants, customers, physicians and others may expose us to broadly applicable fraud and abuse and other healthcare federal and state laws and regulations, including in the United States, that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain regulatory approval. Potentially applicable healthcare laws and regulations include, but are not limited to, the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for, purchasing, leasing, ordering, arranging for, or recommending the purchase, lease, or order of, any good, facility, item or service for which payment may be made under U.S. government healthcare programs such as Medicare and Medicaid;
- the federal civil and criminal false claims laws and civil monetary penalties laws, including civil whistleblower or qui tam actions, which prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to 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, or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay or transmit money or property to the federal government;
- the Privacy Rule or the Security Rule of HIPAA, as amended by HITECH, and its implementing regulations, which impose various obligations with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the health care fraud provisions of HIPAA, which impose criminal liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, or to obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, and knowingly and willfully falsifying, concealing or covering up 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;
- the federal Physician Payments Sunshine Act under PPACA and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies to annually report to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value made by such manufacturers to physicians and teaching hospitals, and ownership and investment interests held by physicians or their immediate family members; and
- analogous laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements, research, distribution and claims involving healthcare items or services reimbursed by state governmental and non-governmental third-party payors, including private insurers, state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, and state requirements for manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures and other restrictions on drug manufacturer marketing practices.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under the U.S. federal Anti-Kickback Statute and analogous state laws, it is possible that some of our current and future business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, PPACA, among other things, amends the intent requirement of the U.S. federal Anti-Kickback Statute and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to be in violation. Moreover, PPACA provides that the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, agency guidance or case law involving applicable healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to, without limitation, significant civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, imprisonment, disgorgement, enhanced government reporting and oversight, contractual damages, reputational harm, diminished profits and future earnings and/or the curtailment or restructuring of our operations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses or divert our management's attention from the operations of our business. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to similar penalties, including, without limitation, criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products abroad once we enter a commercialization phase and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Risks Related to Our Intellectual Property

If we or our licensors are unable to obtain and maintain effective patent or license rights for our approved products, product candidates or any future product candidates, or if the scope of the patent or license rights obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

In addition to the exclusivity maintained by Keveyis and our product candidates with regulatory orphan drug status, we rely upon a combination of patents, trade secret protection, license rights and confidentiality agreements to protect the intellectual property related to our products and product candidates. Our success depends in large part on our

and our licensors' ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries, as well as license rights, with respect to our proprietary technology, products and product candidates. Furthermore, our right to receive royalty payments from Novo from Macrilen sales, and the amount of any royalty payments, will depend on Novo Nordisk's ability to protect the Macrilen patent portfolio.

We have sought to protect our proprietary position by filing, where possible, patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This 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, in a timely manner or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development and manufacturing processes before it is too late to obtain patent protection. Moreover, in some circumstances, we do 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 and involves complex legal and factual questions for which legal principles remain unsolved. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our products or product candidates in the United States or in foreign countries. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions remain confidential for a period of time after filing, and some remain so until issued. Therefore, we cannot be certain that we were the first to file any patent application related to our products or product candidates, or whether we were the first to make the inventions claimed in our owned patents or pending patent applications, nor can we know whether those from whom we license patents were the first to make the inventions claimed or were the first to file. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, and even if such patents cover our products or product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, found unenforceable or invalidated, which could 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. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our products or product candidates, prevent others from designing around our claims or provide us with a competitive advantage. Any of these outcomes could impair our ability to prevent competition from third parties.

We and/or our licensors or partners have filed several patent applications covering various aspects of our products and product candidates. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent, or whether any issued patents will be found invalid and unenforceable or will be challenged by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us after patent issuance, or the loss or other impairment of any license rights relating to our products or product candidates, could deprive us of rights necessary for the successful commercialization of any products or product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product or product candidate under patent protection could be reduced.

We may not have sufficient patent terms to effectively protect our products and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is first filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. 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 product 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 or otherwise provide us with a competitive advantage. Even if patents covering our products or product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

Although patent term extensions in the United States and under supplementary protection certificates in the European Union may be available to extend the patent exclusivity term for our products or product candidates, we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long.

Patent policy and rule changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Assuming the other requirements for patentability are met, in the United States prior to March 15, 2013, the first to invent the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act (the "AIA"), enacted on September 16, 2011, the United States has moved to a first inventor to file system. The AIA also includes a number of significant changes that affect the way patent applications will be prosecuted and may also affect patent litigation. The effects of these changes are currently unclear as the United States Patent and Trademark Office (the "USPTO") is still implementing various regulations, the courts have yet to address many of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. In general, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. In addition, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Third-party claims of intellectual property infringement may expose us to substantial liability or prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our products that have been approved for sale, and to use our proprietary technology without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the USPTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we will market products and are developing product candidates. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our products and product candidates may be subject to claims of infringement of the intellectual property rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to compositions, formulations, methods of manufacture or methods of treatment related to the use or manufacture of Keveyis or our product candidates. We cannot be sure that we know of each and every patent and pending application in the United States and abroad that is relevant or necessary to the commercialization of Keveyis or our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents upon which our products or product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our products or product candidates, any compositions formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to

commercialize such product or product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product or product candidate unless we obtained a license or until such patent expires or is finally determined to be invalid or unenforceable. In either case, such a license may not be available 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.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize Keveyis or one or more of our product candidates, if approved. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

Furthermore, to the extent any claims of infringement are brought by third parties against Novo related to Macrilen, we may be exposed to indemnification claims from Novo under the terms of the Macrilen Acquisition Agreement.

We may become involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Competitors may infringe upon our patents or the patents of our licensors. Although we are not currently involved in any litigation, if we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering one of our products or product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and/or unenforceable, or request declaratory judgment that there is no infringement. In patent litigation in the United States, defendant counterclaims alleging invalidity, noninfringement and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, nonobviousness or non-lack of enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld material relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, or at all. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs, and distract our management and other employees. In addition, the uncertainties associated with litigation could compromise our ability to successfully market Keveyis, raise the funds necessary to continue our clinical trials, continue our research programs, and license necessary technology from third parties or enter into development partnerships that would help us bring our product candidates to market, if approved.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could hurt the market price of our ordinary shares.

Failure to secure or maintain adequate protection for our trademarks could adversely affect our business.

We have filed a U.S., Canadian, Brazilian and International (Madrid Protocol) trademark application designating Australia, China, European Community, India, Israel, Japan, Mexico and Turkey for the mark, "Strongbridge Biopharma." If the U.S. or any foreign trademark offices raise any objections, we may be unable to overcome such objections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Oppositions or cancellation proceedings have been filed and may in the future be filed against our trademarks, and our trademarks may not survive such proceedings.

Furthermore, third parties may allege in the future, that a trademark or trade name that we elect to use for our product candidates may cause confusion in the marketplace. We evaluate such potential allegations in the course of our business, and such evaluations may cause us to change our commercialization or branding strategy for our product candidates, which may require us to incur additional costs. Moreover, any name we propose to use with our product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, domain names or copyrights may be ineffective and could result in substantial costs and diversion of resources.

In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks alleging that the use of a corporate name or logo, product names or other signs by which we distinguish our products and services are infringing their trademark rights. The outcome of such claims is uncertain and may adversely affect our freedom to use our corporate name or other relevant signs. If litigation arises in this area, it may lead to significant costs and diversion of management and employee attention.

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

Because we rely on third parties to develop and manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may harm our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We may employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in

their work for us, and we are not currently subject to any claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties, we may in the future be subject to such claims. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

Although we are not currently experiencing any claims challenging the inventorship of our patents or ownership of our intellectual property, we may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

Filing, prosecuting and defending patents on our products or product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Further, licensing partners may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful.

Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to Our Ordinary Shares

The price of our ordinary shares may be volatile and may fluctuate due to factors beyond our control.

The market price of our ordinary shares may be volatile and subject to wide fluctuations in response to a variety of factors, many of which are beyond our control, including:

- revenues from product sales and royalties;

- positive or negative results of testing and clinical trials by us, strategic partners or competitors;
- delays in in-licensing or acquiring additional complementary product candidates;
- any delay in the commencement, enrollment and the ultimate completion of clinical trials;
- technological innovations or commercial product introductions by us or competitors;
- failure to successfully develop and commercialize any of our product candidates, if approved;
- changes in government regulations;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern relating to the commercial value or safety of any of our products or product candidates;
- financing or other corporate transactions, or inability to obtain additional funding;
- failure to meet or exceed expectations of the investment community;
- announcements of significant licenses, acquisitions, strategic partnerships or joint ventures by us or our competitors;
- publication of research reports or comments by securities or industry analysts; or
- general market conditions in the pharmaceutical industry or in the economy as a whole.

The share price of publicly traded emerging biopharmaceutical and drug discovery and development companies has been highly volatile and is likely to remain highly volatile in the future. In addition, the stock market in general has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of individual companies. Broad market and industry factors may hurt the market price of companies' stock, including ours, regardless of actual operating performance.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, the price of our ordinary shares and our trading volume could decline.

The trading market for our ordinary shares depends in part on the research and reports that securities or industry analysts publish about us or our business. If too few securities or industry analysts commence or continue coverage of our company, the trading price for our ordinary shares would likely be negatively affected. In the event securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our ordinary shares or publish inaccurate or unfavorable research about our business, the price of our ordinary shares would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our ordinary shares could decrease, which might cause the price of our ordinary shares and trading volume to decline.

Future sales, or the possibility of future sales, of a substantial number of our ordinary shares could adversely affect the price of our ordinary shares.

Future sales of a substantial number of our ordinary shares, or the perception that such sales will occur, could cause a decline in the market price of our ordinary shares. We currently have 54,158,948 ordinary shares outstanding, and 15,555,864 shares issuable upon the exercise of outstanding stock options, restricted stock units and warrants.

We have filed a Registration Statement on Form S-8, registering ordinary shares that we may issue under our equity compensation plans. These ordinary shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements. If a large number of our ordinary shares or securities convertible into our ordinary shares are sold in the public market after they become eligible for sale, the sales could reduce the trading price of our ordinary shares and impede our ability to raise future capital.

We are also party to an Equity Distribution Agreement with JMP Securities LLC ("JMP Securities"), pursuant to which we may offer and sell ordinary shares having an aggregate offering price of up to $40 million from time to time through JMP Securities, acting as agent. As of December 31, 2018, we have issued an aggregate of $8.9 million in ordinary shares to JMP Securities under the Equity Distribution Agreement, leaving $31.1 million in ordinary shares available for issuance. Whether we choose to affect future sales under this agreement will depend on a number of factors, including, among others, market conditions and the trading price of our ordinary shares relative to other sources of capital. The issuance from time to time of ordinary shares through this "at-the-market" facility program or in any other equity offering, or the perception that such sales may occur, could reduce the trading price of our ordinary shares.

An active market in our ordinary shares may not be liquid enough for investors to resell our ordinary shares.

The listing of our ordinary shares on the Nasdaq Global Select Market does not assure that a meaningful, consistent and liquid trading market exists. In general trading volume in our ordinary shares has been limited and an active trading market for our shares may not be sustained. If an active market for our ordinary shares is not sustained, it may be difficult for investors to sell their shares without depressing the market price for the shares or at all.

We have never paid cash dividends, do not expect to pay dividends in the foreseeable future and our ability to pay dividends, or repurchase or redeem our ordinary shares, is limited by law.

We have not paid any dividends since our inception and do not anticipate paying any dividends on our ordinary shares in the foreseeable future. Even if future operations lead to significant levels of distributable profits, we currently intend that any earnings will be reinvested in our business and that dividends will not be paid until we have an established revenue stream to support continuing dividends. The proposal to pay future dividends to shareholders will in addition effectively be at the sole discretion of our board of directors after taking into account various factors our board of directors deems relevant, including our business prospects, capital requirements, financial performance and new product development. In addition, payment of future dividends is subject to certain limitations under the Irish Companies Act 2014 (the "Irish Companies Act"). The Irish Companies Act, among other requirements, requires Irish companies to have distributable reserves available for distribution equal to or greater than the amount of the proposed dividend. Accordingly, investors cannot rely on dividend income from our ordinary shares and any returns on an investment in our ordinary shares will likely depend entirely upon any future appreciation in the price of our ordinary shares.

We believe we were classified as a passive foreign investment company ("PFIC") for U.S. federal income tax purposes in past years and we may be classified as a PFIC in future years , which could result in adverse U.S. federal income tax consequences to U.S. Holders of our ordinary shares.

A non-U.S. corporation generally will be classified as a PFIC for U.S. federal income tax purposes for any taxable year if either (1) 75% or more of its gross income for such year consists of certain types of "passive" income or (2) 50% or more of the value of its assets (determined on the basis of a quarterly average) during such year produce or are held for the production of passive income. For this purpose, "passive income" generally includes, among other items of income, dividends, interest, royalties, rents and gains from commodities and securities transactions and from the sale or exchange of property that gives rise to passive income, and a non-U.S. corporation is treated as owning a proportionate share of the assets and earning a proportionate share of the income of any other corporation in which such non-U.S. corporation owns, directly or indirectly, more than 25% of the value of such other corporation's stock. Based on our income, assets and activities in past years, we believe that we were a PFIC in past years, and we may be classified as a PFIC for the current taxable year and for future years depending on the income, assets, and activities in such taxable years.

A U.S. Holder that holds ordinary shares during any taxable year in which we are a PFIC would be subject to substantially increased U.S. federal income tax liability, including upon the receipt of any "excess distributions" from us and upon the sale or other disposition of our ordinary shares. Although certain elections may be available to mitigate the adverse impact of the PFIC rules, such elections may result in a current U.S. federal tax liability prior to any distribution on or disposition of our ordinary shares. Further, there can be no assurances that we will supply U.S. Holders with information that such U.S. Holders are required to report under the rules governing such elections. Accordingly, the acquisition of our ordinary shares may not be an appropriate investment for certain holders that are not tax-exempt

organizations. U.S. Holders should consult their tax advisers regarding the application of the PFIC rules to an investment in our ordinary shares.

Our shareholder's rights are governed by Irish law and differ from the rights of shareholders under U.S. law.

We are a public limited company incorporated under the laws of Ireland. Therefore, the rights of holders of ordinary shares are governed by Irish law and by our memorandum and articles of association. These rights differ from the typical rights of shareholders in U.S. corporations. In certain cases, facts that, under U.S. law, would entitle a shareholder in a U.S. corporation to claim damages may not give rise to a cause of action under Irish law entitling a shareholder in an Irish company to claim damages. For example, the rights of shareholders to bring proceedings against us or against our directors or officers in relation to public statements are more limited under Irish law than under the civil liability provisions of the U.S. securities laws.

Our shareholders may have difficulties enforcing, in actions brought in courts in jurisdictions located outside the United States, judgments obtained in the U.S. courts under the U.S. securities laws. In particular, if a shareholder sought to bring proceedings in Ireland based on U.S. securities laws, the Irish court might consider that:

- it did not have jurisdiction;
- it was not the appropriate forum for such proceedings;
- applying Irish conflict of laws rules, U.S. laws (including U.S. securities laws) did not apply to the relationship between you and us or our directors and officers; or
- the U.S. securities laws were of a penal nature or violated Irish public policy and should not be enforced by the Irish court.

Our shareholders should also be aware that Irish law does not allow for any form of legal proceedings directly equivalent to the class action available in the United States.

Because the PCAOB is not permitted to inspect registered public accounting firms in Ireland, you do not have the benefit of such inspections to the extent our financial statements are audited by a registered public accounting firm in Ireland.

Auditors of U.S. public companies, including our independent registered public accounting firm, are required by the laws of the United States to undergo periodic PCAOB inspections to assess their compliance with U.S. law and professional standards in connection with performance of audits of financial statements filed with the SEC. The laws of certain European Union countries, including Ireland, do not currently permit the PCAOB to conduct inspections of accounting firms established and operating in such European Union countries. Accordingly, to the extent our financial statements will be audited by a registered public accounting firm in Ireland, the PCAOB would be prevented from fully evaluating the effectiveness of our independent registered public accounting firm's audit procedures or quality control procedures. Unlike shareholders or potential shareholders of most U.S. public companies, our shareholders would be deprived of the possible benefits of such PCAOB inspections.

A future transfer of our ordinary shares, other than one effected by means of the transfer of book-entry interests in DTC, may be subject to Irish stamp duty.

The rate of Irish stamp duty, when applicable, on the transfer of shares in an Irish-incorporated company is 1% of the price paid, or the market value of the shares acquired, whichever is greater. Payment of Irish stamp duty is generally a legal obligation of the transferee. We expect that most of our ordinary shares will be traded through the Depositary Trust Company ("DTC"), or through brokers who hold such shares on behalf of customers through DTC. As such, the transfer of ordinary shares should be exempt from Irish stamp duty based on established practice of the Irish Revenue Commissioners. We received written confirmation from the Irish Revenue Commissioners on June 22, 2015 that a transfer of our ordinary shares held through DTC and transferred by means of a book-entry interest would be exempt from Irish stamp duty. However, if you hold your ordinary shares directly of record, rather than beneficially

through DTC, or through a broker that holds your ordinary shares through DTC, any transfer of your ordinary shares may be subject to Irish stamp duty. The potential for Irish stamp duty to arise could adversely affect the price and liquidity of our ordinary shares. In addition, the terms of our eligibility agreement with DTC requires us to provide certain indemnities relating to Irish stamp duty to third parties. If liability were to arise as a result of the indemnities provided under the terms of the eligibility agreement, we may face significant unexpected costs.

Anti-takeover provisions in our Articles and under Irish law could make an acquisition of us more difficult, limit attempts by our shareholders to replace or remove our current directors and management team, and limit the market price of our ordinary shares.

Our Articles contain provisions that may delay or prevent a change of control, discourage bids at a premium over the market price of our ordinary shares and adversely affect the market price of our ordinary shares and the voting and other rights of the holders of our ordinary shares. These provisions include:

- dividing our board of directors into three classes, with each class serving a staggered three-year term;
- permitting our board of directors to issue preference shares without shareholder approval, with such rights, preferences and privileges as they may designate;
- provisions which allow our board of directors to adopt a shareholder rights plan upon such terms and conditions as it deems expedient and in our best interests;
- establishing an advance notice procedure for shareholder proposals to be brought before an annual meeting, including proposed nominations of persons for election to our board of directors; and
- the ability of our board of directors to fill vacancies on our board in certain circumstances.

These provisions do not make us immune from takeovers. However, these provisions will apply even if the offer may be considered beneficial by some shareholders. In addition, these provisions may frustrate or prevent any attempts by our shareholders to replace or remove our current management team by making it more difficult for shareholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Irish law differs from the laws in effect in the United States with respect to defending unwanted takeover proposals and may give our board of directors less ability to control negotiations with hostile offerors.

We are subject to the Irish Takeover Rules. Under the Irish Takeover Rules, our board of directors is not permitted to take any action that might frustrate an offer for our ordinary shares once our board of directors has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (1) the issue of shares, options, restricted share units or convertible securities, (2) material acquisitions or disposals, (3) entering into contracts other than in the ordinary course of business or (4) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which our board of directors has reason to believe an offer is or may be imminent. These provisions may give our board of directors less ability to control negotiations with hostile offerors than would be the case for a corporation incorporated in the United States.

We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to "emerging growth companies" will make our ordinary shares less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. For so long as we continue to be an "emerging growth company," we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, exemptions from the requirements to provide certain executive compensation disclosures, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation or seeking shareholder approval of any golden parachute payments not previously

approved. As an "emerging growth company," in our initial registration statement, we were required to report only two years of financial results and selected financial data compared to three and five years, respectively, for comparable data reported by other public companies. We could be an "emerging growth company" for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our ordinary shares held by non-affiliates exceeds $700 million as of any June 30 before that time, in which case we would no longer be an "emerging growth company" as of the following December 31, our fiscal year end. We cannot predict if investors will find our ordinary shares less attractive because we may rely on these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and the price of our ordinary shares may be more volatile.

Certain provisions of the warrants issued in our 2016 private placement could impede a sale of the company.

In the event of a sale of the company, the terms of the warrants issued to investors in our December 2016 private placement require us to use our best efforts to ensure the holders of such warrants will have a continuing right to purchase shares of the acquirer and, if our efforts are unsuccessful, to make a payment to such warrant holders based on a Black-Scholes valuation (using variables as specified in the warrant agreements). Such payment must be made in cash in the event that the acquisition results in our shareholders receiving cash from the acquirer at the closing of the transaction, and must be made in shares of the Company (with the value of each ordinary share determined according to the calculation specified in the warrant agreements) in the event that the acquisition results in our shareholders receiving shares in the acquirer or other entity at the closing of the transaction. In the event that our shareholders receive both cash and shares at the closing of the transaction, such payment to the warrant holders shall also be made in both cash and shares in the same proportion as the consideration received by the shareholders.

Notwithstanding the foregoing, in the event that as a result of an acquisition the warrants will be exercisable for anything other than shares or securities that are listed on a regulated market (within the meaning of the Markets in Financial Instruments Directive (2004/39(EC))) or a U.S. national securities exchange, the warrant holders will be entitled to demand to receive a cash payment in an amount equal to the Black-Scholes Value per warrant (calculated in accordance with the warrants) contemporaneously with or promptly after the consummation of such acquisition.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None

ITEM 2. PROPERTIES

Our Irish corporate headquarters are located at Suite 206, Fitzwilliam Hall, Fitzwilliam Place, Dublin 2, D02 T292, Ireland. In addition, we lease 22,069 square feet of office space in Trevose, Pennsylvania. We believe that our existing office space is adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we are a party to legal proceedings arising in the ordinary course of business. We are not currently a party to any other legal proceedings that we believe could have a material adverse effect on financial condition or results of operations.

ITEM 4. MINE SAFETY DISCLOSURE

Not applicable.

PART II.

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

Market Information

Our ordinary shares are listed on the Nasdaq Global Select Market under the symbol "SBBP".

Stockholders

As of December 31, 2018, there were approximately 27 stockholders of record of our ordinary shares. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Securities Authorized for Issuance Under Equity Compensation Plans

See Part III, Item 12. "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" for information relating to our equity compensation plans.

Recent Sale of Unregistered Securities and Use of Proceeds

None.

Purchases of Equity Securities By the Issuer and Affiliated Purchasers

None.

ITEM 6. SELECTED FINANCIAL DATA

The following tables set forth a summary of our consolidated financial data. We have derived the consolidated statement of operations data for the years ended December 31, 2018, 2017, 2016, 2015 and 2014 and the balance sheet data as of December 31, 2018, 2017 and 2016 from our consolidated audited financial statements. You should read this data together with the consolidated financial statements and related notes appearing elsewhere in this Annual Report and the section in this filing titled "Management's Discussion and Analysis of Financial Condition and Results of Operations." The historical results are not necessarily indicative of the results to be expected for any future periods. All of our operations are continuing operations and we have not proposed or paid dividends in any of the periods presented.

	December 31,				
	2018	2017	2016	2015	2014
	(in thousands)				
Consolidated Statement of Operations Data:					
Revenues:					
Net product sales	$ 18,027	$ 7,046	$ —	$ —	$ —
Cost and expenses:					
Cost of sales (excluding amortization of intangible assets)	$ 3,986	$ 1,483	$ —	$ —	$ —
Selling, general and administrative	63,336	36,292	14,875	22,719	4,588
Research and development	25,441	17,268	20,023	20,135	5,844
Amortization of intangible assets	7,187	5,022	—	—	—
Impairment of intangible asset	—	20,723	15,828	—	—
Total cost and expenses	99,950	80,788	50,726	42,854	10,432
Operating loss	(81,923)	(73,742)	(50,726)	(42,854)	(10,432)
Total other income (expense), net	114,310	(37,970)	(631)	(1,229)	282
Income (Loss) before income taxes	32,387	(111,712)	(51,357)	(44,083)	(10,150)
Income tax (expense) benefit	(536)	(1,771)	2,638	450	480
Net income (loss)	$ 31,851	$(113,483)	$ (48,719)	$ (43,633)	$ (9,670)

	December 31,		
	2018	2017	2016
	(in thousands)		
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$122,490	$ 57,510	$ 66,837
Total assets	170,285	103,925	137,531
Long-term debt	—	37,794	18,434
Total liabilities	57,330	115,839	70,559
Total stockholders' equity (deficit)	112,955	(11,914)	66,972

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion summarizes the significant factors affecting the operating results, financial condition, liquidity and cash flows of our company as of and for the periods presented below. The following discussion and analysis should be read in conjunction with the financial statements and the related notes thereto included elsewhere in this Annual Report. The statements in this discussion regarding industry outlook, our expectations regarding our future performance, liquidity and capital resources and all other non-historical statements in this discussion are forward-looking statements and are based on the current beliefs of our management, as well as assumptions made by, and information currently available to, our management. Actual results could differ materially from those discussed in or implied by forward-looking statements as a result of various factors, including those discussed below and elsewhere in this Annual Report, particularly in the section titled "Risk Factors."

Overview

We are a global, commercial-stage biopharmaceutical company focused on the development and commercialization of therapies for rare diseases with significant unmet needs.

Our first commercial product is Keveyis (dichlorphenamide), the first and only treatment approved by the FDA for hyperkalemic, hypokalemic, and related variants of PPP, a group of rare hereditary disorders that cause episodes of muscle weakness or paralysis.

In January 2018, Strongbridge Ireland Ltd., one of our wholly-owned subsidiaries, acquired the U.S. and Canadian rights to Macrilen (macimorelin), the first and only oral drug approved by the FDA for the diagnosis of patients with adult growth hormone deficiency. We launched Macrilen in the United States in July 2018. In December 2018, we sold Strongbridge Ireland Ltd., to Novo. As consideration for the sale, we received $145 million from Novo plus the right to receive tiered royalties on net sales of Macrilen through 2027. In addition, we entered into a services agreement with Novo pursuant to which it will fund, for a period of three years (subject to our right to terminate the arrangement upon six months' notice), the costs of 23 of our field-based employees to provide full-time ongoing services to Novo, including the promotion of Macrilen in the United States. We will also be entitled to a performance fee of up to $1.5 million per contract year if certain conditions are met by our field-based employees under the services arrangement, which conditions will be determined and measured by a joint committee comprised of members from Novo and from Strongbridge, with a majority of members from Novo. Novo also purchased 5.2 million of our ordinary shares at a purchase price of $7.00 per share. The excess price paid per share over the fair value of the stock, was included in the gain on sale of our subsidiary.

We have two clinical-stage product candidates for rare endocrine diseases, Recorlev and veldoreotide. Recorlev (levoketoconazole) is a cortisol synthesis inhibitor currently being studied for the treatment of endogenous Cushing's syndrome. Veldoreotide is a next-generation somatostatin analog being investigated for potential applications in conditions amenable to somatostatin receptor activation, such as acromegaly. Both Recorlev and veldoreotide have received orphan designation from the FDA and the EMA.

We are building a rare disease, franchise-based business model focused on expansion through a disciplined in-licensing and acquisition strategy. We will continue to identify and evaluate the acquisition of products and product candidates for licensing or acquisition that would be complementary to our existing rare neuromuscular and endocrine franchises or that would form the basis for new rare disease franchises. We believe this approach will enable us to maximize our commercial potential by further leveraging our existing resources and expertise.

In December 2017, we received letters from the offices of U. S. Senators Amy Klobuchar, Susan Collins and Tammy Baldwin, and Senator Claire McCaskill, Ranking Member of the Homeland Security and Governmental Affairs Committee, that request information relating to the marketing and sales of Keveyis. The letters request information principally relating to the pricing of Keveyis, among other things. We are cooperating with these voluntary requests for information.

Financial Operations Overview

Net Revenue

Our product sales in 2018, resulted from sales of Keveyis and Macrilen. We will no longer record product sales from Macrilen following the sale of our rights to Macrilen to Novo in December 2018. We recognize net product sales at the time our products are received by our customers (primarily wholesalers and specialty pharmacies). The products are subsequently sold to patients, who are covered by payors that may provide for government-mandated or privately negotiated rebates with respect to the purchase of our products. We expense incremental costs related to the set-up of the contracts with our customers when incurred, as these costs do not meet the criteria for capitalization.

Cost of Sales

Cost of sales includes third-party acquisition costs, third-party warehousing and product distribution charges.

Selling, General and Administrative Expenses

Selling, general and administrative expenses include personnel costs, costs for outside professional services and other allocated expenses. Personnel costs consist of salaries, bonuses, benefits, travel and stock-based compensation. Outside professional services consist of legal, accounting and audit services, commercial evaluation and strategy services, sales, marketing and other consulting services.

Research and Development Expenses

Our research and development expenses consist primarily of costs incurred in connection with the development of our product candidates, including:

- personnel-related costs, such as salaries, bonuses, benefits, travel and other related expenses, including stock-based compensation;
- expenses incurred under our agreements with CROs, clinical sites, contract laboratories, medical institutions and consultants that plan and conduct our preclinical studies and clinical trials, including, in the case of consultants, stock-based compensation;
- costs associated with regulatory filings;
- upfront and milestone payments under in-license or acquisition agreements with third parties;
- costs of acquiring preclinical study and clinical trial materials, and costs associated with formulation and process development; and
- depreciation, maintenance and other facility-related expenses.

We expense all research and development costs as incurred. Clinical development expenses for our product candidates are a significant component of our current research and development expenses as we progress our product candidates into and through clinical trials. Product candidates in later stage clinical development generally have higher research and development costs than those in earlier stages of development, primarily due to increased size and duration of the clinical trials. We recognize costs for each grant project, preclinical study or clinical trial that we conduct based on our evaluation of the progress to completion, including the use of information and data provided to us by our external research and development vendors and clinical sites.

We expect our research and development expenses to increase in absolute dollars in the future as we continue to in-license or acquire product candidates and as we advance our existing and any future product candidates into and through clinical trials and pursue regulatory approval of our product candidates. The process of conducting the necessary clinical research to obtain regulatory approval of a product candidate is costly and time consuming. The probability that any of our product candidates receives regulatory approval and eventually is able to generate revenue depends on a

variety of factors, including the quality of our product candidates, early clinical data, investment in our clinical program, competition, manufacturing capability and commercial viability. As a result of these uncertainties, we are unable to determine the duration and completion costs of our research and development projects or if, when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates, if approved. We may never succeed in achieving regulatory approval for any of our product candidates.

We do not allocate personnel-related research and development costs, including stock-based compensation or other indirect costs, to specific programs, as they are deployed across multiple projects under development.

Interest Expense

Interest expense represents interest paid to our lender, amortization of our debt discount, and issuance costs associated with loan and security agreements. In December 2018, we extinguished all of our outstanding debt.

Amortization of Intangible Assets

Amortization of intangible assets relates to the amortization of our product rights to Keveyis and Macrilen. Both intangible assets were (and Keveyis will continue to be) amortized using the straight-line method, using an amortization period of eight years for Keveyis and ten years for Macrilen. In December 2018, we sold the rights to Macrilen and, therefore, will no longer record amortization of the related intangible asset.

Other Income (Expense), Net

Other income (expense), net, consists of our gain on the sale of our subsidiary, unrealized gain (loss) on the remeasurement of the fair value of warrant liability, interest expense recognized on our long-term debt, the loss on the extinguishment of our pre-existing long-term debt, interest income generated from our cash and cash equivalents, foreign exchange gains and losses and gains and losses on investments.

Critical Accounting Policies and Estimates

This operating and financial review of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles ("U.S. GAAP"). The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies and estimates are critical.

Revenue Recognition

We follow Accounting Standards Codification ("ASC") Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). Topic 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation.

Revenues from sales of our products are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and that result from rebates, co-pay assistance and other allowances that are offered by us and the patients' payors. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount is payable to our customer) or a current liability (if the amount is payable to a party other than our customer). Where appropriate, these estimates may take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. For a complete discussion of accounting for net product revenue, see Note 3, "Revenue recognition" to our consolidated financial statements.

Warrant Liability

The fair values of certain outstanding warrants were measured using the Black-Scholes option-pricing model. Inputs used to determine estimated fair value of the warrant liabilities include the fair value of the underlying stock at the valuation date, the term of the warrants, risk-free interest rates, expected dividends and the expected volatility of the underlying stock. The significant unobservable inputs used in the fair value measurement of the warrant liabilities were the fair value of the underlying stock at the valuation date and the estimated term of the warrants. Generally, increases (decreases) in the fair value of the underlying stock and estimated term would result in a directionally similar impact to the fair value measurement.

Intangible Assets

Certain intangible assets were acquired as part of an asset purchase and have been capitalized at their acquisition date at fair value. Acquired definite life intangible assets are amortized using the straight-line method over their respective estimated useful lives. The Company evaluates the potential impairment of intangible assets if events or changes in circumstances indicate that the carrying amount of the assets may not be fully recoverable or that the useful lives of these assets are no longer appropriate.

In connection with the Asset Purchase and Supply Agreement we entered into with Taro Pharmaceuticals North America, Inc., we paid Taro an upfront payment in two installments of $1 million in December 2016 and $7.5 million in March 2017. We have concluded that the supply price payable by us exceeds fair value and, therefore, have used a discounted cash flow method with a probability assumption to value the payments in excess of fair value at $29.3 million, for which we have recorded an intangible asset and corresponding liability. This liability is amortized as we purchase inventory over the term of the agreement. In addition, we incurred transaction costs of $2.4 million resulting in the recording of an intangible asset of $40.2 million. This intangible asset is being amortized over an eight-year period using the straight-line method.

We entered into a License and Assignment Agreement in 2018 with Aeterna Zentaris GmbH, pursuant to which we acquired the U.S. and Canadian rights to manufacture and commercialize Macrilen (macimorelin) for $24 million and incurred transaction costs of $0.7 million, resulting in an initial intangible asset of $24.7 million. We recorded any royalty liability as an increase to the intangible asset. This asset was being amortized over a ten-year period using the straight-line method, until the sale of our subsidiary that held this asset in December 2018.

As of December 31, 2018, no impairment of intangible assets has been identified.

Goodwill

We test goodwill for impairment on an annual basis or whenever events occur that may indicate possible impairment. This analysis requires us to make a series of critical assumptions to (1) evaluate whether any impairment exists and (2) measure the amount of impairment.

Because we have one operating segment, when testing for a potential impairment of goodwill, we are required to estimate the fair value of our business as a whole and determine the carrying value. If the estimated fair value is less than the carrying value of our business, then we are required to estimate the fair value of all identifiable assets and liabilities in a manner similar to a purchase price allocation for an acquired business. Only after this process is completed can the goodwill impairment be determined, if any.

We did not record a charge for impairment for the years ended December 31, 2018, 2017 and 2016. As of December 31, 2018, there were no events or changes in circumstances indicating possible impairment.

Stock-Based Compensation

We account for stock-based compensation awards in accordance with Financial Accounting Standards Board ("FASB") ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments including grants of stock options and restricted stock and modifications to existing stock options, to be recognized in the consolidated statements of operations based on their fair values.

Our stock-based awards are subject to either service-based or performance-based vesting conditions. Vesting of certain awards could also be accelerated upon achievement of defined market-based vesting conditions. Certain awards also contain a combination of service and market conditions or performance and market conditions.

We account for employee stock-based awards at grant date fair value. If we issue awards with an exercise price denominated in a currency other than our functional currency, trading currency or the currency for which we compensate our employee, we account for these as liabilities.

We record compensation expense for service-based awards over the vesting period of the award on a straight-line basis. Compensation expense related to awards with performance-based vesting conditions is recognized over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

Compensation expense for awards with service and market-based vesting conditions is recognized using the accelerated attribution method over the shorter of the requisite service period or the implied period associated with achievement of the market-based vesting provisions.

We estimate the fair value of our awards with service conditions using the Black Scholes option pricing model, which requires the input of subjective assumptions, including (i) the expected stock price volatility, (ii) the expected term of the award, (iii) the risk-free interest rate and (iv) expected dividends. Due to the lack of historical and implied volatility data of our ordinary shares, we based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. We selected companies with comparable characteristics to us, including enterprise value, risk profiles and position within the industry, and with historical share price information sufficient to meet the expected term of the stock-based awards. We compute historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards.

We estimate the fair value of our awards with market conditions using a Monte Carlo simulation to determine the probability of satisfying the market condition. We make this estimate using the conditions that exist at the grant date. The derived service period, which may be the requisite service period, is also determined at this time. Compensation cost for our awards with a market condition is recognized ratably using the accelerated attribution method if the award is subject to graded vesting over the requisite service period. The compensation cost for our awards with a market condition is not reversed if the market condition is not satisfied.

We have estimated the expected term of employee service-based stock options using the "simplified" method, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option, due to our lack of sufficient historical data. We have estimated the expected term of employee awards with service and market conditions using a Monte Carlo simulation model. This approach involves generating random stock price paths through a lattice type structure. Each path results in a certain financial outcome, such as accelerated vesting

or specific option payout. We have estimated the expected term of nonemployee service and performance-based awards based on the remaining contractual term of such awards.

The risk-free interest rates for periods within the expected term of the option are based on the Swedish Government Bond rate or the U.S. Treasury Bond rate with a maturity date commensurate with the expected term of the associated award. We have never paid dividends, and do not expect to pay dividends in the foreseeable future.

We account for forfeitures as they occur as opposed to estimating forfeitures. We record stock-based compensation expense only for those awards that are expected to vest.

Income Taxes

The Tax Act, which was enacted in 2017, made broad and complex changes to the U.S. tax code, including, but not limited to, reducing the top U.S. federal corporate tax rate from 35 percent to 21 percent; requiring companies to pay a one-time transition tax on certain un-repatriated earnings of foreign subsidiaries; generally eliminating U.S. federal income taxes on dividends from foreign subsidiaries; requiring a current inclusion in U.S. federal taxable income of certain earnings of controlled foreign corporations; eliminating the corporate alternative minimum tax ("AMT") and changing how existing AMT credits can be realized; creating the base erosion anti-abuse tax ("BEAT"), a new minimum tax; creating a new limitation on deductible interest expense; and changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017.

The Tax Act reduced our U.S. corporate income tax rate from 34% to 21%, effective January 1, 2018. 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 reverse. As a result of the reduction in the U.S. corporate income tax rate from 34% to 21% under the Tax Act, we revalued our ending net deferred tax assets and liabilities at December 31, 2017.

The Tax Act provided for a one-time transition tax on the deemed repatriation of post-1986 undistributed foreign subsidiary earnings and profits ("E&P"). We did not have to recognize any income tax expense related to the transition tax as we own no controlled foreign corporations.

The global intangible low-taxed income tax and base erosion provisions are effective for taxable years beginning after December 31, 2017. The Company does not currently expect these provisions to have a material impact on its tax rate as they do not own any controlled foreign corporations and they are currently below the gross receipts threshold for purposes of the base erosion provisions.

In accordance with Staff Accounting Bulletin No. 118 ("SAB 118"), we have finalized the accounting for the Tax Act and have recorded no additional amount during the current year.

We recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2018, 2017 and 2016, we had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in our statements of operations.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

The following table sets forth our results of operations for the years ended December 31, 2018 and 2017.

	Year Ended December 31,		Change
	2018	2017	$
	(in thousands)		
Revenues:			
Net product sales	$ 18,027	$ 7,046	$ 10,981
Total revenues	18,027	7,046	10,981
Cost and operating expenses:			
Cost of sales (excluding amortization of intangible assets)	$ 3,986	$ 1,483	$ 2,503
Selling, general and administrative	63,336	36,292	27,044
Research and development	25,441	17,268	8,173
Amortization of intangible assets	7,187	5,022	2,165
Impairment of intangible asset	—	20,723	(20,723)
Total cost and expenses	99,950	80,788	19,162
Operating loss	(81,923)	(73,742)	(8,181)
Other income (expense), net	114,310	(37,970)	152,280
Income (loss) before income taxes	32,387	(111,712)	144,099
Income tax expense	(536)	(1,771)	1,235
Net income (loss)	$ 31,851	$(113,483)	$145,334

Net Revenue and Cost of Sales.

Net revenue was $18.0 million, and cost of sales were $4.0 million for the year ended December 31, 2018, an increase of $11.0 million and $2.5 million, respectively, compared to the year ended December 31, 2017. The increase in product sales is due to increased Keveyis sales of $9.8 million compared to the prior period due to increased volume. We also recorded $1.2 million in sales of Macrilen, which we launched in July 2018.

Selling, General and Administrative Expenses

The following table summarizes our selling, general and administrative expenses during the years ended December 31, 2018 and 2017:

	Year Ended December 31,		Change
	2018	2017	$
	(in thousands)		
Compensation and other personnel costs	$ 28,157	$ 14,743	$ 13,414
Outside professional and consulting services	28,110	17,115	10,995
Stock-based compensation expense	6,012	4,027	1,985
Facility costs	1,057	407	650
Total selling, general and administrative expenses	$ 63,336	$ 36,292	$ 27,044

Selling, general and administrative expenses were $63.3 million for the year ended December 31, 2018, an increase of $27.0 million compared to the year ended December 31, 2017. Compensation and other personnel costs increased by $13.4 million during the year ended December 31, 2018, primarily due to increased headcount of commercial personnel for the continued commercialization of Keveyis and our launch of Macrilen. Outside professional

and consulting services increased $11.0 million due to expenses relating to the commercialization of Keveyis and our launch of Macrilen.

Research and Development Expenses

The following table summarizes our research and development expenses during the years ended December 31, 2018 and 2017:

	Year Ended December 31,		Change
	2018	2017	$
	(in thousands)		
Product development and supporting activities	$ 18,228	$ 12,488	$ 5,740
Compensation and other personnel costs	5,418	3,640	1,778
Stock-based compensation expense	1,795	1,140	655
Total research and development expenses	$ 25,441	$ 17,268	$ 8,173

Research and development expenses were $25.4 million for the year ended December 31, 2018, an increase of $8.2 million compared to the year ended December 31, 2017. The $5.7 million increase in expenses for product development and supporting activities was primarily due to additional clinical development expenses for Recorlev and life cycle management activities for Keveyis. Compensation and other personnel costs increased by $1.8 million for the year ended December 31, 2018 as compared to the same period in 2017 due to increased headcount.

Amortization of Intangible Assets

Amortization of intangible assets was $7.2 million for the year ended December 31, 2018, an increase of $2.2 million, due to the commencement of amortization of the Macrilen product rights that we acquired in January 2018. We subsequently sold the subsidiary that held the asset to Novo in December 2018.

Other Income (Expense), Net

	Year Ended December 31,		Change
	2018	2017	$
	(in thousands)		
Unrealized gain (loss) on fair value of warrants	$ 16,337	$(30,218)	$ 46,555
Interest expense	(12,515)	(4,313)	(8,202)
Foreign exchange loss	(47)	(41)	(6)
Loss on extinguishment of debt	(21,549)	(3,545)	(18,004)
Gain on sale of subsidiary	130,832	—	130,832
Other income, net	1,252	147	1,105
Total other income (expense), net	$114,310	$(37,970)	$152,280

Other income (expense), net, increased by $152.3 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017. The increase was primarily due to a $130.8 million gain on the sale of our subsidiary and a $16.3 million unrealized gain on the fair value of our warrant liability in 2018, offset in part by a $8.2 million increase in interest expense and $21.5 million loss on extinguishment of debt. The 2017 period included a $30.2 million unrealized loss on the fair value of our warrant liability and a $3.5 million of expense relating to the loss on the extinguishment of debt.

Income Tax Expense

We recorded income tax expense of $0.5 million for the year ended December 31, 2018 as a result of tax liability expected in connection with the intercompany transfer of intellectual property. We recorded income tax expense

of $1.8 million for the year ended December 31, 2017 as a result of recording full valuation allowances against our deferred tax asset and deferred tax liability.

Liquidity and Capital Resources

We believe that our cash resources of $122.5 million at December 31, 2018 will be sufficient to allow us to fund planned operations for at least 12 months beyond the issuance date of these financial statements. We expect our funding requirements for operating activities to decrease in 2019 as compared to 2018, due in large part to increased sales of Keveyis and from anticipated payments from Novo Nordisk in the form of royalty income, performance incentives, and subsidy of 23 of our field-based employees. Our funding requirements in future years, however, could increase due to expenses associated with the execution of SONICS, LOGICS, and OPTICS clinical trials for Recorlev and the commercialization of Recorlev, if approved. Our cash needs could also increase in 2019 or future years to fund potential in-licenses, acquisitions or similar transactions as we pursue our strategy.

Cash used to fund operating expenses is affected by the timing of when we pay expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Our future funding requirements will depend on many factors, including the following:

- the amount of revenue that we receive from sales of Keveyis and royalty income from Macrilen;
- the cost and timing of establishing sales, marketing, distribution and administrative capabilities;
- the scope, rate of progress, results and cost of our clinical trials testing and other related activities for Recorlev and veldoreotide;
- the number and characteristics of product candidates that we pursue, including any additional product candidates we may in-license or acquire;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates;
- the cost, timing and outcomes of regulatory approvals;
- the terms and timing of any collaborative, licensing and other arrangements that we may establish, including any required milestone and royalty payments thereunder; and
- the emergence of competing technologies and their achieving commercial success before we do or other adverse market developments.

Although we recorded net income in 2018, we expect to incur losses in future years. Our ability to achieve and maintain profitability is dependent upon the continued successful commercialization of Keveyis, the development, regulatory approval and commercialization of our product candidates and achieving a level of revenues, including royalty revenue from Macrilen sales, adequate to support our cost structure. We may never achieve profitability, and unless and until we do, we will continue to need to raise additional capital. If we need to raise additional capital to fund our operations and complete our ongoing and planned clinical trials, funding may not be available to us on acceptable terms, or at all.

We plan to continue to fund our operations and capital funding needs through equity or debt financing, along with revenues from Keveyis sales and Macrilen royalties, and proceeds from our at-the-market ("ATM") facility**.** The sale of additional equity would result in additional dilution to our shareholders. The incurrence of debt financing would result in debt service obligations and the instruments governing such debt could provide for operating and financing covenants that would restrict our operations. If we are not able to secure adequate additional funding, we may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible or suspend or

curtail planned programs. In addition, lack of funding would limit any strategic initiatives to in-license or acquire additional product candidates or programs.

October 2017 Public Offering of Ordinary Shares

On October 6, 2017, we sold 4,000,000 ordinary shares in a public offering at a price to the public of $6.25 per share for net proceeds of approximately $23.4 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

January 2018 Public Offering of Ordinary Shares

On January 25, 2018, we sold 5,000,000 ordinary shares in a public offering at a price to the public of $6.75 per ordinary share for net proceeds of approximately $31.7 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

On February 26, 2018, we sold an additional 255,683 ordinary shares to the underwriters in connection with their partial exercise of the option to purchase additional shares that was granted to them under the underwriting agreement for additional net proceeds of approximately $1.6 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

At-The-Market Facility

We have entered into an Equity Distribution Agreement with JMP Securities LLC ("JMP Securities"), pursuant to which we may offer and sell ordinary shares having an aggregate offering price of up to $40,000,000 from time to time through JMP Securities, acting as agent. During the year ended December 31, 2018, we sold an aggregate of 1,281,903 ordinary shares under the ATM facility for net proceeds of approximately $8.6 million after payment of fees of $0.3 million to JMP Securities. As of December 31, 2018, we have approximately $31.1 million available for sale under our ATM facility.

Cash Flows

Comparison for the Years Ended December 31, 2018 and 2017:

	Year Ended December 31	
	2018	2017
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (84,576)	$ (45,336)
Investing activities	134,330	(7,500)
Financing activities	15,226	43,509
Net increase (decrease) in cash and cash equivalents	$ 64,980	$ (9,327)

Operating Activities

Net cash used in operating activities was $84.6 million for the year ended December 31, 2018 compared to $45.3 million for the year ended December 31, 2017. The increase in net cash used in operating activities resulted primarily from expenditures during 2018 to support the commercialization of Keveyis and the launch of Macrilen, offset in part by increased net revenues resulting from sales of Keveyis and Macrilen.

Investing Activities

Net cash provided by investing activities was $134.3 million for the year ended December 31, 2018 compared to net cash used by investing activities for the year ended December 31, 2017 of $7.5 million. The increase in net cash

provided by investing activities was primarily due to the $159.3 million proceeds from our sale of Macrilen product rights and Strongbridge Ireland Limited.

Financing Activities

Net cash provided by financing activities was $15.2 million for the year ended December 31, 2018 compared to net cash provided by financing activities of $43.5 million for the year ended December 31, 2017. The decrease in net cash provided by financing activities resulted primarily from our payment to CRG Servicing LLC ("CRG") in December 2018 of $94.5 million to pay off our outstanding debt, offset by receipt in January 2018 of $44.9 million in proceeds from the amendment to our senior credit facility with CRG, and $65.8 million in net proceeds from issuance of our ordinary shares and exercise of warrants and stock options.

Contractual Obligations and Other Commitments

The following is a summary of our contractual obligations and other commitments as of December 31, 2018:

	Payments due by period				
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	Total
	(in thousands)				
Minimum contract purchases pursuant to supply agreements	$ 3,014	$ 11,021	$ 8,025	$ —	$ 22,060
Operating leases	$ 439	$ 1,443	$ 207	$ —	$ 2,089
Total contractual obligations	$ 3,453	$ 12,464	$ 8,232	$ —	$ 24,149

We enter into agreements in the normal course of business with vendors for clinical trials, preclinical studies, and other services and products for operating purposes. Future payment obligations under these agreements, which are cancelable at any time by us, generally upon 30 days prior written notice, are not included in this table of contractual obligations.

We are obligated to make future payments to third parties due to payments that become due and payable upon the achievement certain commercialization milestones. As the amount and timing of these milestones are not probable and estimable, such commitments have not been included on our consolidated balance sheets or in the contractual obligations table above.

Off-Balance Sheet Arrangements

We do not have variable interests in variable interest entities or any off-balance sheet arrangements.

Recent Accounting Pronouncements

See Note 2, "Summary of significant accounting policies and basis of presentation - Recently issued accounting pronouncements" to our consolidated financial statements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to certain market risks in the ordinary course of our business. These risks primarily include interest rate risks as described below.

Interest Rate Risk

We had cash and cash equivalents of $122.5 million as December 31, 2018, which consisted 100% of funds held in the United States. Our cash and cash equivalents are held in a variety of interest-earning instruments, including money market funds. Such interest-earning instruments carry a degree of interest rate risk. To date, fluctuations in interest income have not been significant.

ITEM 8. FINANCIAL STATEMENTS

The financial statements and supplementary data required by this item are listed in Item 15 – "Exhibits and Financial Statement Schedules" of this Annual Report.

ITEM 9. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

None

ITEM 9A. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports under the Exchange Act and the rules and regulations thereunder, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by SEC Rule 13a-15(b), we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as of the end of the period covered by this report. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2018 at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Internal control over financial reporting refers to a process designed by, or under the supervision of, the principal executive and principal financial officer and effected by the 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 generally accepted accounting principles and includes those policies and procedures that: (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Under the supervision and with the participation of management, including the Chief Executive Officer and Chief Financial Officer, the Company carried out an evaluation of the effectiveness of its internal control over financial

reporting as of December 31, 2018, based on the Internal Control-Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based upon this evaluation, management has concluded that, as of December 31, 2018, the Company's internal control over financial reporting was effective in providing reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

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

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our registered public accounting firm regarding our internal control over financial reporting. Management's report was not subject to attestation by our registered public accounting firm pursuant to the rules of the SEC that permit us to provide only management's report in this Annual Report for so long as we qualify as an emerging growth company.

Changes in Internal Control over Financial Reporting

There were no changes in the Company's internal control over financial reporting that occurred during the period covered by this Annual Report that have materially affected, or are reasonably likely to materially affect, the Company's internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None

PART III.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The following table presents information about our officers and directors as of February 22, 2019.

NAME	AGE	POSITION
Executive Officers		
Matthew Pauls	48	Chief Executive Officer and Director
A. Brian Davis	52	Chief Financial Officer
Fredric Cohen, M.D.	54	Chief Medical Officer
Stephen Long	53	Chief Legal Officer
Non-Employee Directors		
John H. Johnson	61	Director, Chairman of the Board
Richard S. Kollender	49	Director
Garheng Kong, M.D., Ph.D.	43	Director
Jeffrey W. Sherman, M.D., FACP	64	Director
Mårten Steen, M.D., Ph.D.	43	Director
Hilde H. Steineger, Ph.D.	52	Director

Unless otherwise indicated, the current business addresses for our executive officers and directors is 900 Northbrook Drive, Suite 200, Trevose, Pennsylvania 19053, United States.

Executive Officers

Matthew Pauls has served as our Chief Executive Officer since August 2014 and as a member of our board of directors since September 2015. Mr. Pauls has served as a member of the board of directors of Savara Inc. (formerly as Mast Therapeutics, Inc.), since October 2015 and Egalet Corporation since January 2019. Prior to joining Strongbridge, Mr. Pauls was Chief Commercial Officer of Insmed, Inc., a publicly traded biopharmaceutical company, from April 2013 to August 2014. Prior to Insmed, Mr. Pauls worked at Shire Pharmaceuticals, a publicly traded specialty biopharmaceutical company, beginning in 2007 until March 2013, most recently as Senior Vice President, Head of Global Commercial Operations. Mr. Pauls also held positions at Bristol-Myers Squibb, a publicly traded pharmaceutical company, in Brand Management and Payor Marketing, and at Johnson & Johnson, a publicly traded medical devices, pharmaceutical and consumer packaged goods manufacturer, in various U.S. and global commercial roles. He is a volunteer board member of the Pennington School in Pennington, New Jersey, and the Boys & Girls Clubs of Philadelphia. Mr. Pauls holds B.S. and M.B.A. degrees from Central Michigan University and a J.D. from Michigan State University College of Law.

A. Brian Davis has served as our Chief Financial Officer since March 2015. Prior to joining Strongbridge, Mr. Davis served as Senior Vice President and Chief Financial Officer at Tengion, Inc., a publicly traded regenerative medicine company, from August 2010 to December 2014. In December 2014, Tengion, Inc. filed a petition for relief under Chapter 7 of Title 11 of the United States Bankruptcy Code. From 2009 to July 2010, Mr. Davis served in a consulting capacity as Chief Financial Officer of Neose Technologies, Inc., a biopharmaceutical company. Mr. Davis worked at Neose Technologies, Inc. from 1994 to 2009, where he held several positions of increasing responsibility, including Senior Vice President and Chief Financial Officer. Mr. Davis is licensed as a certified public accountant, and received a B.S. in accounting from Trenton State College and an M.B.A. from The Wharton School at the University of Pennsylvania.

Fredric Cohen, M.D. has served as our Chief Medical Officer since November 2016. Dr. Cohen joined Strongbridge in August 2015 and held roles of increasing responsibility, including Senior Vice President, Global Research and Development, and Vice President, Clinical Research and Development, prior to his promotion to Chief Medical Officer. Fred is an endocrinologist by training with more than 20 years of drug and business development experience, most recently focused in development and commercialization of rare disease and specialty products. Prior to joining Strongbridge, Fred provided strategic and operational counsel to life science companies, actively supporting their

development and licensing functions. Prior to that, he served as Executive Director, Clinical Pipeline, at Aptalis Pharma, where he was responsible for innovation strategy as well as building and advancing the company's specialty pharma pipeline. He has also held research and development positions with Johnson & Johnson and Eli Lilly & Company. Fred holds an M.D. from Pennsylvania State University College of Medicine and an A.B. in biology from Franklin and Marshall College.

Stephen Long has served as our Chief Legal Officer since March 2015 and as Company Secretary since September 2015. Prior to joining Strongbridge, Mr. Long served as Counsel at the law firm of Reed Smith LLP, from April 2013 to February 2015. He previously served at C.R. Bard, Inc., a medical device manufacturing company, from October 2000 to May 2012 in the roles of Vice President, General Counsel, as Vice President, and Secretary, and as Associate General Counsel. Mr. Long also served as Assistant General Counsel, Consumer Healthcare, at Warner-Lambert Company, and as Counsel for the company's pharmaceutical division from February 1998 to September 2000. Mr. Long held positions earlier in his career at the law firm of Willkie Farr & Gallagher and Bankers Trust Company. Mr. Long received his B.S. from the School of Industrial and Labor Relations at Cornell University and his J.D. from Albany Law School of Union University.

Non-Employee Directors

John H. Johnson has served as Chairman of our board of directors since March 2015. From January 2012 until August 2014, Mr. Johnson served as the President and Chief Executive Officer of Dendreon Corporation and as its Chairman from January 2012 until June 2014. From January 2011 until January 2012, he served as the Chief Executive Officer and a member of the board of Savient Pharmaceuticals, Inc. From November 2008 until January 2011, Mr. Johnson served as Senior Vice President and President of Eli Lilly and Company's Oncology unit. He was also Chief Executive Officer of ImClone Systems Incorporated, which develops targeted biologic cancer treatments, from August 2007 until November 2008, and served on ImClone's board of directors until it was acquired by Eli Lilly in November 2008. From 2005 to 2007, Mr. Johnson served as Company Group Chairman of Johnson & Johnson's Worldwide Biopharmaceuticals unit, President of its Ortho Biotech Products LP and Ortho Biotech Canada units from 2003 to 2005, and Worldwide Vice President of its CNS, Pharmaceuticals Group Strategic unit from 2001 to 2003. Prior to joining Johnson & Johnson, he also held several executive positions at Parkstone Medical Information Systems, Inc., Ortho-McNeil Pharmaceutical Corporation and Pfizer, Inc. Mr. Johnson is the former Chairman of Tranzyme Pharma, Inc., and former lead independent director of Sucampo Pharmaceuticals, Inc. Mr. Johnson currently serves as Chief Executive Officer and a board member of Melinta Pharmaceuticals, Inc., having served as interim Chief Executive Officer since October 2018. Mr. Johnson is also a member of the board of directors of Portola Pharmaceuticals, Inc. He previously served as a member of the board of directors for the Pharmaceutical Research and Manufacturers of America and the Health Section Governing Board of Biotechnology Industry Organization. Mr. Johnson holds a B.S. from the East Stroudsburg University of Pennsylvania.

Richard S. Kollender has served as a member of our board of directors since March 2015. Since January 2011, he has served as a Partner and Executive Manager of Quaker Partners Management, LP, a healthcare investment firm, which he initially joined in 2003, and was promoted to Partner in 2005. From August 2016 through September 2018, Mr. Kollender also served as Chief Business Officer and Chief Financial Officer of Rapid Micro Biosystems, where he continues to serve on the board of directors. Mr. Kollender previously served as a director of Celator Pharmaceuticals, Inc., Insmed, Inc., Nupathe, Inc., and Precision Therapeutics, Inc. Mr. Kollender has held positions in sales, marketing and worldwide business development at GlaxoSmithKline or GSK, and served as investment manager at S.R. One, the corporate venture capital arm of GSK. Mr. Kollender holds a B.A. in accounting from Franklin and Marshall College and an M.B.A. and Health Administration and Policy Degree (with Honors) from the University of Chicago and practiced as a certified public accountant for six years at public accounting firms including KPMG.

Garheng Kong, M.D., Ph.D. has served as a member of our board of directors since September 2015. In July 2013, he founded, and has since served as managing partner of, HealthQuest Capital, a healthcare venture growth fund. Dr. Kong was a general partner at Sofinnova Ventures, a venture firm focused on life sciences, from September 2010 to December 2013. From May 2000 to September 2010, he worked at Intersouth Partners, a venture capital firm, serving most recently as a general partner. Dr. Kong currently serves as a director of Melinta Therapeutics, Inc., Avedro, Inc.,

Alimera Sciences, Inc. and Laboratory Corporation of America Holdings. Dr. Kong holds a B.S. from Stanford University and an M.D., Ph.D. and M.B.A. from Duke University.

Jeffrey W. Sherman, MD, FACP, currently serves as Chief Medical Officer and Executive Vice President at Horizon Pharma plc, and has served as a member of our board of directors since October 2016. He has also served as a member of the Xeris Pharmaceuticals board of directors since April 2018. He brings more than 25 years of research, clinical development, regulatory and commercialization experience within the biopharmaceutical industry. He is a member of a number of professional societies, a diplomat of the National Board of Medical Examiners and the American Board of Internal Medicine, and also serves on the Board of Advisors of the Center for Information and Study on Clinical Research Participation (CISCRP). He previously held positions at IDM Pharma, Takeda Global Research and Development, NeoPharm, Searle/Pharmacia, Bristol-Myers Squibb, and is a past president of the Drug Information Association (DIA). Dr. Sherman earned his MD from the Rosalind Franklin University of Medicine and Science/The Chicago Medical School. He completed internship, residency and chief residency programs in internal medicine at Northwestern University Feinberg School of Medicine, where he currently serves as an adjunct assistant professor and a member of the alumni board, and a fellowship program in infectious diseases at the University of California San Francisco, where he was also a research associate at the Howard Hughes Medical Institute in allergy and immunology. He received a BA in Biology from Lake Forest College.

Mårten Steen, M.D., Ph.D. has served as a member of our board of directors since December 2014. Since April 2010, he has served as a Partner of HealthCap VI LP, a venture capital firm investing in life science companies. Prior to HealthCap, from February 2008 until March 2010, Dr. Steen served as director at Merck Serono SA, a biopharmaceutical company. He previously served on the boards of Ultragenyx Pharmaceutical Inc., Wilson Therapeutics AB, Altimmune, Inc. and FerroKin Biosciences. Dr. Steen holds a B.Sc. in Business Administration, an M.D., and a Ph.D. in Clinical Chemistry, all from Lund University.

Hilde H. Steineger, Ph.D. has served as a member of our board of directors since January 2014. She is currently Chief Executive Officer at Staten Biotechnology. Also, she serves as Chief Operations Officer and Co-founder of NorthSea Therapeutics B.V. She previously served as Head of Strategic Innovation Management in Nutrition & Health Division of BASF, and as Head of Global Omega-3 Innovation Management at Pronova BioPharma ASA, a BASF company, from April 2013 to May 2015. From August 2007 to June 2010, Dr. Steineger was Head of Investor Relations for Pronova BioPharma and Vice President Business Development in Pronova BioPharma from November 2009 to April 2013. Dr. Steineger is a board member and Head of the Audit Committee of Nordic Nanovector ASA. Dr. Steineger also serves as a director of PCI Biotech AS. She previously served as a member of the board of directors of Afiew AS, Algeta ASA, Weifa AS, Inven2 AS, Alertis AS, Clavis Pharma ASA and Biotech Pharmacon ASA. Dr. Steineger holds a Ph.D. in medical biochemistry from University of Oslo and an MSc in molecular biology/biotechnology.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our officers and directors, and persons who own more than 10% of a registered class of our equity securities, to file reports of securities ownership and changes in such ownership with the SEC. Officers, directors, and greater than 10% stockholders also are required by SEC rules to furnish us with copies of all Section 16(a) forms they file.

Based solely upon a review of the copies of such forms furnished to us, and on written representations from the reporting persons, we believe that all Section 16(a) filing requirements applicable to our directors and officers and 10% stockholders were timely met during 2018.

Code of Business Conduct and Ethics

Our Code of Business Conduct and Ethics is applicable to all of our directors, officers and employees and is posted on the Investors section of our website, which is located at *www.strongbridgebio.com*. Our Code of Business Conduct and Ethics provides that our directors, officers and employees are expected to avoid any action, position or interest that conflicts with the interests of our company or gives the appearance of a conflict. We expect that any amendment to this

code, or any waivers of its requirements, will be disclosed on our website. Information contained on, or that can be accessed through, our website is not incorporated by reference into this document, and you should not consider information on our website to be part of this document.

Audit Committee

The current members of our audit committee are, Richard S. Kollender, Hilde H. Steineger and Jeffrey Sherman, with Mr. Kollender serving as chairman. Our board of directors has determined that each member of our audit committee is independent under Rule 10A-3 of the Exchange Act and the applicable listing requirements of Nasdaq, and that each member of our audit committee satisfies the other listing requirements of Nasdaq for audit committee membership. Our board of directors has also determined that two of the three members of our audit committee, Mr. Kollender and Dr. Steineger, qualify as an "audit committee financial expert," as such term is defined by the SEC, and that he or she has the requisite level of financial sophistication required by the continued listing standards of Nasdaq.

ITEM 11. EXECUTIVE COMPENSATION

Summary Compensation Table

The following table sets forth information concerning cash and non-cash compensation paid for 2018 and 2017 to certain of our executive officers (referred to herein as "our executive officers").

Name and position	Year	Salary ($)	Bonus ($)[1]	Stock options ($)[2]	All Other Compensation ($)[3]	Total
Matthew Pauls	2018	$ 540,000	$ 400,000	$ 1,692,093	$ 18,837	$ 2,650,930
Chief Executive Officer	2017	500,000	350,000	764,965	10,124	1,625,089
A. Brian Davis	2018	374,351	201,676	555,973	23,414	1,155,414
Chief Financial Officer	2017	354,835	182,030	367,183	8,639	912,687
Fredric Cohen, M.D.	2018	411,403	235,987	560,808	25,056	1,233,254
Chief Medical Officer	2017	395,200	200,366	352,904	8,089	956,559

(1) The amounts in this column represent the discretionary bonuses paid with respect to 2018 and 2017 performance.

(2) The fair value of all stock options granted during the periods covered by the table are calculated on the grant date in accordance with ASC 718-10-30-3 which represented the grant date fair value.

(3) All other compensation received that does not properly report in any other column of the table including insurance premiums paid by Strongbridge with respect to term life insurance, company match on employee's 401(k) contributions and club membership fees.

Narrative to Summary Compensation Table

We have entered into employment agreements with Matthew Pauls, A. Brian Davis and Fredric Cohen. The employment agreements outline the terms of the employment relationship, including any potential severance benefits. We believe that the employment agreements provide certainty to our management team and help to retain the leadership necessary for our company to succeed.

Employment Agreements

We entered into employment agreements with each of Messrs. Pauls and Davis and Dr. Cohen for their service as President and Chief Executive Officer, Chief Financial Officer and Chief Medical Officer, respectively. The agreements are effective until terminated by either the Company or the executive officer, in either case in accordance with the terms of the agreement. Pursuant to the agreement, the annual incentive bonus targets for Messrs. Pauls and Davis, and Dr. Cohen are 55%, 40% and 40%, respectively. Under the agreements, our executive officers are entitled to participate in benefits offered by us for similarly situated employees, including the Company's paid time-off policy.

Each employment agreement provides for severance benefits detailed below under "Potential Payments upon Terminations of Employment or Following a Change in Control." Each employment agreement also contains a non-competition provision, which applies during the term of employment and for one year following termination, and a restrictive covenant with respect to non-disclosure of confidential information, which remains in effect during the term of employment and at all times thereafter.

Other Benefits

Our executive officers are eligible to participate in our employee benefit plans on the same basis as our other employees, including our health and welfare plans and our 401(k) plan. Under our 401(k) plan, participants may elect to make both pre- and post-tax contributions to their accounts in the plan, and we match 100% of those contributions up to 4% of compensation. Our executive officers are not eligible for retirement benefits other than under our 401(k) plan. The company is not required to, and has not, set aside any amounts relating to pension or retirements.

Outstanding Equity Awards as of December 31, 2018

The following table includes certain information with respect to option that were outstanding as of December 31, 2018 for our executive officers.

	Option Awards				
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Grant Date	Option Expiration Date
Matthew Pauls	72,727	—	$ 8.06	8/23/2014	8/23/2019
	72,727	—	$10.74	8/23/2014	8/23/2019
	81,818	—	$13.43	8/23/2014	8/23/2019
	255,812	198,733 (1)	$15.71	5/26/2015	5/26/2025
	94,001	70,312 (2)	$ 3.94	2/26/2016	2/26/2026
	93,750	210,937 (2)	$ 2.90	2/23/2017	2/23/2027
	65,625	284,375 (2)	$ 6.65	2/5/2018	2/5/2028
A. Brian Davis	30,681	23,864 (1)	$15.71	5/26/2015	5/26/2025
	133,363	— (3)	$18.80	7/21/2015	7/21/2020
	44,688	20,312 (2)	$ 3.94	2/26/2016	2/26/2026
	78,750	101,250 (2)	$ 2.90	2/23/2017	2/23/2027
	21,563	93,437 (2)	$ 6.65	2/5/2018	2/5/2028
Fredric Cohen, M.D.	66,478	15,340 (4)	$18.12	8/5/2015	8/5/2025
	20,625	9,375 (2)	$ 3.94	2/26/2016	2/26/2026
	25,000	15,000 (4)	$ 4.16	6/13/2016	6/13/2026
	5,000	5,000 (4)	$ 3.90	11/23/2016	11/23/2026
	75,688	97,312 (2)	$ 2.90	2/23/2017	2/23/2027
	21,750	94,250 (2)	$ 6.65	2/5/2018	2/5/2028

(1) These stock options vest in three separate tranches. The first tranche vests in 16 equal quarterly installments commencing the first quarter subsequent to the grant date; the second tranche vests in 16 equal quarterly installments commencing on the date on which our shares begin trading on NASDAQ; and the third tranche vests one-half on the date on which the closing price of our shares as reported on NASDAQ equals $33.66 for Mr. Pauls, and $31.46 for Mr. Davis, for 20 consecutive trading days, so long as this occurs prior to May 26, 2019, and one-half on the one year anniversary of such initial vesting date. All of these options will fully vest and become exercisable upon a change of control provided that the executive is employed on the date of such change in control.

(2) These options vest in 16 equal quarterly installments commencing with the first quarter subsequent to the grant date. These options will fully vest and become exercisable upon a change of control provided that the executive is employed on the date of such change of control.

(3) These options vest in three equal annual tranches. The first tranche of these options vested on March 23, 2016. The second tranche vests on March 23, 2017. The third tranche vests on March 23, 2018. These options will fully vest and become exercisable upon a change of control provided that the executive is employed on the date of such change of control.

(4) One-fourth of the shares underlying these options vested on the one-year anniversary of the Date of Grant and the remaining three-fourths of the shares underlying these options vest/vested in quarterly installments after the one-year anniversary of the Date of Grant. These options will fully vest and become exercisable upon a change in control provided that the executive is employed on the date of such change in control.

Prior to September 3, 2015, we did not have an equity compensation plan. Grants of stock options to the executive officers and other individuals were made through individual grant agreements.

2019 Equity Awards

On February 20, 2019, our board of directors approved grants of stock options and restricted stock units, or RSUs, to Messrs. Pauls and Davis, and Dr. Cohen. Messrs. Pauls and Davis, and Dr. Cohen were awarded stock options in the amounts of 400,000, 108,500 and 118,000, respectively. These stock options vest in sixteen equal quarterly installments beginning May 20, 2019, provided the executive officer is employed by the Company on each vesting date. All stock options will fully vest upon a change of control of our company. Messrs. Pauls and Davis, and Dr. Cohen were awarded RSUs in the amounts of 50,000, 20,000 and 24,500, respectively. These RSUs vest, with respect to 100% of the grants, on the second anniversary following the date of grant, provided that the executive officer is employed by the Company on such vesting date. All RSUs will fully vest upon a change of control of our company. If and when the RSUs vest, the Company will issue to the executive one ordinary share of the Company for each whole RSU that has vested, subject to satisfaction of the executive's tax withholding obligations. The RSUs will cease to be outstanding upon such issuance of shares.

Potential Payments Upon Terminations of Employment or Following a Change of Control

The employment agreements with Messrs. Pauls and Davis, and Dr. Cohen provide that, upon a termination of employment by our company without "cause," or by the executive for "good reason," or due to the executive's death, subject to the execution of a release of claims, he or she will be entitled to (1) an amount equal to the sum of 18 months of base salary and the target bonus for Mr. Pauls, or 12 months of base salary and the target bonus for our other executive officers, paid in installments over the 18-month period following termination for Mr. Pauls or the 12-month period following termination for our other executive officers, (2) a pro rata portion of the annual bonus that he or she would have been entitled to receive for the calendar year that includes the termination date, based on the actual achievement of the applicable performance goals, and (3) medical and dental benefits provided by us that are at least equal to the level of benefits provided to other similarly situated active employees until the earlier of (a) 18 months following the termination date for Mr. Pauls, or 12 months following the termination date for our other executive officers and (b) the date the executive becomes covered under a subsequent employer's medical and dental plans.

In the event there is a change of control of our company and, during the 24-month period following the change of control, any of our executive officers is terminated by us without cause, by the executive for good reason, or due to the executive's death or, he or she will be entitled to the severance benefits detailed below and all unvested equity or equity-based awards held by the executive will accelerate and vest. The severance benefits include (1) an amount equal to the sum of 24 months base salary and the target bonus for Mr. Pauls, or the sum of 18 months base salary and the target bonus for our other executive officers, paid in installments over the 24-month period following termination for Mr. Pauls or the 18-month period following termination for our other executive officers; and (2) the medical and dental benefits provided by us until the earlier of (a) 18 months following the termination date for Mr. Pauls or one year following the termination date of our other executive officers and (b) the date the executive becomes covered under a subsequent employer's medical and dental plans.

Under the employment agreements, "cause" is defined as (1) the conviction of, or plea of guilty or nolo contendere to, any felony or any crime involving theft, embezzlement, dishonesty or moral turpitude, (2) any act constituting willful misconduct, deliberate malfeasance, dishonesty, or gross negligence in the performance of the individual's duties, (3) the willful and continued failure to perform any of the individual's duties, which has not been cured within 30 days following written notice from us, or (4) any material breach by the individual of the employment

agreement or any other agreement with us, which has not been cured within 30 days following written notice from us. “Good reason” is defined as any of the following reasons unless cured by us within a specified period: (1) a material reduction of the individual’s base salary, other than a reduction that is applicable to other senior executives in the same manner and proportion, (2) the assignment of duties or responsibilities which are materially inconsistent with the individual’s position, (3) a change in the principal location at which the individual performs his or her duties to a new location that is more than 50 miles from the prior location or (4) a material breach of the employment agreement by us. “Change of control ” is defined as the occurrence of any of the following: (a) any person or group of persons becomes the beneficial owner, directly or indirectly, of securities of the Company representing more than fifty percent (50%) of the combined voting power of the Company’s then outstanding securities; provided that if the person or group of persons is already deemed to own more than 50% of the total fair market value or total voting power, then the acquisition of additional stock by such person or group of persons shall not constitute an additional change of control; (b) the stockholders of the Company approve a plan of complete liquidation of the Company; (c) the sale or disposition of all or substantially all of the Company’s assets; or (d) a merger, consolidation or reorganization of the Company with or involving any other entity, other than a merger, consolidation or reorganization that would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity) at least a 50% of the combined voting power of the Company (or such surviving entity) outstanding immediately after such merger, consolidation or reorganization owned in approximately the same proportion of such ownership by each of the prior shareholders as prior to the transaction. The following acquisitions are not considered to be a change of control of the Company: (A) an acquisition by the Company or entity controlled by the Company, or (B) an acquisition by an employee benefit plan (or related trust) sponsored or maintained by the Company.

The employment agreements also provide that, in the event that any of our other executive officers is subject to the excise tax under Section 4999 of the Code, the payments that would be subject to the excise tax will be reduced to the level at which the excise tax will not be applied unless such executive would be in a better net after-tax position by receiving the full payments and paying the excise tax.

Director Compensation

Our board of directors’ compensation program for fiscal year 2018 provided for the following:

- Annual Cash Retainer—$40,000
- Additional Annual Cash Retainers
    - Non-Executive Chairman of the Board Retainer—$35,000
    - Audit Committee Chair Retainer—$16,000
    - Compensation Committee Chair Retainer—$12,000
    - Nomination and Governance Committee Chair Retainer—$9,000
    - Transaction Committee Chair Retainer—$16,000
    - Audit Committee Member (other than Chairman) Retainer—$8,000
    - Compensation Committee Member (other than Chairman) Retainer—$6,000
    - Nomination and Governance Committee Member (other than Chairman) Retainer—$4,500
    - Transaction Committee Member (other than Chairman) Retainer—$8,000
- Equity Compensation
    - Initial Equity Grant—Option to purchase 60,000 shares, with one-third of the shares vesting on the first anniversary of the date of grant and the remaining two-thirds of the shares vesting in equal

monthly installments over the 24-month period that follows the first anniversary of the date of grant, provided that the director continues to provide services as a member of our board of directors continuously from the date of grant through the applicable vesting date

- Annual Equity Grant—Option to purchase 40,000 shares with such option vesting in full on the first anniversary of the date of grant, provided that the director continues to provide services as a member of our board of directors continuously from the date of grant through the vesting date

Our directors earned compensation in 2018 for their service on the board as summarized below:

Name	Year	Fees earned ($)	Options Awards (1) ($)	Total ($)
John H. Johnson	2018	$91,500	$ 220,526	$312,026
Richard S. Kollender	2018	70,000	220,526	290,526
Garheng Kong, M.D., Ph.D.	2018	50,500	220,526	271,026
Jeffrey W. Sherman, M.D., FACP	2018	48,000	220,526	268,526
Mårten Steen, M.D., Ph.D.	2018	57,000	220,526	277,526
Hilde H. Steineger, Ph.D.	2018	48,000	220,526	268,526

(1) Amounts shown represent the aggregate grant date fair value of the option awards, computed in accordance with FASB ASC Topic 718.

The following table includes a summary of outstanding stock options as of December 31, 2018 for our directors:

Name	Options Outstanding
John H. Johnson	187,767
Richard S. Kollender	157,188
Garheng Kong, M.D., Ph.D.	154,385
Jeffrey W. Sherman, M.D., FACP	140,000
Mårten Steen, M.D., Ph.D.	154,918
Hilde H. Steineger, Ph.D.	154,918

Non-Employee Director Equity Compensation Plan

Our board of directors has adopted, and our shareholders have approved, the Non-Employee Director Equity Compensation Plan (the "Non-Employee Director Plan"). The Non-Employee Director Plan provides for the grant of nonstatutory stock options, stock awards, and restricted stock units to our non-employee directors. The Non-Employee Director Plan is effective as of September 3, 2015.

Authorized Shares. As of the date of this report, a total of 1,099,514 ordinary shares have been reserved for issuance pursuant to the Non-Employee Director Plan. The ordinary shares that we have reserved for issuance pursuant to the Non-Employee Director Plan (the "Share Pool") will be increased on the first day of each fiscal year, in an amount equal to one-half percent (0.5%) of the outstanding shares on the last day of the immediately preceding fiscal year. The Share Pool will be reduced on the date of grant, by one ordinary share of our ordinary for each award under the Non-Employee Director Plan; provided that awards that are valued by reference to shares of our ordinary but are required to be paid in cash pursuant to their terms will not reduce the Share Pool. If and to the extent options terminate, expire, or are canceled, forfeited, exchanged, or surrendered without having been exercised, or if any stock awards or awards of restricted stock units (including restricted stock received upon the exercise of options) are forfeited, the ordinary shares subject to such awards will again be available for awards under the Share Pool. Notwithstanding the foregoing, shares tendered by individual grantees, or withheld by us, as full or partial payment to us upon the exercise of options will not become available for issuance again under the Non-Employee Director Plan.

Plan Administration. Our board administers the Non-Employee Director Plan. Subject to the provisions of the Non-Employee Director Plan, our board has the power to determine the terms of the awards, including the exercise price, the number of shares of our ordinary shares subject to each such award, the exercisability of the awards and the form of consideration, if any, payable upon exercise. To the maximum extent permitted by law, no member of our board will be liable for any action taken or decision made in good faith relating to the Non-Employee Director Plan or any award granted thereunder.

Stock Options. The exercise price of options granted under the Non-Employee Director Plan may be equal to or greater than the fair market value of our ordinary shares on the date of grant. The term of an option may not exceed ten years. After the termination of service of a non-employee director for any reason other than death, disability or cause (as defined in the Non-Employee Director Plan), he or she may exercise the vested portion of his or her option for 90 days. If termination is due to death (or death occurs within 90 days after the director's termination date) or disability, the vested portion of the option will remain exercisable for one year. However, in no event may an option be exercised later than the expiration of its term. The entire option is forfeited upon a termination for Cause. In addition, if a non-employee director has engaged in conduct that constitutes cause, any shares acquired upon exercise of an option for which we have not yet delivered the share certificates shall be automatically forfeited to us in exchange for payment of the exercise price paid for such shares.

Stock Awards. Stock awards may be granted under the Non-Employee Director Plan. Stock awards are grants of our ordinary shares that vest in accordance with terms and conditions established by the board. The board will determine the number of shares granted as stock awards to a non-employee director and the consideration, if any, to be paid for such shares. The board may impose whatever conditions to vesting it determines to be appropriate (for example, the board may set restrictions based on the achievement of specific performance goals or continued service to us); provided, however, that the board, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Ordinary shares subject to stock awards that do not vest are subject to forfeiture.

Restricted Stock Units. Restricted stock units may be granted under the Non-Employee Director Plan. Restricted stock units are bookkeeping entries representing an amount equal to the fair market value of one ordinary share. The board determines the terms and conditions of restricted stock units, including the vesting criteria (which may include accomplishing specified performance criteria or continued service to us) and the form and timing of payment. The amount payable as a result of the vesting of a restricted stock unit will be distributed as soon as practicable following the vesting date and in no event later than the fifteenth date of the third calendar month of the year following the vesting date of the restricted stock unit (or as otherwise permitted under Section 409A of the Internal Revenue Code); provided, however, that an individual grantee may, if and to the extent permitted by our board, elect to defer payment of restricted stock units in a manner permitted by Section 409A of the Internal Revenue Code. Notwithstanding the foregoing, the board, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed.

Non-Transferability of Awards. Unless our board provides otherwise, the Non-Employee Director Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime.

Certain Adjustments. In the event of certain changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under the Non-Employee Director Plan, the board will adjust the number and class of shares that may be delivered under the Non-Employee Director Plan and/or the number, class and price per share of shares covered by each outstanding award.

Change of Control. The Non-Employee Director Plan provides that in the event of a change of control, as defined in the Non-Employee Director Plan, where we are not the surviving corporation (or we survive only as a subsidiary of another corporation), unless our board determines otherwise, all outstanding awards will be assumed by, or replaced with comparable awards by, the surviving corporation (or a parent or subsidiary of the surviving corporation). In the event the surviving corporation in such change of control (or a parent or subsidiary of the surviving corporation) does not assume or replace the outstanding awards with comparable awards, (i) we will provide written notice of such change of control to each individual grantee with outstanding awards; (ii) all outstanding options will automatically accelerate and become fully vested and exercisable; (iii) all outstanding stock awards will become vested and deliverable

in accordance with the Non-Employee Director Plan; and (iv) all outstanding restricted stock units will become vested and deliverable in accordance with the Non-Employee Director Plan.

Notwithstanding the foregoing, if there is a change of control, our board may require that grantees surrender outstanding options in exchange for a payment of cash or stock equal to the amount by which the fair market value of the shares exceeds the exercise price and/or, after giving grantees an opportunity to exercise options, terminate all unexercised options, with such surrender or termination taking place as of the date of the change of control or such other date that our board specifies.

Amendment; Termination. Our board has the authority to amend, suspend or terminate the Non-Employee Director Plan provided such action does not impair the existing rights of any participant. The Non-Employee Director Plan automatically terminates in 2025, unless we terminate it sooner. We will obtain shareholder approval of any amendment to the Non-Employee Director Plan as required by applicable law or listing requirements.

Equity Compensation Plan

Our board of directors has adopted, and our shareholders have approved, the 2015 Equity Compensation Plan (the "2015 Plan"). The 2015 Plan provides for the grant of incentive stock options, within the meaning of Section 422 of the Internal Revenue Code, to our employees and any parent or subsidiary corporations' employees, and for the grant of nonstatutory stock options, stock awards, and restricted stock units to our employees, directors and consultants and our parent or subsidiary corporations' employees and consultants. The 2015 Plan is effective as of September 3, 2015.

Authorized Shares. As of the date of this report, a total of 7,114,308 ordinary shares have been reserved for issuance pursuant to the 2015 Plan. The ordinary shares that we have reserved for issuance pursuant to the 2015 Plan (the "Share Pool") will be increased on the first day of each fiscal year in an amount equal to four percent (4.0%) of the outstanding ordinary shares on the last day of the immediately preceding fiscal year. A maximum of 1,000,000 ordinary shares may be subject to awards made under the 2015 Plan to any individual during a calendar year, subject to adjustment as provided in the 2015 Plan. The maximum number of ordinary shares that may be issued under the 2015 Plan as incentive stock options is 7,114,308. The Share Pool will be reduced on the date of grant, by one ordinary share for each award under the 2015 Plan; provided that awards that are valued by reference to ordinary shares but are required to be paid in cash pursuant to their terms will not reduce the Share Pool. If and to the extent options terminate, expire, or are canceled, forfeited, exchanged, or surrendered without having been exercised, or if any stock awards or awards of restricted stock units (including restricted stock received upon the exercise of options) are forfeited, the ordinary shares subject to such awards will again be available for awards under the Share Pool. Notwithstanding the foregoing, the following ordinary shares will not become available for issuance under the 2015 Plan: (i) shares tendered by individual grantees, or withheld by us, as full or partial payment to us upon the exercise of options granted under the 2015 Plan and (ii) shares withheld by, or otherwise remitted to us to satisfy an individual grantee's tax withholding obligations upon the lapse of restrictions on stock awards, or the exercise of options granted under the 2015 Plan.

Plan Administration. Our compensation committee administers the 2015 Plan. Subject to the provisions of the 2015 Plan, our compensation committee has the power to determine the terms of the awards, including the exercise price, the number of shares of our ordinary shares subject to each such award, the exercisability of the awards and the form of consideration, if any, payable upon exercise. To the maximum extent permitted by law, no member of our board or our compensation committee will be liable for any action taken or decision made in good faith relating to the 2015 Plan or any award granted thereunder.

Stock Options. The exercise price of options granted under the 2015 Plan may be equal to or greater than the fair market value of our ordinary shares on the date of grant. The term of an option may not exceed ten years, except that the term of an incentive stock option granted to any employee who owns more than 10% of the voting power of all classes of our outstanding stock must not exceed five years and the exercise price must equal to at least 110% of the fair market value of our ordinary shares on the grant date. After the termination of service of an employee, director or consultant for any reason other than death, disability or cause (as defined in the 2015 Plan), he or she may exercise the vested portion of his or her option for 90 days. If termination is due to death (or death occurs within 90 days after the individual's termination date) or disability, the vested portion of the option will remain exercisable for one year. However, in no event may an option be exercised later than the expiration of its term. The entire option is forfeited upon a termination for Cause. In addition, if an employee, director or consultant has engaged in conduct that constitutes cause,

any shares acquired upon exercise of an option for which we have not yet delivered the share certificates shall be automatically forfeited to us in exchange for payment of the exercise price paid for such shares.

Stock Awards. Stock awards may be granted under the 2015 Plan. Stock awards are grants of ordinary shares that vest in accordance with terms and conditions established by the compensation committee. The compensation committee will determine the number of shares granted as stock awards to any employee, director, or consultant and the consideration, if any, to be paid for such shares. The compensation committee may impose whatever conditions to vesting it determines to be appropriate (for example, the compensation committee may set restrictions based on the achievement of specific performance goals or continued service to us); provided, however, that the compensation committee, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Ordinary shares subject to stock awards that do not vest are subject to forfeiture.

Restricted Stock Units. Restricted stock units may be granted under the 2015 Plan. Restricted stock units are bookkeeping entries representing an amount equal to the fair market value of one ordinary share. The compensation committee determines the terms and conditions of restricted stock units, including the vesting criteria (which may include accomplishing specified performance criteria or continued service to us) and the form and timing of payment. The amount payable as a result of the vesting of a restricted stock unit will be distributed as soon as practicable following the vesting date and in no event later than the fifteenth date of the third calendar month of the year following the vesting date of the restricted stock unit (or as otherwise permitted under Section 409A of the Internal Revenue Code); provided, however, that an individual grantee may, if and to the extent permitted by our compensation committee, elect to defer payment of restricted stock units in a manner permitted by Section 409A of the Internal Revenue Code. Notwithstanding the foregoing, the compensation committee, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed.

Performance-Based Awards. Certain stock awards or restricted stock units granted under the 2015 Plan may be granted in a manner that should be deductible by us under Section 162(m) of the Internal Revenue Code. These awards, referred to as performance-based awards, will be determined based on the attainment of written performance goals approved by the compensation committee. The performance-based awards will be based upon one or more of the following objective criteria: (i) consolidated earnings before or after taxes (including earnings before interest, taxes, depreciation and amortization); (ii) net income; (iii) operating income; (iv) earnings per share; (v) return on shareholders' equity; (vi) attainment of strategic and operational initiatives; (vii) customer income; (viii) economic value-added models; (ix) maintenance or improvement of profit margins; (x) stock price (including total shareholder return), including, without limitation, as compared to one or more stock indices; (xi) market share; (xii) revenues, sales or net sales; (xiii) return on assets; (xiv) book value per share; (xv) expense management; (xvi) improvements in capital structure; (xvii) costs; and (xviii) cash flow. The foregoing criteria may relate to the company, one or more of our subsidiaries or one or more of our divisions or units, or any combination of the foregoing, and may be applied on an absolute basis and/or be relative to one or more peer group companies or indices, or any combination thereof, all as determined by the compensation committee. In addition, to the degree consistent with the Internal Revenue Code, the performance criteria may be calculated without regard to extraordinary, unusual and/or non-recurring items. With respect to performance-based awards, (i) the compensation committee will establish the objective performance goals applicable to a given period of service while the outcome for that performance period is substantially uncertain and no later than 90 days after the commencement of that period of service (but in no event after 25% of that period of service has elapsed) and (ii) no awards will be granted to any participant for a given period of service until the compensation committee certifies that the objective performance goals (and any other material terms) applicable to that period have been satisfied.

Non-Transferability of Awards. Unless our compensation committee provides otherwise, the 2015 Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime.

Certain Adjustments. In the event of certain changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under the 2015 Plan, the compensation committee will adjust the number and class of shares that may be delivered under the 2015 Plan and/or the number, class and price per share of shares covered by each outstanding award, and the numerical share limits set forth in the 2015 Plan.

Change of Control. The 2015 Plan provides that in the event of a change of control, as defined in the 2015 Plan, where we are not the surviving corporation (or we survive only as a subsidiary of another corporation), unless our compensation committee determines otherwise, all outstanding awards will be assumed by, or replaced with comparable awards by, the surviving corporation in such change of control (or a parent or subsidiary of the surviving corporation). In the event the surviving corporation (or a parent or subsidiary of the surviving corporation) in such change of control does not assume or replace the outstanding awards with comparable awards, (i) we will provide written notice of such change of control to each individual grantee with outstanding awards; (ii) all outstanding options will automatically accelerate and become fully vested and exercisable; (iii) all outstanding stock awards will become vested and deliverable in accordance with the 2015 Plan; and (iv) all outstanding restricted stock units will become vested and deliverable in accordance with the 2015 Plan.

Notwithstanding the foregoing, if there is a change of control, our board may require that grantees surrender outstanding options in exchange for a payment of cash or stock equal to the amount by which the fair market value of the shares exceeds the exercise price or, after giving grantees an opportunity to exercise options, terminate all unexercised options, with such surrender or termination taking place as of the date of the change of control or such other date that our board specifies.

Amendment; Termination. Our board has the authority to amend, suspend or terminate the 2015 Plan provided such action does not impair the existing rights of any participant. The 2015 Plan automatically terminates in 2025, unless we terminate it sooner. We will obtain shareholder approval of any amendment to the 2015 Plan as required by applicable law or listing requirements.

2017 Inducement Plan

On February 23, 2017, our board of directors adopted the 2017 Inducement Plan (the "Inducement Plan"), pursuant to which we (along with our affiliates and subsidiaries) may grant equity-based awards to new employees. The purpose of the Inducement Plan is to attract valued employees by offering them a greater stake in our success and a closer identity with us, and to encourage ownership of our ordinary shares by such employees.

The Inducement Plan was adopted without shareholder approval pursuant to Rule 5635(c)(4) of the NASDAQ Listing Rules. In accordance with Rule 5635(c)(4) of the NASDAQ Listing Rules, awards under the Inducement Plan may only be made to individuals who were not previously an employee or a non-employee director of the Company or any of our subsidiaries (or who had a bona fide period of non-employment with the Company and our subsidiaries) who is hired by the Company or a subsidiary. Subject to adjustments described in the Inducement Plan, we may issue up to 2,750,000 of our ordinary shares in the form of stock options, stock awards and restricted stock units to eligible recipients.

Administration. Our compensation committee administers the Inducement Plan and is authorized to determine, among other things, the persons to whom inducement awards will be made and the terms of such awards.

Stock Options. The exercise price of options granted under the Inducement Plan will be equal to or greater than the fair market value of our ordinary shares on the date the options are granted, and the term of any option will not exceed ten years from the date of the grant. After a termination of service for any reason other than death, disability or cause (as defined in the Inducement Plan), the grantee of an option award may exercise the vested portion of his or her option for 90 days. If termination is due to death (or death occurs within 90 days after the individual's termination date) or disability, the vested portion of the option will remain exercisable for one year. However, in no event may an option be exercised later than the expiration of its term. The entire option will be forfeited upon a termination for cause. In addition, if an employee, director or consultant has engaged in conduct that constitutes cause, any shares acquired upon exercise of an option for which we have not yet delivered the share certificates will be automatically forfeited to us in exchange for payment of the exercise price paid for such shares.

Stock Awards and Restricted Stock Units. Ordinary shares issued or transferred pursuant to stock awards may be issued or transferred for consideration or for no consideration, and may be subject to restrictions or no restrictions, as determined by the compensation committee. Each restricted stock unit will be granted with respect to one ordinary share

or will have a value equal to the fair market value of one ordinary share. Restricted stock units will be paid in cash, ordinary shares, or other securities, other awards or other property, as determined by the compensation committee, upon the lapse of the restrictions applicable thereto. The amount payable as a result of the vesting of a restricted stock unit will be distributed as soon as practicable following the vesting date and in no event later than the fifteenth date of the third calendar month of the year following the vesting date of the restricted stock unit (or as otherwise permitted under Section 409A of the Internal Revenue Code); provided, however, that an individual grantee may, if and to the extent permitted by our compensation committee, elect to defer payment of restricted stock units in a manner permitted by Section 409A of the Internal Revenue Code. Except as otherwise set forth in an award agreement, if a grantee ceases to be employed by, or provide services to, us, any stock award or restricted stock units held by the grantee that are subject to transfer restrictions will be forfeited.

Non-Transferability of Awards. Except as otherwise permitted by an award agreement or by our compensation committee, the Inducement Plan generally does not allow for the transfer of awards made under the Inducement Plan, except by will or by the laws of descent and distribution.

Certain Adjustments. In the event of certain changes in our capitalization, to prevent dilution or enlargement of the benefits or potential benefits available under the Inducement Plan, the compensation committee will adjust the number and class of shares that may be delivered under the Inducement Plan and/or the number, class and price per share of shares covered by each outstanding award, and the numerical share limits set forth in the Inducement Plan.

Change of Control. The Inducement Plan provides that in the event of a change of control, as defined in the Inducement Plan, where we are not the surviving corporation (or we survive only as a subsidiary of another corporation), unless our compensation committee determines otherwise, all outstanding awards will be assumed by, or replaced with comparable awards by, the surviving corporation in such change of control (or a parent or subsidiary of the surviving corporation). In the event the surviving corporation (or a parent or subsidiary of the surviving corporation) in such change of control does not assume or replace the outstanding awards with comparable awards, (i) we will provide written notice of such change of control to each individual grantee with outstanding awards; (ii) all outstanding options will automatically accelerate and become fully vested and exercisable; (iii) all outstanding stock awards will become vested and deliverable in accordance with the Inducement Plan; and (iv) all outstanding restricted stock units will become vested and deliverable in accordance with the Inducement Plan.

Notwithstanding the foregoing, if there is a change of control, our board may require that grantees surrender outstanding options in exchange for a payment of cash or stock equal to the amount by which the fair market value of the shares exceeds the exercise price or, after giving grantees an opportunity to exercise options, terminate all unexercised options, with such surrender or termination taking place as of the date of the change of control or such other date that our board specifies.

Amendment; Termination. Our board has the authority to amend or terminate the Inducement Plan at any time; provided, however, that the board will not amend the Inducement Plan without shareholder approval if such approval is required in order to comply with applicable laws or stock exchange requirements. The Inducement Plan automatically terminates in 2027, unless we terminate it sooner.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of February 20, 2019 by:

- each of our directors and director nominees;
- each of our “named executive officers”;
- all of our directors and executive officers as a group; and

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our ordinary shares.

The percentages in the columns entitled "Percentage of Shares Beneficially Owned" are based on a total of 54,158,948 ordinary shares outstanding as of February 20, 2019.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our ordinary shares. Our ordinary shares subject to options that are currently exercisable or exercisable within 60 days of February 20, 2019 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the ordinary shares beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o Strongbridge Biopharma plc, 900 Northbrook Drive, Suite 200, Trevose, Pennsylvania 19053.

		Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% Shareholders			
Caxton Alternative Management LP	(1)	9,127,987	16.2%
Novo Nordisk A/S	(2)	5,242,000	9.7%
Longitude Venture Partners III, L.P	(3)	4,500,000	8.3%
Growth Equity Opportunities Fund III, LLC	(4)	4,141,308	7.6%
HealthCap VI, L.P.	(5)	3,741,008	6.9%
Armistice Capital, LLC	(6)	2,878,000	5.3%
Broadfin	(7)	2,821,722	5.2%
Executive Officers and Directors			
Matthew Pauls	(8)	846,850	1.5%
A. Brian Davis	(9)	348,319	*
Fredric Cohen, M.D.	(10)	256,150	*
John H. Johnson	(11)	147,767	*
Richard S. Kollender	(11)	117,188	*
Garheng Kong, M.D., Ph.D.	(11)	114,385	*
Jeffrey W. Sherman, M.D., F.A.C.P.	(12)	90,000	*
Mårten Steen, M.D., Ph.D.	(11)	114,918	*
Hilde H. Steineger, Ph.D.	(11)	114,918	*
All current directors and executive officers as a group (10 persons)		**2,491,610**	**4.4%**

* less than one percent

(1) Based on the information disclosed in a Schedule 13D/A filed with the SEC on August 27, 2018 by Caxton Corporation ("Caxton"), CDK Associates, L.L.C. ("CDK") and Bruce Kovner, and subsequent Section 16 filings made with the SEC. According to the SEC filings, Caxton, the manager of CDK, and Mr. Kovner, the Chairman and sole shareholder of Caxton, each share voting and dispositive power with respect to 9,127,987 ordinary shares, which includes 8,681,305 ordinary shares beneficially owned by CDK and 446,682 ordinary shares beneficially owned by employees of an affiliate of Caxton. According to the SEC reports, CDK shares voting and dispositive power with respect to 8,681,305 ordinary shares. The 8,681,305 ordinary shares beneficially owned by CDK represent 6,581,305 ordinary shares and warrants to purchase up to an aggregate of 2,100,000 ordinary shares. The 446,682 ordinary shares beneficially owned by employees of an affiliate of Caxton represent 326,682 ordinary shares and warrants to purchase up to an aggregate of 120,000 ordinary shares. The reporting persons will be prohibited from exercising the warrants, if after giving effect to such exercise, they (together with any of their affiliates) would together beneficially own in excess of 4.99% of our ordinary shares outstanding immediately after giving effect to such exercise or 9.99% if the holder beneficially owns greater than 4.99% of the number of ordinary shares outstanding notwithstanding the ordinary shares issuable upon exercise of this warrant. The address of the reporting persons is 731 Alexander Road, Princeton, NJ, 08540.

(2) Based on the information disclosed in a Schedule 13G filed with the SEC on December 21, 2018 by Novo Nordisk A/S, in which the reporting person reported sole voting and dispositive power with respect to 5,242,000 ordinary shares. The address of the reporting person is Novo All, DK-2880 Bagsværd, Denmark.

(3) Based on the information disclosed in a Schedule 13G/A filed with the SEC on February 12, 2019 by Longitude Venture Partners III, L.P. ("LVPIII"), Longitude Capital Partners III, LLC ("LCPIII"), Juliet Tammenoms Bakker and Patrick G. Enright, in which the reporting persons reported shared voting and dispositive power with respect to 4,500,000 ordinary shares. The address of the reporting persons is 2740 Sand Hill Road, Second Floor, Menlo Park, California 94025.

(4) Based on the information disclosed in a Schedule 13D/A filed with the SEC on January 6, 2017 by Growth Equity Opportunities Fund III, LLC ("GEO"), New Enterprise Associates 14, L.P. ("NEA 14"), NEA Partners 14, L.P. ("NEA Partners 14"), NEA 14 GP, LTD ("NEA 14 GP"), M. James Barrett, Peter J. Barris, Forest Baskett, Anthony A. Florence, Jr., Patrick J. Kerins, David M. Mott, Scott D. Sandell, Peter W. Sonsini, and Ravi Viswanathan, in which each reporting person reported shared voting and dispositive power with respect to 4,141,308 ordinary shares. The number reported in the table above includes warrants to purchase up to an aggregate of 1,000,000 ordinary shares, which became exercisable subsequent to the Schedule 13D/A filed by the reporting persons. The reporting persons will be prohibited from exercising the warrants, if after giving effect to such exercise, they (together with any of their affiliates) would together beneficially own in excess of 4.99% of our ordinary shares outstanding immediately after giving effect to such exercise or 9.99% if the holder beneficially owns greater than 4.99% of the number of ordinary shares outstanding notwithstanding the ordinary shares issuable upon exercise of this warrant. NEA 14 is the sole member of GEO, NEA Partners 14 is the sole general partner of NEA 14, and NEA 14 GP is the sole general partner of NEA Partners 14. Messrs. Barrett, Barris, Baskett, Florence, Kerins, Mott, Sandell, Sonsini and Viswanathan are the directors of NEA 14 GP. Each reporting person disclaims beneficial ownership of the ordinary shares reported other than those ordinary shares which such person owns of record. The address of each of GEO, NEA 14, NEA Partners 14, and NEA 14 GP is New Enterprise Associates, 1954 Greenspring Drive, Suite 600, Timonium, MD 21093. The address of the principal business office for each of Messrs. Barris, Florence, Kerins and Mott is New Enterprise Associates, 5425 Wisconsin Avenue, Suite 800, Chevy Chase, MD 20815. The address of the principal business officer for each of Messrs. Baskett, Sandell, Sonsini and Viswanathan is New Enterprise Associates, 2855 Sand Hill Road, Menlo Park, CA 94025.

(5) Based on the information disclosed in a Schedule 13G/A filed with the SEC on February 1, 2019 by HealthCap VI, L.P. ("HealthCap") and HealthCap VI GP S.A. ("HealthCap GP"), in which each reporting person reported shared voting and dispositive power with respect to 3,741,008 ordinary shares, which includes (i) 114,918 ordinary shares issuable upon exercise of options that are exercisable within 60 days and (ii) a warrant to purchase up to an additional 400,000 ordinary shares. The reporting persons will be prohibited from exercising the warrants, if after giving effect to such exercise, they (together with any of their affiliates) would together beneficially own in excess of 4.99% of our ordinary shares outstanding immediately after giving effect to such exercise or 9.99% if the holder beneficially owns greater than 4.99% of the number of ordinary shares outstanding notwithstanding the ordinary shares issuable upon exercise of this warrant. HealthCap GP is the sole general partner of HealthCap. The address of HealthCap and HealthCap GP is 18, Avenue d'Ouchy, 1006 Lausanne, Switzerland.

(6) Based on the information disclosed in a Schedule 13G/A filed with the SEC on February 14, 2019 by Armistice Capital, LLC, Armistice Capital Master Fund Ltd. and Steven Boyd, in which each reporting person reported shares voting and dispositive power with respect to 2,878,000 ordinary shares. The address of Armistice Capital, LLC and Mr. Boyd is 510 Madison Avenue, 7th Floor, New York, New York 10022 and the address for Armistice Capital Master Fund Ltd. is c/o dms Corporate Services Ltd., 20 Genesis Close, P.O. Box 314, Grand Cayman KY1-1104, Cayman Islands.

(7) Based on the information disclosed in a Schedule 13G/A filed with the SEC on February 13, 2019 by Broadfin Capital, LLC ("Broadfin Capital"), Broadfin Healthcare Master Fund, Ltd. ("Broadfin Fund") and Kevin Kotler, in which each reporting person reported shared voting and dispositive power with respect to 2,821,722 ordinary shares. The address of Broadfin Capital and Mr. Kotler is Broadfin Capital, 300 Park Avenue, 25th floor, New York, NY 10022. The address of Broadfin Fund is 20 Genesis Close, Ansbacher House, Second Floor, PO Box 1344, Grand Cayman KY1-1108, Cayman Islands.

(8) This number includes 56,447 ordinary shares that are subject to options that are or will vest and become exercisable within 60 days.

(9) This number includes 17,584 ordinary shares that are subject to options that are or will vest and become exercisable within 60 days.

(10) This number includes 15,812 ordinary shares that are subject to options that are or will vest and become exercisable within 60 days.

(11) This number includes 0 ordinary shares that are subject to options that are or will vest and become exercisable within 60 days.

(12) This number includes 3,333 ordinary shares that are subject to options that are or will vest and become exercisable within 60 days.

Equity Compensation Plan Information

The table below sets forth information with respect to ordinary shares that may be issued under our equity compensation plans issued as of December 31, 2018:

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a))
	(a)	(b)	(c)
Equity compensation plans approved by security holders	5,217,839 [1]	$ 5.35	218,171
Equity compensation plans not approved by security holders[3]	1,852,431 [2]	5.59	638,200
Total	7,070,270		856,371

(1) This number includes the following: (i) 4,390,476 ordinary shares subject to outstanding awards granted under the 2015 Equity Compensation Plan as of December 31, 2018, of which 4,275,376 ordinary shares were subject to outstanding stock options and 115,100 ordinary shares were subject to outstanding restricted stock unit awards; and (ii) 827,363 ordinary shares were subject to outstanding awards granted in the form of options under the Non-Employee Director Equity Compensation Plan as of December 31, 2018.

(2) This number represents ordinary shares subject to outstanding awards granted under the 2017 Inducement Plan, of which 1,824,431 ordinary shares were subject to outstanding stock options and 28,000 ordinary shares were subject to outstanding restricted stock unit awards as of December 31, 2018.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

Related Party Transactions

On October 6, 2017, we sold 4,000,000 ordinary shares in a public offering. Two of our existing shareholders holding in excess of 5% of our outstanding shares prior to the public offering, Armistice Capital LLC and Broadfin Capital LLC, purchased shares in the public offering for $6.0 million and $2.5 million, respectively.

On January 25, 2018, we sold 5,000,000 ordinary shares in a public offering. One of our existing shareholders holding in excess of 5% of our outstanding shares prior to the public offering, Broadfin Capital LLC, purchased shares in the public offering for $2.0 million.

Policies and Procedures for Related Party Transactions

We have adopted a policy that our executive officers, directors, nominees for election as a director, beneficial owners of more than 5% of any class of our voting securities and any members of the immediate family of any of the foregoing persons are not permitted to enter into a related person transaction with us without the prior consent of our audit committee. Any request for us to enter into a transaction with an executive officer, director, nominee for election as a director, beneficial owner of more than 5% of any class of our voting securities or any member of the immediate family of any of the foregoing persons, in which the amount involved exceeds $120,000 and such person would have a direct or indirect material interest, must first be presented to our audit committee for review, consideration and approval. In approving or rejecting any such proposal, our audit committee is to consider the material facts of the transaction, including, but not limited to: the benefits to the Company; the impact on a director's independence in the event the transaction involves a director, an immediate family member of a director or an entity in which a director is a general partner, shareholder or executive officer; the availability of other sources for comparable products or services; the terms

of the transaction; and the terms available to unrelated third parties or to employees generally. All of the transactions described above were entered into prior to the adoption of such policy, but after presentation, consideration and approval by our board of directors.

Director Independence

Based upon information requested from and provided by each director concerning their background, employment and affiliations, including family relationships, our board of directors has determined that each of Messrs. Johnson and Kollender and Drs. Kong, Sherman, Steen and Steineger, representing six of our seven directors, is independent under the applicable rules and regulations of Nasdaq. In making such determinations, the board of directors considered the relationships that each such non-employee director has with the Company and all other facts and circumstances the board of directors deemed relevant in determining their independence.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Principal Accountant Fees and Services

The following table sets forth the aggregate fees billed by Ernst & Young our independent registered public accounting firm as described below:

	2018	2017
Fee Category:	(in thousands)	
Audit Fees[1]	$ 730	$ 582
Audit-Related Fees[2]	144	162
Tax Fees[3]	—	—
All Other Fees	—	—
Total Fees	$ 874	$ 744

(1) Audit fees consist of fees for the audit of our financial statements, the review of our interim financial statements and statutory audits.

(2) Audit-related fees included fees for consultations concerning financial and accounting matters not classified as audit services.

(3) Tax fees consists of fees incurred for tax compliance, tax advice and tax planning and includes fees for tax return preparation and tax consulting.

The aggregate fees included in the Audit Fees are billed for the fiscal year. The aggregate fees included in the Audit-related fees and Tax Fees are fees billed in the fiscal year.

All such accountant services and fees were pre-approved by our audit committee in accordance with the "Pre-Approval Policies and Procedures" described below.

Pre-approval policies and procedures

The audit committee of our board of directors has adopted policies and procedures for the pre-approval of audit and non-audit services for the purpose of maintaining the independence of our independent auditor. We may not engage our independent auditor to render any audit or non-audit service unless either the service is approved in advance by the audit committee, or the engagement to render the service is entered into pursuant to the audit committee's pre-approval policies and procedures.

ITEM 15. EXHIBITS

EXHIBIT INDEX

2.1	Macrilen Acquisition Agreement, dated as of October 31, 2018, between Strongbridge Biopharma plc and Novo Nordisk Healthcare AG (incorporated by reference to Exhibit 2.2 to the Form 8-K (File No. 001-37569) filed with the SEC on October 31, 2018)
2.2	Share Purchase Agreement, dated as of October 31, 2018 between Strongbridge Biopharma plc and Novo Nordisk A/S (incorporated by reference to Exhibit 2.2 to the Form 8-K (File No. 001-37569) filed with the SEC on October 31, 2018)
3.1	Constitution of Strongbridge Biopharma plc (incorporated by reference to Exhibit 3.1 to the Form F-1/A (No. 333-206654) filed with the SEC on September 9, 2015)
3.2	Articles of Association of Strongbridge Biopharma plc (incorporated by reference to Exhibit 3.2 to the Form F-1/A (No. 333-206654) filed with the SEC on September 9, 2015)
10.1	Sublease Agreement, dated March 30, 2015, by and between Insight Pharmaceuticals LLC and Cortendo AB (incorporated by reference to Exhibit 10.1 to the Form F-1 (No. 333-206654) filed with the SEC on August 28, 2015)
10.2	Lease, dated November 21, 2017, by and between Northbrook TC Equities LLC, et. al. as Landlord, and Strongbridge U.S. Inc., as Tenant (incorporated by reference to Exhibit 10.2 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.3	Securities Purchase Agreement, dated December 22, 2016, by and among Strongbridge Biopharma plc and the several purchasers signatory thereto (incorporated by reference to Exhibit 10.1 to the Form 6-K (File No. 001-37569) filed with the SEC on December 23, 2016)
10.4	Asset Purchase Agreement, dated as of May 14, 2015, by and among Cortendo AB, and Aspireo Pharmaceuticals, Ltd. and TVM V Life Science Ventures GmbH & Co. KG (incorporated by reference to Exhibit 10.3 to the Form F-1 (No. 333-206654) filed with the SEC on August 28, 2015)
10.5†	Asset Purchase Agreement, dated December 12, 2016, between Taro Pharmaceutical North America, Inc. and Strongbridge plc (incorporated by reference to Exhibit 10.3 to the Form F-3 (No. 333-215531) filed with the SEC on January 12, 2017)
10.6†	Supply Agreement, dated December 12, 2016, between Taro Pharmaceutical North America, Inc. and Strongbridge plc (incorporated by reference to Exhibit 10.4 to the Form F-3 (No. 333-215531) filed with the SEC on January 12, 2017)
10.7	Amended and Restated Employment Agreement, dated as of October 13, 2017, by and between Strongbridge U.S. Inc. and Matthew Pauls (incorporated by reference to Exhibit 10.7 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.8	Form of Amended and Restated Employment Agreement, dated as of October 13, 2017, by and between Strongbridge U.S. Inc. and certain of its executive officers (incorporated by reference to Exhibit 10.8 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.9	Share Purchase Agreement, dated as of January 12, 2015, by and among Cortendo AB, BioPancreate Inc., Cortendo Invest AB and the Investors listed therein (incorporated by reference to Exhibit 10.10 to the Company's Form F-1 (No. 333-206654) filed with the SEC on August 28, 2015)
10.10	Investors' Rights Agreement, dated as of February 10, 2015, by and among Cortendo AB and the Investors listed therein (incorporated by reference to Exhibit 10.11 to the Company's Form F-1 (No. 333-206654) filed with the SEC on August 28, 2015)
10.11	Share Purchase Agreement, dated as of May 14, 2015, by and among Cortendo AB, BioPancreate Inc., Cortendo Invest AB and the Investors named therein (incorporated by reference to Exhibit 10.12 to the Company's Form F-1 (No. 333-206654) filed with the SEC on August 28, 2015)
10.12	Form of Indemnification Agreement (incorporated by reference to Exhibit 10.13 to the Company's Form F-1/A (No. 333-206654) filed with the SEC on September 25, 2015)
10.13*	Strongbridge Biopharma plc 2015 Equity Compensation Plan.
10.14*	Strongbridge Biopharma plc Non-Employee Director Equity Compensation Plan
10.15*	Strongbridge Biopharma plc 2017 Inducement Plan

10.16	Form of Incentive Stock Option Award Agreement under the Strongbridge Biopharma plc 2015 Equity Compensation Plan (incorporated by reference to Exhibit 10.16 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.17	Form of Nonqualified Stock Option Award Agreement under the Strongbridge Biopharma plc 2015 Equity Compensation Plan (incorporated by reference to Exhibit 10.17 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.18	Form of Restricted Stock Unit Award Agreement under the Strongbridge Biopharma plc 2015 Equity Compensation (incorporated by reference to Exhibit 10.18 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.19	Form of Nonqualified Stock Option Award Agreement under the Strongbridge Biopharma plc Non-Employee Director Equity Compensation Plan (incorporated by reference to Exhibit 10.19 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.20	Form of Stock Option Award Agreement under the Strongbridge Biopharma plc 2017 Inducement Plan (incorporated by reference to Exhibit 10.20 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.21	Form of Restricted Stock Unit Award Agreement under the Strongbridge Biopharma plc 2017 Inducement Plan (incorporated by reference to Exhibit 10.21 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.22	Form of Warrant Securities Agreement, by and among Strongbridge Biopharma plc and the several purchasers signatory thereto (incorporated by reference to Exhibit 10.3 to the Company's Form 6-K (File No. 001-37569) filed with the SEC on December 23, 2016)
10.23	Form of Warrant Securities Agreement, by and among Oxford Finance LLC, Horizon Technology Finance Corporation, the other Lenders listed therein, and Strongbridge Biopharma plc, Cortendo Cayman Ltd, Cortendo AB (publ) and Strongbridge U.S. Inc. (incorporated by reference to Exhibit 10.20 to the Form 20-F (File No. 001-37569) filed with the SEC on April 4, 2017)
10.24†	Term Loan Agreement, dated as of July 14, 2017, by and among Strongbridge U.S. Inc., Strongbridge Biopharma plc, Cortendo AB (publ), Cortendo Cayman Ltd., CRG Servicing LLC, as administrative agent and collateral agent, and the lenders named therein (incorporated by reference to Exhibit 10.1 to the Report on Form 6-K (File No. 001-37569) filed with the SEC on July 17, 2017)
10.25	Securities Purchase Agreement, dated as of July 14, 2017, by and among Strongbridge Biopharma plc, CRG Partners III L.P., CRG Partners III — Parallel Fund "A" L.P., CRG Partners III — Parallel Fund "B" (Cayman) L.P., CRG Partners III (Cayman) Lev AIV I. L.P. and CRG Partners III (Cayman) Unlev AIV I L.P. (incorporated by reference to Exhibit 10.2 to the Report on Form 6-K (File No. 001-37569) filed with the SEC on July 17, 2017)
10.26	Form of Warrant to CR Group Lenders, dated July 14, 2017 (incorporated by reference to Exhibit 10.3 to the Report on Form 6-K (File No. 001-37569) filed with the SEC on July 17, 2017)
10.27	Amendment No. 1 to Securities Purchase Agreement, dated as of December 22, 2016, by and between Strongbridge Biopharma plc and the purchasers named therein (incorporated by reference to Exhibit 10.4 to the Report on Form 6-K (File No. 001-37569) filed with the SEC on July 17, 2017)
10.28††	Amendment No. 1 to Term Loan Agreement, dated January 16, 2018, by and among Strongbridge U.S. Inc., Strongbridge Biopharma plc, Cortendo Cayman Ltd., Strongbridge Ireland Limited, Cortendo AB (Publ), CRG Servicing LLC, as administrative agent and collateral agent, and the lenders listed therein (incorporated by reference to Exhibit 10.29 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.29	Form of Warrant to CR Group Lenders, dated January 16, 2018 (incorporated by reference to Exhibit 10.30 to the Form 10-K (File No. 001-37569) filed with the SEC on March 12, 2018)
10.30	Amendment No. 2 to Term Loan Agreement, dated as of June 6, 2018, by and among and among Strongbridge U.S. Inc., Strongbridge Biopharma Public Limited Company, Cortendo Cayman Ltd., Strongbridge Ireland Limited, Cortendo AB (publ), CRG Servicing LLC, as administrative agent and collateral agent, and the lenders listed therein. (incorporated by reference to Exhibit 10.1 to the Form 10-Q (File No. 001-37569) filed with the SEC on August 8, 2018)
21.1*	Subsidiaries of the Company
23.1*	Consent of Ernst & Young LLP
31.1*	Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1*	Certification of Chief Executive Officer and Chief Financial Officer pursuant to Exchange Act Rules 13a-14(b) and 15d-14(b) and 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS**	XBRL Instance Document
101.SCH**	XBRL Taxonomy Extension Schema Document
101.CAL**	XBRL Taxonomy Extension Calculation Linkbase Document
101.LAB**	XBRL Taxonomy Extension Label Linkbase Document
101.PRE**	XBRL Taxonomy Extension Presentation Linkbase Document
101.DEF**	XBRL Taxonomy Extension Definitions Linkbase Document

* Filed herewith.

† Confidential treatment granted as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

†† Portions of the exhibit are omitted pursuant to a confidential treatment request with the U.S. Securities and Exchange commission.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

STRONGBRIDGE BIOPHARMA PLC

By: /s/ Matthew Pauls
Name: Matthew Pauls
Title: *Chief Executive Officer and Director*

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Matthew Pauls and A. Brian Davis, jointly and severally, his or her attorneys-in-fact, each with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this report has been signed by the following persons on the dates and in the capacities indicated below:

NAME	TITLE	DATE
/s/ Matthew Pauls Matthew Pauls	President and Chief Executive Officer (principal executive officer) and Director	February 27, 2019
/s/ A. Brian Davis A. Brian Davis	Chief Financial Officer (principal financial officer and principal accounting officer) and authorized representative in the United States	February 27, 2019
/s/ John H. Johnson John H. Johnson	Chairman, Director	February 27, 2019
/s/ Richard Kollender Richard S. Kollender	Director	February 27, 2019
/s/ Garheng Kong Garheng Kong	Director	February 27, 2019

/s/ Jeffrey Sherman Jeffrey Sherman	Director	February 27, 2019
/s/ Marten Steen Marten Steen	Director	February 27, 2019
/s/ Hilde Steineger Hilde Steineger	Director	February 27, 2019

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Strongbridge Biopharma plc

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Strongbridge Biopharma Plc. (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations, shareholders' equity and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2015.

Philadelphia, Pennsylvania
February 27, 2019

STRONGBRIDGE BIOPHARMA plc
Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	$ 122,490	$ 57,510
Accounts receivable	1,626	1,584
Inventory	3,946	511
Prepaid expenses and other current assets	4,236	1,208
Total current assets	132,298	60,813
Property and equipment, net	294	15
Intangible assets, net	30,132	35,155
Goodwill	7,256	7,256
Other assets	305	686
Total assets	$ 170,285	$ 103,925
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 1,184	$ 1,247
Accrued liabilities	16,065	11,232
Total current liabilities	17,249	12,479
Long-term debt	—	37,794
Warrant liability	15,513	41,308
Supply agreement liability, noncurrent	24,568	24,258
Total liabilities	57,330	115,839
Commitments and contingencies (Note 9)		
Stockholders' equity (deficit):		
Deferred shares, $1.098 par value, 40,000 shares authorized, issued and outstanding at December 31, 2018 and December 31, 2017	44	44
Ordinary shares, $0.01 par value, 600,000,000 shares authorized at December 31, 2018 and December 31, 2017; 54,122,074 and 40,149,812 shares issued and outstanding at December 31, 2018 and December 31, 2017	541	401
Additional paid-in capital	323,402	230,524
Accumulated deficit	(211,032)	(242,883)
Total stockholders' equity (deficit)	112,955	(11,914)
Total liabilities and stockholders' equity (deficit)	$ 170,285	$ 103,925

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

STRONGBRIDGE BIOPHARMA plc
Consolidated Statements of Operations
(In thousands, except share and per share data)

	Year Ended December 31,		
	2018	2017	2016
Revenues:			
Net product sales	$ 18,027	$ 7,046	$ —
Total revenues	18,027	7,046	—
Cost and expenses:			
Cost of sales (excluding amortization of intangible assets)	3,986	1,483	—
Selling, general and administrative	63,336	36,292	14,875
Research and development	25,441	17,268	20,023
Amortization of intangible assets	7,187	5,022	—
Impairment of intangible asset	-	20,723	15,828
Total cost and expenses	99,950	80,788	50,726
Operating loss	(81,923)	(73,742)	(50,726)
Other income (expense), net:			
Unrealized gain (loss) on fair value of warrants	16,337	(30,218)	638
Interest expense	(12,515)	(4,313)	(20)
Foreign exchange loss	(47)	(41)	(69)
Loss on extinguishment of debt	(21,549)	(3,545)	—
Gain on sale of subsidiary	130,832	—	—
Other income (expense), net	1,252	147	(1,180)
Total other income (expense), net	114,310	(37,970)	(631)
Income (loss) before income taxes	32,387	(111,712)	(51,357)
Income tax (expense) benefit	(536)	(1,771)	2,638
Net income (loss)	31,851	(113,483)	(48,719)
Net income (loss) attributable to non-controlling interest	—	—	122
Net income (loss) attributable to Strongbridge Biopharma	$ 31,851	$ (113,483)	$ (48,597)
Net income (loss) attributable to ordinary shareholders:			
Basic	$ 31,851	$ (113,483)	$ (48,597)
Diluted	$ 15,514	$ (113,483)	$ (49,236)
Net income (loss) per share attributable to ordinary shareholders:			
Basic	$ 0.69	$ (3.11)	$ (2.26)
Diluted	$ 0.31	$ (3.11)	$ (2.27)
Weighted-average shares used in computing net loss per share attributable to ordinary shareholders:			
Basic	46,297,088	36,544,825	21,550,353
Diluted	49,724,503	36,544,825	21,655,564

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

STRONGBRIDGE BIOPHARMA plc
Consolidated Statements of Shareholders' Equity (Deficit)
(In thousands except share amounts)

	Ordinary Shares		Deferred Shares		Additional Paid-In	Accumulated	Non-Controlling	Total Shareholders' (Deficit)
	Shares	Amount	Shares	Amount	Capital	Deficit	Interest	Equity
Balance—December 31, 2015	21,205,382	$ 212	40,000	$ 44	$ 170,910	$ (80,803)	$ 564	$ 90,927
Net loss	—	—	—	—	—	(48,597)	(122)	(48,719)
Stock-based compensation	—	—	—	—	4,606	—	—	4,606
Acquisition of non-controlling interest	—	—	—	—	(972)	—	(442)	(1,414)
Issuance of shares, net of offering costs	14,000,000	140	—	—	20,430	—	—	20,570
Exercise of stock options	129,644	1	—	—	119	—	—	120
Issuance of warrants related to the loan agreement	—	—	—	—	882	—	—	882
Balance—December 31, 2016	35,335,026	$ 353	40,000	$ 44	$ 195,975	$ (129,400)	$ —	$ 66,972
Net loss	—	—	—	—	—	(113,483)	—	(113,483)
Stock-based compensation	—	—	—	—	5,167	—	—	5,167
Issuance of shares, net of offering costs	4,429,799	44	—	—	26,340	—	—	26,384
Issuance of shares in connection with at-the-market facility, net of costs	10,300	*	—	—	73	—	—	73
Exercise of stock options	196,081	2	—	—	624	—	—	626
Exercise of warrants	178,606	2	—	—	(2)	—	—	—
Issuance of warrants related to loan agreements, net	—	—	—	—	2,347	—	—	2,347
Balance—December 31, 2017	40,149,812	$ 401	40,000	$ 44	$ 230,524	$ (242,883)	$ —	$ (11,914)
Net income	—	—	—	—	—	31,851	—	31,851
Stock-based compensation	—	—	—	—	7,807	—	—	7,807
Issuance of shares, net of offering costs	5,255,683	53	—	—	33,455	—	—	33,508
Issuance of shares to Novo	5,242,000	52	—	—	22,331	—	—	22,383
Issuance of shares to CRG	656,929	7	—	—	2,798	—	—	2,805
Issuance of shares in connection with at-the-market facility, net of costs	1,281,903	13	—	—	8,583	—	—	8,596
Exercise of warrants	1,384,062	14	—	—	10,619	—	—	10,633
Issuance of warrants related to loan agreements	—	—	—	—	7,663	—		7,663
Exercise of stock options	50,654	*	—	—	96	—	—	96
Ordinary shares issued, net of shares withheld for employee taxes	101,031	1	—	—	(474)	—	—	(473)
Balance—December 31, 2018	54,122,074	$ 541	40,000	$ 44	$ 323,402	$ (211,032)	—	$ 112,955

* Represents an amount less than $1.

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

STRONGBRIDGE BIOPHARMA plc
Consolidated Statements of Cash Flow
(In thousands)

	Year Ended December 31,		
	2018	**2017**	**2016**
Cash flows from operating activities:			
Net income (loss)	$ 31,851	$ (113,483)	$ (48,719)
Adjustments to reconcile net income (loss) to net cash used in operating activities:			
Change in fair value of warrant liability	(16,337)	30,218	(638)
Impairment of intangible asset	-	20,723	15,828
Stock-based compensation	7,807	5,167	4,606
Amortization of intangible assets	7,187	5,022	—
Interest and related guarantee fees paid in kind	-	896	—
Amortization of debt discounts and debt issuance costs	1,484	482	—
Loss on extinguishment of debt	21,549	3,545	—
Gain on sale of subsidiary	(130,832)	—	—
Deferred income tax expense (benefit)	-	1,958	(2,884)
Depreciation	46	10	10
Impairment/loss on investment in Antisense Therapeutics	—	—	550
Changes in operating assets and liabilities:			
Accounts receivable	(42)	(1,584)	—
Inventory	(3,437)	(511)	—
Prepaid expenses and other current assets	(3,028)	(444)	848
Other assets	381	(536)	(88)
Accounts payable	(63)	158	(1,702)
Accrued liabilities and other liabilities	(1,142)	3,043	475
Net cash used in operating activities	(84,576)	(45,336)	(31,714)
Cash flows from investing activities:			
Payment for acquisitions	(24,655)	(7,500)	(3,392)
Purchases of property and equipment	(326)	—	—
Proceeds from sale of subsidiary	159,311	—	—
Net cash provided by (used in) investing activities	134,330	(7,500)	(3,392)
Cash flows from financing activities:			
Proceeds from long-term debt, net	44,930	39,987	19,316
Payment for loss on extinguishment of debt	(9,990)	(1,300)	—
Repayment of long-term debt	(85,000)	(22,261)	—
Proceeds from issuance of ordinary shares, net	33,508	26,384	32,298
Proceeds from share subscription to Novo	22,383	—	—
Proceeds from issuance of ordinary shares in connection with at-the-market offering	8,596	73	—
Proceeds from exercise of warrants	1,176	—	—
Proceeds from exercise of stock options	96	626	120
Payments related to tax withholding for net-share settled equity awards	(473)	—	—
Acquisition of non-controlling interest	-	—	(1,414)
Net cash provided by financing activities	15,226	43,509	50,320
Effect of exchange rate changes on cash and cash equivalents	—	—	—
Net increase (decrease) in cash and cash equivalents	64,980	(9,327)	15,214
Cash and cash equivalents—beginning of period	57,510	66,837	51,623
Cash and cash equivalents—end of period	$ 122,490	$ 57,510	$ 66,837
Supplemental disclosures of cash flow information:			
Cash paid during the year for:			
Interest	$ 11,122	$ 2,935	$ 20
Income taxes other, net of refunds	$ 1	$ 127	$ —
Supplemental non-cash financing activities:			
Issuance of shares to settle debt	$ 2,805	$ —	$ —

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

STRONGBRIDGE BIOPHARMA plc
Notes to Consolidated Financial Statements

1. Organization

We are a global, commercial-stage biopharmaceutical company focused on the development and commercialization of therapies for rare diseases with significant unmet needs.

Our first commercial product is Keveyis (dichlorphenamide), the first and only treatment approved by the U.S. Food and Drug Administration (the "FDA") for hyperkalemic, hypokalemic, and related variants of primary periodic paralysis ("PPP"), a group of rare hereditary disorders that cause episodes of muscle weakness or paralysis.

In January 2018, Strongbridge Ireland Ltd., one of our wholly-owned subsidiaries, acquired the U.S. and Canadian rights to Macrilen (macimorelin), the first and only oral drug approved by the FDA for the diagnosis of patients with adult growth hormone deficiency. We launched Macrilen in the United States in July 2018. In December 2018, we sold Strongbridge Ireland Ltd. to Novo Nordisk Healthcare AG ("Novo") for $145 million plus the right to receive tiered royalties on net sales of Macrilen through 2027. In addition, Strongbridge U.S. Inc, another of our wholly-owned subsidiaries, entered into an agreement with Novo Nordisk Inc., subsidiary of Novo ("NNI"), pursuant to which NNI will fund the costs of 23 of our field-based employees to provide full-time ongoing services to NNI, including the promotion of Macrilen in the United States, for a period of three years. Novo also purchased 5.2 million of our ordinary shares at a purchase price of $7.00 per share

We have two clinical-stage product candidates for rare endocrine diseases, Recorlev and veldoreotide. Recorlev (levoketoconazole) is a cortisol synthesis inhibitor currently being studied for the treatment of endogenous Cushing's syndrome. Veldoreotide is a next-generation somatostatin analog being investigated for potential applications in conditions amenable to somatostatin receptor activation, such as acromegaly. Both Recorlev and veldoreotide have received orphan designation from the FDA and the European Medicines Agency ("EMA").

Liquidity

We believe that our cash resources of $122.5 million at December 31, 2018 will be sufficient to allow us to fund planned operations for at least 12 months beyond the issuance date of these financial statements.

We may never achieve profitability, and unless and until we do, we will continue to need to raise additional capital. We plan to continue to fund our operations and capital funding needs through equity or debt financing along with revenues from Keveyis and royalty income from Macrilen. There can be no assurances, however, that additional funding will be available on terms acceptable to us.

2. Summary of significant accounting policies and basis of presentation

Basis of presentation and principles of consolidation

The accompanying consolidated financial statements include the accounts of our wholly owned subsidiaries, Strongbridge U.S. Inc. (Trevose, Pennsylvania, United States), Strongbridge Dublin Limited (Dublin, Ireland), Cortendo AB (Gothenburg, Sweden) and Cortendo Cayman (Georgetown, Cayman Islands). All intercompany balances and transactions have been eliminated in consolidation. These audited consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the FASB.

Revenue recognition

We follow ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"), effective for revenue accounting. Topic 606 applies to all contracts with customers, except for contracts that are within the scope of other

standards, such as leases, insurance, collaboration arrangements and financial instruments. Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We apply the five-step model to contracts only when it is probable that we will collect the consideration we are entitled to receive in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract, determine those that are performance obligations, and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For a complete discussion of accounting for net product revenue, see Note 3.

Inventory and cost of sales

Inventory is stated at the lower of cost or net realizable value where cost is determined using the first-in, first-out method. Our inventory consists of only finished goods.

Cost of sales includes the cost of inventory sold, which includes third-party acquisition costs, third-party warehousing and product distribution charges.

Foreign currency translation

The consolidated financial statements are reported in United States dollars, which is the functional currency of our subsidiaries. Transactions in foreign currencies are remeasured into our functional currency at the rate of exchange prevailing at the date of the transaction. Any monetary assets and liabilities arising from these transactions are remeasured into our functional currency at exchange rates prevailing at the balance sheet date or on settlement. Resulting gains and losses are recorded in foreign exchange loss in our consolidated statements of operations.

Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires us to make estimates and assumptions that affect the reported amounts in the financial statements and accompanying notes. We must apply significant judgment in this process. Actual results could materially differ from those estimates.

Cash and cash equivalents

We consider all short-term highly liquid investments with an original maturity at the date of purchase of three months or less to be cash equivalents. Cash and cash equivalents consist of account balances at banks and money market accounts, respectively.

Concentration of credit risk and other risks and uncertainties

As part of our cash and investment management processes, we perform periodic evaluations of the credit standing of the financial institutions with which we deposit our cash or purchase cash equivalents, and we have not sustained any credit losses from instruments held at these financial institutions.

Fair value of financial instruments

Fair value accounting is applied for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually).

We are required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. FASB ASC Topic 820, *Fair Value Measurements and Disclosures* ("ASC 820"), establishes a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of us. Unobservable inputs are inputs that reflect our assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described as follows:

Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that we have the ability to access at the measurement date.

Level 2—Valuations based on quoted prices for similar assets or liabilities, or quoted prices in markets that are not active, and for which all significant inputs are observable, either directly or indirectly.

Level 3—Valuations that require inputs that reflect our own assumptions that are both significant to the fair value measurement and unobservable. To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment we exercise in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

In December 2016, we issued warrants in connection with our private placement of ordinary shares. Pursuant to the terms of the warrant agreement, the Company could be required to settle the warrants in cash in the event of an acquisition of the Company and, as a result, the warrants are required to be measured at fair value and reported as a liability in the consolidated balance sheet. We recorded the fair value of the warrants upon issuance using the Black-Scholes Model and are required to revalue the warrants at each reporting date with any changes in fair value recorded on our statement of operations. The valuation of the warrants is considered under Level 3 of the fair value hierarchy due to the need to use assumptions in the valuation that that are both significant to the fair value measurement and unobservable. The change in the fair value of the Level 3 warrant liabilities is reflected in the statement of operations for the years ended December 31, 2018, 2017 and 2016.

Property and equipment, net

Property and equipment, net, consists of office equipment such as furniture, fixtures and computers. Depreciation expense for the years ended December 31, 2018 and 2017 was not significant. The following useful lives were used for the various classifications of property and equipment, net:

	Amortization Periods
Computer hardware	3 - 5 years
Computer software	2 - 5 years
Furniture and fixtures	2 - 5 years
Leasehold improvements	Lesser of useful life or remaining lease term

Intangible assets

Certain intangible assets were acquired as part of an asset purchase and have been capitalized at their acquisition date fair value. Acquired definite life intangible assets are amortized using the straight-line method over their respective estimated useful lives. The Company evaluates the potential impairment of intangible assets if events or

changes in circumstances indicate that the carrying amount of the assets may not be fully recoverable or that the useful lives of these assets are no longer appropriate.

Purchased identifiable intangible assets with indefinite lives are evaluated for impairment annually in accordance with our policy and whenever events or changes in circumstances indicate that it is more likely than not that the fair value of these assets may not be recovered.

Goodwill

We test goodwill for impairment on an annual basis or whenever events occur that may indicate possible impairment. This analysis requires us to make a series of critical assumptions to (1) evaluate whether any impairment exists and (2) measure the amount of impairment.

Because we have one operating segment, when testing for a potential impairment of goodwill, we are required to estimate the fair value of our business and determine the carrying value. If the estimated fair value is less than the carrying value of our business, then we are required to estimate the fair value of all identifiable assets and liabilities in a manner similar to a purchase price allocation for an acquired business. Only after this process is completed can the goodwill impairment be determined, if any.

To estimate the fair value of the business, primarily a market-based approach is applied, utilizing our public market value. We did not record a charge for impairment for our goodwill for the years ended December 31, 2018, 2017, and 2016.

Research and development expenses

Research and development costs are expensed as incurred. Research and development expenses consist of internal and external expenses. Internal expenses include compensation and related expenses. External expenses include development, clinical trials, report writing, and regulatory compliance costs incurred with clinical research organizations and other third-party vendors. At the end of the reporting period, we compare payments made to third-party service providers to the estimated progress toward completion of the research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the progress that we estimate has been made as a result of the service provided, we may record net prepaid or accrued expense relating to these costs. Upfront and milestone payments made to third parties who perform research and development services on our behalf are expensed as services are rendered.

Stock-based compensation

We account for stock-based compensation awards in accordance with Financial Accounting Standards Board ("FASB") ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments including grants of stock options and restricted stock and modifications to existing stock options, to be recognized in the consolidated statements of operations based on their fair values.

Our stock-based awards are subject to either service-based or performance-based vesting conditions. Vesting of certain awards could also be accelerated upon achievement of defined market-based vesting conditions. Certain awards also contain a combination of service and market conditions or performance and market conditions.

We record compensation expense for service-based awards over the vesting period of the award on a straight-line basis. Compensation expense related to awards with performance-based vesting conditions is recognized over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable. For those awards in which the performance condition was the completion of our IPO, we did not recognize compensation expense until the close of the IPO as we did not deem the IPO probable until it occurred.

Compensation expense for awards with service and market-based vesting conditions is recognized using the accelerated attribution method over the shorter of the requisite service period or the implied period associated with achievement of the market-based vesting provisions.

We estimate the fair value of our awards with service conditions using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including (i) the expected stock price volatility, (ii) the expected term of the award, (iii) the risk-free interest rate and (iv) expected dividends. Due to the lack of historical and implied volatility data of our ordinary shares, we based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. We selected companies with comparable characteristics to us, including enterprise value, risk profiles and position within the industry, and with historical share price information sufficient to meet the expected term of the stock-based awards. We compute historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards.

We estimate the fair value of our awards with market conditions using a Monte Carlo simulation to determine the probability of satisfying the market condition. We make this estimate using the conditions that exist at the grant date. The derived service period, which may be the requisite service period, is also determined at this time. Compensation cost for our awards with a market condition is recognized ratably using the accelerated attribution method if the award is subject to graded vesting over the requisite service period. The compensation cost for our awards with a market condition is not reversed if the market condition is not satisfied.

We have estimated the expected term of employee service-based stock options using the "simplified" method, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option, due to our lack of sufficient historical data. We have estimated the expected term of employee awards with market conditions using a Monte-Carlo simulation model. This approach involves generating random stock-price paths through a lattice-type structure. Each path results in a certain financial outcome, such as accelerated vesting or specific option payout. We have estimated the expected term of nonemployee service- and performance-based awards based on the remaining contractual term of such awards.

The risk-free interest rates for periods within the expected term of the option are based on the U.S. Treasury Bond rate with a maturity date commensurate with the expected term of the associated award. We have never paid dividends and do not expect to pay dividends in the foreseeable future.

We account for forfeitures as they occur.

Income taxes

On December 22, 2017, the U.S. government enacted comprehensive tax legislation commonly referred to as the Tax Cuts and Jobs Act (the "Tax Act"). The Tax Act makes broad and complex changes to the U.S. tax code, including, but not limited to, reducing the top U.S. federal corporate tax rate from 35 percent to 21 percent; requiring companies to pay a one-time transition tax on certain un-repatriated earnings of foreign subsidiaries; generally eliminating U.S. federal income taxes on dividends from foreign subsidiaries; requiring a current inclusion in U.S. federal taxable income of certain earnings of controlled foreign corporations; eliminating the corporate alternative minimum tax ("AMT") and changing how existing AMT credits can be realized; creating the base erosion anti-abuse tax ("BEAT"), a new minimum tax; creating a new limitation on deductible interest expense; and changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017.

The Tax Act reduces our U.S. corporate income tax rate from 34% to 21%, effective January 1, 2018. 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 reverse. As a result of the reduction in the U.S. corporate income tax rate from 34% to 21% under the Tax Act, we revalued our ending net deferred tax assets and liabilities at December 31, 2017.

The Tax Act provided for a one-time transition tax on the deemed repatriation of post-1986 undistributed foreign subsidiary earnings and profits ("E&P"). Strongbridge did not have to recognize any income tax expense related to the transition tax as they own no controlled foreign corporations.

The global intangible low-taxed income tax and base erosion provisions are effective for taxable years beginning after December 31, 2017. The Company does not currently expect these provisions to have a material impact on its tax rate as they do not own any controlled foreign corporations and they are currently below the gross receipts threshold for purposes of the base erosion provisions.

In accordance with Staff Accounting Bulletin No. 118 ("SAB 118"), the Company has finalized the accounting for the Tax Act and has recorded no additional amount during the current year.

We recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2018, 2017 and 2016, we had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in our statements of operations.

Net income (loss) per share

Basic net income (loss) per share is calculated by dividing the net income (loss) attributable to shareholders by the weighted-average number of ordinary shares outstanding during the period. Diluted net income (loss) per share is calculated by dividing the net income (loss) attributable to shareholders by the weighted-average number of ordinary shares outstanding for the period, including any dilutive effect from outstanding stock options and other equity-based awards.

Net income (loss) per share was calculated as follows for the periods indicated below:

	Year Ended December 31,		
(in thousands, except per share data)	**2018**	**2017**	**2016**
Basic Net Income (Loss) Per Share			
Basic net income (loss)	$ 31,851	$ (113,483)	$ (48,597)
Weighted-average ordinary shares outstanding	46,297,088	36,544,825	21,550,353
Basic net income (loss per share)	$ 0.69	$ (3.11)	$ (2.26)
Diluted Net Income (Loss) Per Share			
Diluted net income (loss)	$ 15,514	$ (113,483)	$ (49,236)
Weighted-average ordinary shares outstanding	46,297,088	36,544,825	21,550,353
Dilutive warrants, stock options and RSUs	3,427,415	-	105,211
Weighted-average shares used to compute diluted net income (loss) per share	49,724,503	36,544,825	21,655,564
Diluted net income (loss) per share	$ 0.31	$ (3.11)	$ (2.27)

Shares used in the diluted net loss per share calculations exclude anti-dilutive ordinary share equivalents, which consist of outstanding stock options, unvested restricted stock units and warrants, if applicable.

	Year Ended December 31,		
	2018	**2017**	**2016**
Warrants	1,642,539	7,555,003	7,000,000
Stock options issued and outstanding	4,444,830	6,104,715	3,249,784
Unvested RSUs	—	267,250	184,000

Recently issued accounting pronouncements

In January 2017, the FASB issued Accounting Standards Update ("ASU") 2017-04, *Intangibles - Goodwill and Other*: *Simplifying the Accounting for Goodwill Impairment*. ASU 2017-04 removes Step 2 of the goodwill impairment test, which requires a hypothetical purchase price allocation. A goodwill impairment will now be the amount by which a reporting unit's carrying value exceeds its fair value, not to exceed the carrying amount of goodwill. This standard,

which will be effective for us beginning in the first quarter of fiscal year 2020, is required to be applied prospectively. Early adoption is permitted for interim or annual goodwill impairment tests performed on testing dates after January 1, 2017. We are currently evaluating the impact this new accounting guidance will have on our consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases*, that requires lessees to recognize leases on-balance sheet and disclose key information about leasing arrangements. The new standard establishes a right-of-use ("ROU") model that requires a lessee to recognize a ROU asset and lease liability on the balance sheet for all leases with a term longer than 12 months. Leases will be classified as finance or operating, with classification affecting the pattern and classification of expense recognition in the income statement. The standard is effective on January 1, 2019, with early adoption permitted. We adopted the new standard on January 1, 2019 and use the effective date as our date of initial application. In July 2018, the FASB issued an update that provided an additional transition option that allows companies to continue applying the guidance under the lease standard in effect at that time in the comparative periods presented in the consolidated financial statements. Companies that elect this option would record a cumulative-effect adjustment to the opening balance of retained earnings on the date of adoption. We elected this optional transition method. We also elected the "package of practical expedients", which permits us not to reassess under the new standard our prior conclusions about lease identification, lease classification and initial direct costs. We continue to evaluate other practical expedients available under the standard.

We have substantially completed our assessment of the standard. We continue to finalize our calculations, including our discount rate assumptions, related to the new standard. We are also continuing to establish new processes and internal controls that may be required to comply with the new lease accounting and disclosure requirements set by the new standard.

We expect the impact of the standard adoption to increase our assets and liabilities no more than 5% within our consolidated balance sheet as a result of the recognition of new ROU assets and liabilities in accordance with the new leasing standard.

3. Revenue recognition

Product revenue, net

We launched our second commercial product, Macrilen, in July 2018. Our product sales result from sales of Keveyis and Macrilen. We will no longer record product sales of Macrilen following its sale to Novo in December 2018. We recognize net product sales at the time our products are received by our customers (primarily wholesalers and specialty pharmacies). The products are subsequently sold to patients, who are covered by payors that may provide for government-mandated or privately negotiated rebates with respect to the purchase of our products.

Disaggregation of Revenue

The following table summarizes revenue by product for the twelve months ended December 31, 2018 and 2017 (in thousands):

	Twelve Months Ended December 31, 2018	Twelve Months Ended December 31, 2017
Products		
Keveyis	$ 16,802	$ 7,046
Macrilen	1,225	—
Total	$ 18,027	$ 7,046

Reserves for variable consideration

Revenues from sales of our products are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and that result from rebates, co-pay assistance and other allowances that are offered by us and the patients' payors. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount is payable to our customer) or a current liability (if the amount is payable to a party other than our customer). Where appropriate, these estimates may take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. We reassess our estimates on an ongoing basis. If actual results in the future vary from our estimates, we will adjust our estimates. Any such adjustments would affect net product revenue and earnings in the period such variances become known.

Trade discount: Our contracts with our customers provide for a discount, that is recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we receive sales order management, data and distribution services from our customers. To the extent the services received are distinct from our sale of products to our customers, these payments are classified in selling, general and administrative expenses in our consolidated statement of operations.

Prompt Pay Discount: We offer cash discounts to our customers, generally 2% of the sales price, as an incentive for prompt payment. We estimate for cash discounts using the most likely amount method by reducing accounts receivable by the prompt pay discount amount. The discount is recognized as a reduction of revenue in the same period as the related revenue.

Funded Co-pay Assistance Program: We contract with a third-party to manage the co-pay assistance program intended to provide financial assistance to qualified insured patients. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that we expect to receive associated with the product that has been recognized as revenue but remains in the distribution channel inventories at the end of each reporting period. These payments are consideration payable to our customers and the related reserve is recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses on the consolidated balance sheet.

Government rebates: We are subject to discount obligations under state Medicaid programs and Medicare. We estimate our Medicaid and Medicare rebates based upon a range of possible outcomes that are probability-weighted for the estimated patient mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability, which is included in accrued expenses on the consolidated balance sheet. For Medicaid, accruals are based on estimates of future Medicaid beneficiary utilization applied to the Medicaid unit rebate formula established by the Center for Medicaid and Medicare Services. Effective January 1, 2011, manufacturers of pharmaceutical products are responsible for 50% of the patient's cost of branded prescription drugs related to the Medicare Part D Coverage Gap. In order to estimate the cost to us of this Medicare coverage gap responsibility, we estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. Our liability for these rebates consists of estimates of claims for the current quarter and estimated future claims that will be made that have been recognized as revenue but remain in the distribution channel inventories at the end of each reporting period.

Temporary Supply and Patient Assistance Programs: We provide free product to uninsured patients who satisfy pre-established criteria for either the Temporary Supply Program for Keveyis or the Patient Assistance Program for Keveyis. Patients who meet the Temporary Supply Program eligibility criteria may receive a temporary supply of free Keveyis for no more than sixty days while we determine the patient's third-party insurance, prescription drug benefit or

other third-party coverage for Keveyis. The Patient Assistance Program provides free Keveyis for up to twelve months to patients who satisfy pre-established criteria for financial need. We do not recognize any revenue related to these free products and the associated costs are classified in selling, general and administrative expenses in our consolidated statements of operations.

4. Fair value measurement

The following table sets forth the fair value measurements by level within the fair value hierarchy, that are measured on a recurring basis. Our level 3 instrument consist of the ordinary share warrant liability. The fair values of the outstanding warrants were measured using the Black-Scholes option-pricing model. Inputs used to determine estimated fair value of the warrant liabilities include the estimated fair value of the underlying stock at the valuation date, the estimated term of the warrants, risk-free interest rates, expected dividends and the expected volatility of the underlying stock. The significant unobservable inputs used in the fair value measurement of the warrant liabilities were the volatility rate and the estimated term of the warrants. Generally, increases (decreases) in the fair value of the underlying stock and estimated term would result in a directionally similar impact to the fair value measurement.

The following table presents the Company's assets and liabilities that are measured at fair value on a recurring basis for the periods presented (in thousands):

	As of December 31, 2018			
	Level I	Level II	Level III	Total
Cash equivalents	122,300	—	—	122,300
Total assets	$ 122,300	$ —	$ —	$ 122,300
Warrant liability	—	—	15,513	15,513
Total liabilities	$ —	$ —	$ 15,513	$ 15,513

	As of December 31, 2017			
	Level I	Level II	Level III	Total
Cash equivalents	57,024	—	—	57,024
Total assets	$ 57,024	$ —	$ —	$ 57,024
Warrant liability	—	—	41,308	41,308
Total liabilities	$ —	$ —	$ 41,308	$ 41,308

5. Intangible assets and goodwill

The gross carrying amount of in-process research and development, acquired developed product rights and goodwill is as follows (in thousands):

	As of December 31, 2018				
	Beginning of Period	Additions	Sold	Amortization	End of Period
Keveyis	$ 35,155	$ —	$ —	$ (5,023)	$ 30,132
Macrilen	—	24,834	(22,670)	(2,164)	—
Goodwill	7,256	—	—	—	7,256
Total	$ 42,411	$ 24,834	$ (22,670)	$ (7,187)	$ 37,388

	As of December 31, 2017				
	Beginning of Period	Additions	Impairment	Amortization	End of Period
IPR&D	$ 20,723	$ —	$ (20,723)	$ —	$ —
Keveyis	40,177	—	—	(5,022)	35,155
Goodwill	7,256	—	—	—	7,256
Total	$ 68,156	$ —	$ (20,723)	$ (5,022)	$ 42,411

Estimated amortization of our acquired developed product rights intangible asset for the five years subsequent to December 31, 2018 is as follows (in thousands):

2019	$ 5,022
2020	5,022
2021	5,022
2022	5,022
2023	5,022

Goodwill and in-process research and development resulted from our acquisition of BioPancreate and our 2015 acquisition of veldoreotide from Aspireo Pharmaceuticals, Ltd. In-process research and development is initially measured at its fair value and is not amortized until commercialization. We recorded $20.7 million of impairment relating for our veldoreotide in-process research and development during the year ended December 31, 2017. The significant inputs to the fair value measurement were future revenues expected to be generated, estimated costs to manufacture and appropriate risk-adjusted discount rate. The impairment of veldoreotide was due to estimated increased development costs and longer time lines related to the development process resulting in a decrease in the valuation of our intangible asset.

Our finite lived intangible asset consists of acquired developed product rights obtained from the asset acquisition of Keveyis (dichlorphenamide) from a subsidiary of Taro Pharmaceutical Industries Ltd. (“Taro”). In connection with the Asset Purchase and Supply Agreement we entered into with Taro, we have paid Taro an upfront payment in two installments of $1 million in December 2016 and $7.5 million in March 2017. We concluded that the supply price payable by us exceeds fair value and, therefore, have used a discounted cash flow method with a probability assumption to value the payments in excess of fair value at $29.3 million, for which we have recorded an intangible asset and corresponding liability. This liability will be amortized as we purchase inventory over the term of the agreement. In addition, we incurred transaction costs of $2.4 million resulting in the recording of an Intangible Asset of $40.2 million. This asset began being amortized in 2017 and is being amortized over an 8-year period.

In January 2018, we entered into a License and Assignment Agreement with Aeterna Zentaris GmbH, pursuant to which we acquired the U.S. and Canadian rights to manufacture and commercialize Macrilen (macimorelin) for $24 million and incurred transaction costs of $0.7 million, resulting in an initial intangible of $24.7 million. We recorded any royalty liability as an increase to the intangible asset. This asset was being amortized over a ten-year period using the straight-line method until our sale of the rights to the asset to Novo in December 2018.

6. Accrued liabilities

Accrued liabilities consist of the following (in thousands):

	December 31, 2018	December 31, 2017
Consulting and professional fees	$ 4,145	$ 2,465
Supply agreement - current portion	1,638	4,237
Employee compensation	5,717	3,668
Accrued sales allowances	2,233	742
Accrued royalties	802	—
Other	1,530	120
Total accrued liabilities	$ 16,065	$ 11,232

7. Long-term debt

On January 16, 2018 (the “First Loan Amendment Effective Date”), we and our subsidiaries, Strongbridge U.S. Inc., Strongbridge Ireland Limited, Cortendo AB (publ) and Cortendo Cayman Ltd., entered into an amendment

(the "First Loan Amendment"), to the Term Loan Agreement (the "Loan Agreement"), dated July 14, 2017, with CRG Servicing LLC ("CRG"), as administrative agent and collateral agent, and the lenders named therein (the "Lenders").

The primary purpose of the First Loan Amendment was to increase the total potential borrowing under the Loan Agreement from $50 million to $100 million. The First Loan Amendment provided for (i) an additional disbursement of $45.0 million (the "Second Tranche") to the Company on the First Loan Amendment Effective Date, and (ii) an additional disbursement of $5.0 million (the "Fourth Tranche") to us at our election, contingent upon our achievement of certain revenue milestones and a market capitalization condition on or before December 31, 2018, as described in the First Loan Amendment. Under the First Loan Amendment, we continued to be eligible to borrow up to an additional $10.0 million (the "Third Tranche"), contingent upon our achievement of certain revenue milestones on or before June 30, 2018, as previously provided in the Loan Agreement; provided, however, that under the Loan Agreement, as amended, the Third Tranche would be subject to a market capitalization condition, as described in the First Loan Amendment. As a condition to the addition of the Second Tranche under the First Loan Amendment, we issued to the Lenders on the First Loan Amendment Effective Date warrants to purchase an aggregate of 1,248,250 of our ordinary shares, at an exercise price of $10.00 per share.

On June 6, 2018, we and our subsidiaries, Strongbridge U.S. Inc., Cortendo Cayman Ltd., Strongbridge Ireland Limited and Cortendo AB (publ), entered into a second amendment (the "Second Loan Amendment"), to the Loan Agreement. The primary purposes of the Second Loan Amendment (as requested by the Company) was to reduce the aggregate commitments under the Loan Agreement from $100 million to $95 million and to combine the Third Tranche and the Fourth Tranche under the Loan Agreement into one final borrowing tranche for up to $10 million (the "Final Tranche"). Under the terms of the Second Loan Amendment, the Final Tranche borrowing must occur on or before March 19, 2019. The Final Tranche is subject to the Company's achievement of a certain revenue milestone, which under the Second Loan Amendment must be satisfied on or prior to December 31, 2018, and satisfaction of a market capitalization condition for the 20 consecutive trading days ending on the trading day immediately prior to the Final Tranche borrowing date (as described in the Loan Agreement, as amended).

The amendment in January 2018, resulted in a greater than 10% change in cash flows as compared to the original debt instrument under the First Loan Amendment, the First Loan Amendment was accounted for as a debt extinguishment, which resulted in a $0.5 million loss during year ended December 31, 2018.

In December 2018, we extinguished our outstanding debt of $88.3 million, in which we incurred final payment fees of $12.5 million, wrote-off unamortized debt discounts of $9.4 million which resulted in a loss on early extinguishment of debt of $21.0 million. We also issued CRG 656,259 of our ordinary shares as part of our debt extinguishment.

8. Warrants

Ordinary share warrants are accounted for in accordance with applicable accounting guidance provided in ASC Topic 815*, Derivatives and Hedging — Contracts in Entity's Own Equity* ("ASC Topic 815"), as either derivative liabilities or as equity instruments depending on the specific terms of the warrant agreement.

Warrants outstanding and warrant activity for the year ended December 31, 2018 is as follows:

	Classification	Exercise Price	Expiration Date	Warrants Issued	Warrants Exercised	Warrants Outstanding December 31, 2018
Warrants in connection with private equity placement	Liability	$ 2.50	6/28/2022	7,000,000	(1,970,000)	5,030,000
Warrants in connection with Horizon and Oxford loan agreement	Equity	$ 2.45	12/28/2026	428,571	(267,857)	160,714
Warrants in connection with CRG loan agreement	Equity	$ 7.37	7/14/2024	394,289	—	394,289
Warrants in connection with CRG loan amendment in January 2018	Equity	$ 10.00	1/16/2025	1,248,250	—	1,248,250
				9,071,110		6,833,253

9. Commitments and contingencies

(a) Lease

In March 2015, we entered into a 52-month building sublease agreement for 14,743 square feet of office space in Trevose, Pennsylvania. The lease has annual rent escalations and is recognized on a straight-line basis over the term of the lease. In November 2017, we entered into a 60-month building lease agreement for an additional 7,326 square feet of office space in the same building in Trevose, Pennsylvania. The lease has annual rent escalations. We obtained access to this newly leased space on November 27, 2017, which was considered the lease commencement date for accounting purposes. Thus, rent expense began on this date and is recognized on a straight-line basis over the term of the lease. The lease provides for us the ability to continue leasing its currently subleased office space upon expiration of the sublease described above.

As of December 31, 2018, future minimum commitments under facility operating leases were as follows (in thousands):

	Operating leases
2019	439
2020	470
2021	481
2022	492
2023	207
Total minimum lease payments	$ 2,089

Rent expense recognized under our operating leases was $719,000, $285,000 and $273,000 for the years ended December 31, 2018, 2017 and 2016, respectively.

(b) Commitments to Taro Pharmaceuticals Industries Ltd.

In December 2016, we acquired the U.S. marketing rights to Keveyis (dichlorphenamide) from Taro. Under the terms of an asset purchase agreement, we paid Taro an upfront payment in two installments of $1 million in December 2016 and $7.5 million in March 2017, and will pay an aggregate of $7.5 million in potential milestones upon the achievement of certain product sales targets. Taro has agreed to continue to manufacture Keveyis for us under an exclusive supply agreement through the orphan exclusivity period. We are obligated to purchase certain annual minimum amounts of product totaling approximately $29 million over a six-year period. As of December 31, 2018, our remaining obligation was $22.1 million. The supply agreement may extend beyond the orphan exclusivity period unless terminated by either party pursuant to the terms of the agreement. If terminated by Taro at the conclusion of the orphan exclusivity period, we

have the right to manufacture the product on our own or have the product manufactured by a third party on our behalf. We are required to reimburse Taro for their royalty obligation resulting from their sale of Keveyis to us.

(c) Indemnifications

In the ordinary course of business and in connection with the sale of assets and businesses and other transactions, we often indemnify our counterparties against certain liabilities that may arise in connection with the transaction or that are related to events and activities prior to or following a transaction, such as breaches of contracts, unfavorable tax consequences and employee liabilities. If the indemnified party were to make a successful claim pursuant to the terms of the indemnification, we may be required to reimburse the loss and such amount could be material to our financial statements. Where appropriate, the obligation for such indemnifications is recorded as a liability. Because the amount of these types of indemnifications generally is not specifically stated, the overall maximum amount of the obligation under such indemnifications cannot be reasonably estimated. However, we believe that the likelihood of a material liability being triggered under these indemnification obligations is not probable at this time.

10. Defined contribution plan

Our 401(k) Employee Savings Plan ("401(k) Plan") is available to all employees. We have elected a Safe-Harbor provision for the 401(k) Plan in which participants are always fully vested in their employer contributions. We match 100% of the first 4% of participating employee contributions. In 2018, we contributed approximately $704,000. Our contributions are made in cash. Our ordinary shares are not an investment option available to participants in the 401(k) Plan.

11. Income taxes

For the years ended December 31, 2018, 2017 and 2016, the components of income (loss) before income taxes were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Sweden	$ 4,712	$ (19,249)	$(16,433)
Ireland	73,409	(47,211)	(11,653)
Cayman Islands	(701)	(21,709)	(19,550)
U.S.	(45,033)	(23,543)	(3,721)
Total	$ 32,387	$(111,712)	$(51,357)

The components of income tax expense (benefit) for the years ended December 31, 2018, 2017 and 2016 were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Current tax (benefit) expense:			
Sweden	$ 535	$ —	$ —
Ireland	—	(22)	22
U.S.			
Federal	—	(151)	151
State	1	(14)	73
Total current tax expense (benefit)	$ 536	$ (187)	$ 246
Deferred tax expense (benefit):			
Sweden	$ 12,395	$ (4,586)	$ (834)
Ireland	(13,337)	1,280	(1,547)
U.S.			
Federal	(1,785)	39	(3,412)
State	(354)	(2,392)	(678)
Change in valuation allowance	3,081	7,617	3,587
Total deferred tax expense (benefit)	—	1,958	(2,884)
Total tax expense (benefit)	$ 536	$ 1,771	$ (2,638)

With the exception of Sweden, we have net operating loss carryforwards in all other countries. For the Ireland and Swedish operations, we have not reflected any benefit of net operating loss carryforwards ("NOLs") in the accompanying financial statements. Strongbridge US, Inc., as a result of the intercompany service agreements, was in taxable income and determined they were able to recognize all deferred tax assets in 2016. In 2017, Strongbridge US, Inc. generated book loss as we decided this entity will market and commercialize certain products. As such, given the expenses incurred, it is not more likely than not we will recognize all deferred tax assets which results in us establishing a full valuation allowance against its deferred tax assets. During 2018, we transferred all our intercompany intellectual property to Ireland, resulting in current taxes due in Sweden, the utilization of NOLs in Sweden, which previously had a full valuation allowance, and the creation of amortizable deferred tax assets in Ireland, which have a full valuation allowance.

Deferred taxes are recognized for temporary differences between the bases of assets and liabilities for financial statement and income tax purposes. The tax effect of temporary differences that give rise to significant portions of the deferred tax assets are as follows (in thousands):

	Year Ended December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$ 4,576	$ 28,570
Stock-based compensation	4,944	2,824
Other deferred activity	960	617
Tax credits	10,826	9,182
Interest disallowance	9,889	—
Intangibles	13,240	—
Capitalized research and development costs	—	161
Total deferred tax assets	44,435	41,354
Valuation allowance	(44,435)	(41,354)
Deferred tax assets recognized	—	—

We have evaluated the positive and negative evidence bearing upon the realizability of our deferred tax assets. Based on our history of operating losses, aside from the gain associated with the sale of our subsidiary, we have concluded that it is more likely than not that the benefit of our deferred tax assets will not be realized. The valuation allowance increased by approximately $2.7 million and $7.6 million during the years ended December 31, 2018 and 2017, respectively, due primarily to net operating losses.

Our effective income tax rate differs from the ultimate parent company, Strongbridge Biopharma plc, Irish domestic statutory rate of 12.5% for the year ended December 31, 2018, 2017 and 2016.

	Year Ended December 31,		
	2018	2017	2016
Ireland statutory income tax rate	12.50 %	12.50 %	12.50 %
Foreign tax differential between Sweden, U.S., Cayman Island and Ireland	7.55	3.99	2.28
Federal tax credits	(4.58)	—	—
Change in valuation allowance	9.51	(6.82)	(6.69)
State income taxes	(1.09)	1.43	0.92
Permanent differences	4.01	(5.04)	1.59
Rate change - tax impact	—	(7.09)	—
Foreign exchange remeasurement of Swedish deferred tax asset	—	0.83	(5.42)
Provision to return	3.95	(1.33)	—
Sale of subsidiary	(37.58)	—	—
Net operating loss adjustment	7.72	—	—
Other	(0.34)	(0.06)	(0.04)
Effective income tax rate	1.65 %	(1.59)%	5.14 %

At December 31, 2018, as a result of the transfer of our intellectual property to Ireland, we have no Swedish NOLs and approximately $1.6 million of Irish NOLs, which have an indefinite life, and approximately $13,8 million of U.S. federal and $14.6 million of state NOLs, which begin to expire in 2031. Due to tax reform, federal U.S. net operating losses generated after January 1, 2018 will have an indefinite life. Through December 31, 2015 we operated through a permanent establishment in both Sweden and the United States. As a result of utilizing the Swedish NOLs, we have written off all attributes associated with the prior U.S. branch. At December 31, 2018, we had $10.7 million of U.S. federal orphan drug tax credit carryforwards, which begin to expire in 2032, and $0.2 million of U.S. federal research and development tax credit carryforwards, which begin to expire in 2031. The orphan drug credit carryforward is attributable to the permanent establishment of the Swedish entity within the U.S.

Utilization of the NOLs may be subject to limitations under Swedish tax regulations or U.S. Internal Revenue Code Section 382 if there is a greater than 50% ownership change as determined under applicable regulations.

We file income tax returns in Sweden, Ireland, the United States, and various states within the United States. In the normal course of business, we are subject to examination by federal, state and foreign jurisdictions, where applicable. Our tax years are still open under statute from inception to present. All open years may be examined to the extent that tax credit or net operating loss carryforwards are used in future periods.

12. Ordinary shares

Voting rights and privileges

As of December 31, 2018, and December 31, 2017, there are 600,000,000 authorized shares and 54,122,074 and 40,149,812 outstanding shares, respectively.

The holders of our ordinary shares are entitled to one vote for each ordinary share held at all meetings of shareholders without limitation and written actions in lieu of meetings. The holders are entitled to receive dividends if

and when declared by our Board of Directors. No dividends have been declared or paid since our inception. The holders are entitled to share ratably in our assets available for distribution to stockholders, in the event of any voluntary or involuntary liquidation.

In addition, on May 26, 2015 the Company issued 40,000 deferred shares with a €1.00 par value per share (US$1.098). The deferred shares are issued in order to satisfy an Irish legislative requirement to maintain a minimum level of issued share capital denominated in euro. The deferred shares carry no voting rights and are not entitled to any dividend or distribution.

Equity financings

On December 18, 2018, we sold 5,242,000 shares of our ordinary shares to Novo for $7.00 per share and an aggregate purchase price of $36.7 million. We accounted for the $14.3 million premium paid over the market price of our ordinary shares as additional gain on the sale of our subsidiary.

On January 25, 2018, we sold 5,000,000 ordinary shares in a public offering at a price to the public of $6.75 per ordinary share for net proceeds of approximately $31.7 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

On February 26, 2018, we sold an additional 255,683 ordinary shares as part of our January 2018 public offering at a price of $6.75 per ordinary share for net proceeds of approximately $1.6 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

On October 6, 2017, we sold 4,000,000 ordinary shares in a public offering at a price to the public of $6.25 per ordinary share for net proceeds of approximately $23.4 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

Concurrent with the CRG credit facility from July 2017, CRG purchased 429,799 shares of our ordinary shares at a price of $6.98 per share for total proceeds to us of approximately $3.0 million.

We entered into an equity distribution agreement with JMP Securities LLC ("JMP Securities") on April 28, 2017, pursuant to which we may sell, at our option, from time to time, up to an aggregate of $40 million in ordinary shares of the Company through JMP Securities, as sales agent. We will pay JMP Securities a commission equal to 3% of the gross proceeds from the sale of ordinary shares under the ATM Facility. Pursuant to the terms of the equity distribution agreement, we reimbursed JMP Securities for certain out-of-pocket expenses, including the fees and disbursements of counsel to JMP Securities, incurred in connection with establishing the ATM Facility and have provided JMP Securities with customary indemnification rights. During the year ended December 31, 2018, we sold an aggregate of 1,281,903 ordinary shares under the ATM Facility for net proceeds of approximately $8.6 million and paid fees of $0.3 million to JMP Securities. As December 31, 2018, we have approximately $31.1 million available for sale under our ATM facility.

Shares reserved for issuance

There were 8,579,511 and 6,104,715 ordinary shares reserved for future issuance upon exercise of stock options as of December 31, 2018 and 2017, respectively. As of December 31, 2018, we have 6,833,253 shares reserved for outstanding warrants.

13. Stock-based compensation

Our board of directors has adopted the 2017 Inducement Plan (the "Inducement Plan"). The Inducement Plan provides for the grant of equity-based awards to new employees. The purpose of the Inducement Plan is to attract valued employees by offering them a greater stake in our success and a closer identity with us, and to encourage ownership of our ordinary shares by such employees. The Inducement Plan became effective on February 23, 2017. As of December 31, 2018, 638,200 shares are available for issuance pursuant to the Inducement Plan.

Our board of directors has adopted, and our shareholders have approved, the 2015 Equity Compensation Plan (the "2015 Plan"). The 2015 Plan provides for the grant of incentive stock options to our employees and any parent or subsidiary corporation's employees, and for the grant of nonstatutory stock options, stock awards, and RSUs to our employees, directors and consultants and our parent or subsidiary corporations' employees and consultants. The 2015 Plan became effective on September 3, 2015. As of December 31, 2018, 216,630 shares are available for issuance pursuant to the 2015 Plan.

Our board of directors has adopted, and our shareholders have approved, the Non-Employee Director Equity Compensation Plan (the "Non-Employee Director Plan"). The Non-Employee Director Plan provides for the grant of nonstatutory stock options, stock awards, and RSUs to our non-employee directors. The Non-Employee Director Plan became effective on September 3, 2015. As of December 31, 2018, 1,541 shares are available for issuance pursuant to the Non-Employee Director Plan.

A summary of the outstanding stock options activity for the year ended December 31, 2018 is as follows:

	Options Outstanding			
	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding—January 1, 2018	6,104,715	$ 7.50	7.70	$ 14,021
Granted	2,969,255	$ 6.72		
Forfeited and cancelled	(407,421)	$ 5.95		
Exercised	(87,038)	$ 4.25		
Outstanding—December 31, 2018	8,579,511	$ 7.35	7.57	$ 3,281
Vested and exercisable—December 31, 2018	3,873,952	$ 8.85	6.30	$ 1,427

Included in the stock options outstanding at December 31, 2018 are unvested stock options to purchase 88,908 shares at a weighted-average exercise price of $18.80 per share for which the vesting of certain tranches will accelerate if the fair value per share of our stock reaches $31.46. In addition, the options outstanding include 97,652 shares that vest upon a market appreciation event, so long as it occurs prior to the date specified in the applicable award agreement and 97,652 shares that will vest upon the one-year anniversary of the market appreciation event. The market appreciation event, which had not yet occurred as of December 31, 2018, is defined as the last trading day in the period in which our closing stock price on each of 20 consecutive trading days reported on NASDAQ has been at least $30.14 or $33.66 for the respective grantee.

Stock-based compensation expense

We recognized stock-based compensation expense for employees and non-employees in the accompanying consolidated statements of operations as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Selling, general and administrative	$ 6,012	$ 4,027	$ 4,005
Research and development	1,795	1,140	601
Total stock-based compensation	$ 7,807	$ 5,167	$ 4,606

As of December 31, 2018, the total unrecognized compensation expense related to unvested options was $15.6 million, which we expect to recognize over an estimated weighted-average period of 2.70 years.

In determining the estimated fair value of the stock-based awards, we use the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment.

The fair value of stock option awards was estimated with the following assumptions:

	Year Ended December 31,		
	2018	2017	2016
Expected term (in years)	6.11	5.98	5.9
Risk-free interest rate	2.25% - 3.04%	1.78% - 2.26%	1.21% - 2.23%
Expected volatility	78.2% - 85.0%	78.2% - 85.0%	78.1% - 83.6%
Dividend rate	—%	—%	—%

Our board of directors have approved grants of restricted stock units ("RSUs") to employees. These RSUs vest two years from the date of issuance, provided that the employee is employed by us on such vesting date. All RSUs will fully vest upon a change of control of our company. If and when the RSUs vest, we will issue one ordinary share for each whole RSU that has vested, subject to satisfaction of the employees' tax withholding obligations. The RSUs will cease to be outstanding upon such issuance of ordinary shares. We recorded expense, which is included in the stock-based compensation table above, of $454,000 and $436,000 for the year ended December 31, 2018 and 2017, respectively. As of December 31, 2018, the total unrecognized compensation expense related to unvested RSUs is $0.4 million, which we expect to recognize over an estimated weighted-average period of 0.99 years.

A summary of our unvested RSUs as of December 31, 2018 is as follows:

	Number of Shares
Outstanding—January 1, 2018	267,250
Granted	69,150
Forfeited	(18,300)
Vested	(175,000)
Unvested—December 31, 2018	143,100

14. Segment and other information

Operating segments are identified as components of an enterprise about which separate discreet financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions on how to allocate resources and assess performance. We view our operations and manage our business in one operating segment.

All of our sales were in the United States.

The following table represents total long-lived assets by location (in thousands):

	December 31, 2018	December 31, 2017
United States	$ 294	$ 15
Total long-lived assets (1)	$ 294	$ 15

(1) Long-lived assets consist of property and equipment.

Customer concentration

The following table presents the gross sales from customers that represented more than 10% of our gross sales included in our single operating segment:

	2018	2017
Customer A	92%	100%

15. Sale of Subsidiary

In December 2018, we sold Strongbridge Ireland Ltd, whose only asset was the rights to Macrilen, to Novo for $145 million. As part of the sale, we are entitled to received tiered royalties based on net sales of Macrilen through 2027. In addition, Strongbridge U.S. Inc entered into an agreement with NNI pursuant to which we have agreed to provide 23 field-based employees of Strongbridge U.S. to NNI to provide commercial services related to Macrilen, including the promotion of Macrilen in the United States, for a period of three years which will be accounted over the course of the contract with the income and expense being recorded as non-operating income and expense, respectively. Novo also purchased 5.2 million of our ordinary shares at a purchase price of $7.00 per share. We accounted for the $14.3 million excess fair value of Novo's share purchase over the market price of our ordinary shares as additional gain on the sale. We incurred $5.8 million of expenses relating to the sale, which were recorded as part of the gain on the sale. We originally acquired the product rights to Macrilen in January 2018 for $24.8 million and recorded amortization in 2018 of $2.2 million resulting in a net book value of $22.6 million at the time of sale.

16. Quarterly financial information (unaudited)

This table summarizes the unaudited consolidated financial results of operations for the quarters ended:

(in thousands, except share and per share data)	March 31,	June 30,	September 30,	December 31,
2018 Quarter Ended				
Total revenues	$ 3,870	$ 4,296	$ 5,347	$ 4,514
Cost of sales (excluding amortization of intangible assets)	667	753	1,441	1,125
Total costs and expenses	19,012	22,535	28,639	25,778
Other (expense) income	(12,914)	16,070	4,174	106,980
Income tax (expense) benefit	—	(1)	—	(535)
Net (loss) income	(28,723)	(2,923)	(20,559)	84,056
Net (loss) income per ordinary share, basic (1)	(0.66)	(0.06)	(0.44)	1.73
Net (loss) income per ordinary share, diluted (1)	(0.66)	(0.43)	(0.55)	1.64
2017 Quarter Ended				
Total revenues	$ —	$ 1,529	$ 2,533	$ 2,984
Cost of sales (excluding amortization of intangible asset)	—	377	591	515
Total costs and expenses	12,179	15,525	34,967	16,634
Other expenses	(15,712)	(15,910)	(2,885)	(3,463)
Income tax (expense) benefit	(1,594)	92	850	(1,119)
Net loss	(29,485)	(30,191)	(35,060)	(18,747)
Net loss per ordinary share, basic and diluted (1)	(0.83)	(0.86)	(0.98)	(0.47)

(1) Net loss per share amounts may not agree to the per share for the full year due to the use of weighted-average shares for each period.

Exhibit 10.13

STRONGBRIDGE BIOPHARMA PLC
2015 EQUITY COMPENSATION PLAN

The purpose of the Strongbridge Biopharma plc 2015 Equity Compensation Plan (the "Plan") is to provide (i) designated employees of Strongbridge Biopharma plc (the "Company") and its parents and subsidiaries; (ii) certain consultants and advisors who perform services for the Company or its parents or subsidiaries; and (iii) non-employee members of the Board of Directors of the Company (the "Board") with the opportunity to receive grants of incentive stock options, nonqualified stock options and stock awards. The Company believes that the Plan will encourage the participants to contribute materially to the growth of the Company, thereby benefitting the Company's shareholders, and will align the economic interests of the participants with those of the shareholders.

1. **Administration**

(a) Committee. The Plan shall be administered and interpreted by the Board or by a committee consisting of members of the Board, which shall be appointed by the Board. After an initial public offering of the Company's stock as described in Section 19(b) (a "Public Offering"), the Plan shall be administered by a committee of Board members, which may consist of "outside directors" as defined under section 162(m) of the Internal Revenue Code of 1986, as amended (the "Code"), and related Treasury regulations, and "non-employee directors" as defined under Rule 16b-3 under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The Board, however, may ratify or approve any grants as it deems appropriate, and the Board shall approve and administer all grants made to non-employee directors. The committee may delegate authority to one or more subcommittees as it deems appropriate. To the extent that a committee or subcommittee administers the Plan, references in the Plan to the "Board" shall be deemed to refer to the committee or subcommittee.

(b) Board Authority. The Board shall have the sole authority to (i) determine the individuals to whom grants shall be made under the Plan; (ii) determine the type, size, and terms of the grants to be made to each such individual; (iii) determine the time when the grants will be made and the duration of any applicable exercise or restriction period, including the criteria for exercisability and the acceleration of exercisability; (iv) amend the terms of any previously issued grant; (v) accelerate the vesting, exercisability, or lapse of any forfeiture condition with respect to an Award; and (vi) deal with any other matters arising under the Plan.

(c) Board Determinations. The Board shall have full power and authority to administer, construe and interpret the Plan, correct any defect, supply any omission, or reconcile any inconsistency in the Plan or any Award or Award Agreement, make factual determinations and adopt or amend such rules, regulations, agreements, and instruments for implementing the Plan and for the conduct of its business as it deems necessary or advisable, in its sole discretion. The Board's interpretations of the Plan and all determinations made by the Board pursuant to the powers vested in it hereunder shall be conclusive and binding on all persons having any interest in the Plan or in any awards granted hereunder. All powers of the Board shall be executed in its sole discretion, in the best interest of the Company, not as a fiduciary, and in

keeping with the objectives of the Plan and need not be uniform as to similarly situated individuals.

(d) Limitation of Liability. To the maximum extent permitted by law, no member of the Board shall be liable for any action taken or decision made in good faith relating to the Plan or any Award thereunder. The Board may employ counsel, consultants, accountants, appraisers, brokers or other persons. The Board, the Company, and the officers and directors of the Company shall be entitled to rely upon the advice, opinions or valuations of any such persons.

2. **Awards**

Awards under the Plan may consist of grants of incentive stock options as described in Section 5 ("Incentive Stock Options"), nonqualified stock options as described in Section 5 ("Nonqualified Stock Options") (Incentive Stock Options and Nonqualified Stock Options are collectively referred to as "Options"), as stock awards as described in Section 6 ("Stock Awards"), and restricted stock units as described in Section 6 ("RSUs") (hereinafter collectively referred to as "Awards"). All Awards shall be subject to the terms and conditions set forth herein and to such other terms and conditions consistent with the Plan as the Board deems appropriate and as are specified in writing by the Board to the individual in a grant instrument or an amendment to the grant instrument (the "Award Agreement"). The Board shall approve the form and provisions of each Award Agreement. Awards under a particular Section of the Plan need not be uniform as among the grantees.

3. **Shares Subject to the Plan**

(a) Shares Authorized. Subject to adjustment as described below, the aggregate number of ordinary shares of par value US$0.01 each of the Company ("Company Stock") that may be issued or transferred under the Plan is 7,114,308 (the "Share Pool") and the maximum aggregate number of shares that may be issued under the Plan under Incentive Stock Options is 7,114,308. After a Public Offering, the maximum aggregate number of shares of Company Stock that shall be subject to Awards made under the Plan to any individual during any calendar year shall be 1,000,000 shares, subject to adjustment as described below. The shares may be authorized but unissued shares of Company Stock or reacquired shares of Company Stock, including shares purchased by the Company on the open market for purposes of the Plan.

(b) Automatic Share Pool Increase. The Share Pool shall be increased on the first day of each Fiscal Year beginning with the 2016 fiscal year, in an amount equal to four percent (4.0%) of the outstanding shares of Company Stock on the last day of the immediately preceding fiscal year.

(c) Adjustments to Share Pool. The Share Pool shall be reduced, on the date of grant, by one share for each Award granted under the Plan; provided that Awards that are valued by reference to shares of Company Stock but are required to be paid in cash pursuant to their terms shall not reduce the Share Pool. If and to the extent Options terminate, expire, or are canceled, forfeited, exchanged, or surrendered without having been exercised, or if any Stock Awards or RSUs (including restricted stock received upon the exercise of Options) are forfeited, the shares of Company Stock subject to such Awards shall again be available for Awards under the Share Pool. Notwithstanding the foregoing, the following shares of Company Stock shall not

become available for issuance under the Plan: (A) shares tendered by Grantees, or withheld by the Company, as full or partial payment to the Company upon the exercise of stock options granted under the Plan; and (B) shares withheld by, or otherwise remitted to, the Company to satisfy a Grantee's tax withholding obligations upon the lapse of restrictions on Stock Awards or the exercise of Options granted under the Plan.

(d) Adjustments. If there is any change in the number or kind of shares of Company Stock outstanding (i) by reason of a stock dividend, spinoff, recapitalization, stock split, or combination or exchange of shares; (ii) by reason of a merger, reorganization, or consolidation; (iii) by reason of a reclassification or change in par value; or (iv) by reason of any other extraordinary or unusual event affecting the outstanding Company Stock as a class without the Company's receipt of consideration, or if the value of outstanding shares of Company Stock is substantially reduced as a result of a spinoff or the Company's payment of an extraordinary dividend or distribution, the maximum number of shares of Company Stock available for Awards, the maximum number of shares of Company Stock that any individual participating in the Plan may be granted in any year, the number of shares covered by outstanding Awards, the kind of shares issued under the Plan, and the price per share of such Awards shall be adjusted by the Board to reflect any increase or decrease in the number of, or change in the kind or value of, issued shares of Company Stock to preclude the enlargement or dilution of rights and benefits under such Awards; provided, however, that any fractional shares resulting from such adjustment shall be eliminated. Any adjustments determined by the Board shall be final, binding, and conclusive.

4. **Eligibility for Participation**

(a) Eligible Persons. All employees of the Company and its parents or subsidiaries ("Employees"), including Employees who are officers or members of the Board, and members of the Board who are not Employees ("Non-Employee Directors") shall be eligible to participate in the Plan. Consultants and advisors who perform services for the Company or any of its parents or subsidiaries ("Key Advisors") shall be eligible to participate in the Plan if the Key Advisors render bona fide services to the Company or its parents or subsidiaries, the services are not in connection with the offer and sale of securities in a capital-raising transaction, and the Key Advisors do not directly or indirectly promote or maintain a market for the Company's securities.

(b) Selection of Grantees. The Board shall select the Employees, Non-Employee Directors, and Key Advisors to receive Awards and shall determine the number of shares of Company Stock subject to a particular Award in such manner as the Board determines. Employees, Key Advisors, and Non-Employee Directors who receive Awards under the Plan shall hereinafter be referred to as "Grantees."

5. **Granting of Options**

The Company may grant Options to purchase shares of Company Stock to Employees, Non-Employee Directors, and Key Advisors. The following provisions are applicable to Options.

(a) Number of Shares. The Board shall determine the number of shares of Company Stock that shall be subject to each Award of Options.

(b) Type of Option and Price.

(i) The Board may grant Incentive Stock Options that are intended to qualify as "incentive stock options" within the meaning of section 422 of the Code or Nonqualified Stock Options that do not qualify as Incentive Stock Options. Incentive Stock Options may be granted only to employees of the Company or its parents or subsidiaries, as defined in section 424 of the Code.

(ii) The purchase price (the "Exercise Price") of Company Stock subject to an Option shall be determined by the Board and may be equal to or greater than the Fair Market Value (as defined below) of a share of Company Stock on the date the Option is granted. An Incentive Stock Option may not be granted to an Employee who, at the time of grant, owns stock possessing more than ten percent of the total combined voting power of all classes of stock of the Company or any parent or subsidiary of the Company, unless the Exercise Price per share is not less than 110% of the Fair Market Value of Company Stock on the date of grant.

(iii) If the Company Stock is publicly traded, the Fair Market Value per share shall be determined as follows: (x) if the principal trading market for the Company Stock is a national securities exchange or the Nasdaq National Market, the last reported sale price thereof on the relevant date or (if there were no trades on that date) the latest preceding date upon which a sale was reported, or (y) if the Company Stock is not principally traded on such exchange or market, the mean between the last reported "bid" and "asked" prices of Company Stock on the relevant date, as reported on Nasdaq or, if not so reported, as reported by the National Daily Quotation Bureau, Inc. or as reported in a customary financial reporting service, as applicable and as the Board determines.

(iv) If the Company Stock is not publicly traded or, if publicly traded, is not subject to reported transactions or "bid" or "asked" quotations as set forth above, the Fair Market Value per share shall be as determined by the Board. The Board shall determine the Fair Market Value based upon the application of a reasonable valuation method that considers all material information available to the Board. The Board may engage outside advisors, valuation experts and counsel to assist the Board in making a determination of Fair Market Value for purpose of the Plan.

(c) Option Term. The Board shall determine the term of each Option. The term of any Option shall not exceed ten years from the date of grant. An Incentive Stock Option that is granted to an Employee who, at the time of grant, owns stock possessing more than ten percent of the total combined voting power of all classes of stock of the Company, or any parent or subsidiary of the Company, however, may not have a term that exceeds five years from the date of grant.

(d) Exercisability of Options. Options shall become exercisable in accordance with such terms and conditions, consistent with the Plan, as may be determined by the Board and specified in the Award Agreement. The Board may accelerate the exercisability of any or all

outstanding Options at any time for any reason. The Board may provide in an Award Agreement that the Grantee may elect to exercise part or all of an Option before it otherwise has become exercisable. Any shares so purchased shall be restricted shares and shall be subject to a repurchase right in favor of the Company during a specified restriction period, with the repurchase price equal to the lesser of (A) the Exercise Price or (B) the Fair Market Value of such shares at the time of repurchase, and (C) any other restrictions determined by the Company.

(e) Termination of Employment, Disability, or Death.

(i) Except as provided below, an Option may only be exercised while the Grantee is employed by, or providing service to, the Employer (as defined below) as an Employee, Key Advisor, or member of the Board. In the event that a Grantee ceases to be employed by, or provide service to, the Employer for any reason other than Disability, death, or termination for Cause, any Option which is otherwise exercisable by the Grantee shall terminate unless exercised within 90 days after the date on which the Grantee ceases to be employed by, or provide service to, the Employer (or within such other period of time as may be specified by the Board), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Board or in the Award Agreement, any of the Grantee's Options that are not otherwise exercisable as of the date on which the Grantee ceases to be employed by, or provide service to, the Employer shall terminate as of such date.

(ii) In the event the Grantee ceases to be employed by, or provide service to, the Employer on account of a termination for Cause by the Employer, any Option held by the Grantee shall terminate as of the date the Grantee ceases to be employed by, or provide service to, the Employer. In addition, notwithstanding any other provisions of this Section 5, if the Board determines that the Grantee has engaged in conduct that constitutes Cause at any time while the Grantee is employed by, or providing service to, the Employer or after the Grantee's termination of employment or service, any Option held by the Grantee shall immediately terminate, and the Grantee shall automatically forfeit all shares underlying any exercised portion of an Option for which the Company has not yet delivered the share certificates, upon refund by the Company of the Exercise Price paid by the Grantee for such shares. Upon any exercise of an Option, the Company may withhold delivery of share certificates pending resolution of an inquiry that could lead to a finding resulting in a forfeiture.

(iii) In the event the Grantee ceases to be employed by, or provide service to, the Employer because the Grantee is Disabled, any Option which is otherwise exercisable by the Grantee shall terminate unless exercised within one year after the date on which the Grantee ceases to be employed by, or provide service to, the Employer (or within such other period of time as may be specified by the Board), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Board, any of the Grantee's Options which are not otherwise exercisable as of the date on which the Grantee ceases to be employed by, or provide service to, the Employer shall terminate as of such date.

(iv) If the Grantee dies while employed by, or providing service to, the Employer or within 90 days after the date on which the Grantee ceases to be employed or provide service on account of a termination specified in Section 5(f)(i) above (or within such other period of time as may be specified by the Board), any Option that is otherwise exercisable

by the Grantee shall terminate unless exercised within one year after the date on which the Grantee ceases to be employed by, or provide service to, the Employer (or within such other period of time as may be specified by the Board), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Board, any of the Grantee's Options that are not otherwise exercisable as of the date on which the Grantee ceases to be employed by, or provide service to, the Employer shall terminate as of such date.

(v) For purposes of this Plan:

(A) The term "Employer" shall mean the Company and its parent and subsidiary corporations or other entities, as determined by the Board.

(B) "Employed by, or provide service to, the Employer" shall mean employment or service as an Employee, Key Advisor, or member of the Board (so that, for purposes of exercising Options and satisfying conditions with respect to Stock Awards or RSUs, a Grantee shall not be considered to have terminated employment or service until the Grantee ceases to be an Employee, Key Advisor, or member of the Board), unless the Board determines otherwise.

(C) "Disability" shall mean a Grantee's becoming disabled within the meaning of section 22(e)(3) of the Code, within the meaning of the Employer's long-term disability plan applicable to the Grantee, or as otherwise determined by the Board.

(D) "Cause" shall mean, except to the extent specified otherwise by the Board or as defined in any other agreement between the Grantee and the Company, a finding by the Board that the Grantee has (i) been convicted of a felony or crime involving moral turpitude; (ii) disclosed trade secrets or confidential information of the Employer to persons not entitled to receive such information; (iii) breached any written noncompetition or nonsolicitation agreement between the Grantee and the Employer; or (iv) engaged in willful and continued negligence in the performance of the duties assigned to the Grantee by the Employer, after the Grantee has received notice of and failed to cure such negligence.

(f) Exercise of Options. A Grantee may exercise an Option that has become vested and exercisable, in whole or in part, by delivering a notice of exercise to the Company. The Grantee shall pay the Exercise Price for an Option by the Board (i) in cash; (ii) by delivering shares of Company Stock owned by the Grantee (including Company Stock acquired in connection with the exercise of an Option, subject to such restrictions as the Board deems appropriate) and having a Fair Market Value on the date of exercise equal to the Exercise Price or by attestation (on a form prescribed by the Board) to ownership of shares of Company Stock having a Fair Market Value on the date of exercise equal to the Exercise Price; (iii) after a Public Offering, payment through a broker in accordance with procedures permitted by Regulation T of the Federal Reserve Board; or (iv) by such other method as the Board may approve. In addition, the Grantee may elect to settle the Option on a "net basis" by taking delivery of the number of Company Stock equal to Fair Market Value of the shares subject to any Option less the exercise price, any tax (or other governmental obligation) or other

administration fees due. Shares of Company Stock used to exercise an Option shall have been held by the Grantee for the requisite period of time to avoid adverse accounting consequences to the Company with respect to the Option. The Grantee shall pay the Exercise Price and the amount of any withholding tax due (pursuant to Section 7) as specified by the Board.

(g) Limits on Incentive Stock Options. Each Incentive Stock Option shall provide that, if the aggregate Fair Market Value of the stock on the date of the grant with respect to which Incentive Stock Options are exercisable for the first time by a Grantee during any calendar year, under the Plan or any other stock option plan of the Company or a parent or subsidiary, exceeds $100,000, then the Option, as to the excess, shall be treated as a Nonqualified Stock Option. An Incentive Stock Option shall not be granted to any person who is not an Employee of the Company or a parent or subsidiary (within the meaning of section 424(f) of the Code) of the Company.

6. **Stock Awards and RSUs**

The Company may issue or transfer shares of Company Stock to an Employee, Non-Employee Director, or Key Advisor under a Stock Award or RSU, upon such terms as the Board deems appropriate. The following provisions are applicable to Stock Awards and RSUs:

(a) General Requirements. Shares of Company Stock issued or transferred pursuant to Stock Awards may be issued or transferred for consideration or for no consideration, and subject to restrictions or no restrictions, as determined by the Board. The Board shall determine the number of shares of Company Stock subject to a Stock Award and the number of RSUs to be granted to a Grantee, the duration of the period during which, and the conditions, if any, under which, the Stock Award and RSUs may vest or may be forfeited to the Company and the other terms and conditions of such Awards. The Board may require different periods of service or different performance goals and objectives with respect to different Grantees holding different Stock Awards or RSUs or to separate, designated portions of shares constituting Stock Awards.

(b) Transfer Restrictions and Legend on Stock Certificate. Stock Awards and RSUs may not be sold, assigned, transferred, pledged or otherwise encumbered except as provided in the Plan or as may be provided in the applicable Award Agreement; provided, however, that the Board may determine that Stock Awards and RSUs may be transferred by the Grantee. Each certificate for Stock Awards shall contain a legend giving appropriate notice of the restrictions in the Award. The Grantee shall be entitled to have the legend removed from the stock certificate covering the shares subject to restrictions when all restrictions on such shares have lapsed. The Board may determine that the Company shall not issue certificates for Stock Awards until all restrictions on such shares have lapsed, or that the Company shall retain possession of certificates for Stock Awards until all restrictions on such shares have lapsed. Upon the lapse of the restrictions applicable to a Stock Award, the Company or other custodian, as applicable, shall deliver such certificates to the Grantee or the Grantee's legal representative.

(c) Payment/Lapse of Restrictions. Each RSU shall be granted with respect to one share of Company Stock or shall have a value equal to the Fair Market Value of one share of Company Stock. RSUs shall be paid in cash, shares of Company Stock, other securities, other Awards or other property, as determined in the sole discretion of the Board, upon the lapse of

restrictions applicable thereto, or otherwise in accordance with the applicable Award Agreement. The amount payable as a result of the vesting of an RSU shall be distributed as soon as practicable following the vesting date and in no event later than the fifteenth date of the third calendar month of the year following the vesting date of the RSU (or as otherwise permitted under Section 409A of the Code); provided, however, that a Grantee may, if and to the extent permitted by the Board, elect to defer payment of RSUs in a manner permitted by Section 409A of the Code.

(d) Termination of Employment or Service. Except as otherwise set forth in the Award Agreement, if the Grantee ceases to be employed by, or provide service to, the Employer (as defined in Section 5(e)), any Stock Award or RSUs held by the Grantee that are subject to the transfer restrictions set forth in Section 6(b) above at such time shall be forfeited. The Board may, however, provide for complete or partial exceptions to this requirement as it deems appropriate.

(e) No Right to Vote and to Receive Dividends. Prior to the lapse of the transfer restrictions set forth in Section 6(b) above, the Grantee shall not have the right to vote shares subject to Stock Awards or to receive any dividends or other distributions paid on such shares, subject to any restrictions deemed appropriate by the Board.

7. **Performance-Based Awards**

Notwithstanding anything to the contrary herein, certain Stock Awards or RSUs granted under the Plan may be granted in a manner which is deductible by the Company under Section 162(m) of the Code (or any successor section thereto). Such Stock Awards or RSUs shall be designated "Performance-Based Awards". The following provisions are applicable to Performance-Based Awards:

(a) Performance Goals. A Grantee's Performance-Based Awards shall be determined based on the attainment of written performance goals approved by the Board for a performance period established by the Board (i) while the outcome for that performance period is substantially uncertain and (ii) no more than 90 days after the commencement of the performance period to which the performance goal relates or, if less, the number of days which is equal to 25 percent of the relevant performance period, or as otherwise permitted pursuant to Section 162(m) of the Code (or any successor section thereto). The performance goals, which must be objective, shall be based upon one or more of the following criteria: (i) consolidated earnings before or after taxes (including earnings before interest, taxes, depreciation and amortization); (ii) net income; (iii) operating income; (iv) earnings per share; (v) return on shareholders' equity; (vi) attainment of strategic and operational initiatives; (vii) customer income; (viii) economic value-added models; (ix) maintenance or improvement of profit margins; (x) stock price (including total shareholder return), including, without limitation, as compared to one or more stock indices; (xi) market share; (xii) revenues, sales or net sales; (xiii) return on assets; (xiv) book value per share; (xv) expense management; (xvi) improvements in capital structure; (xvii) costs and (xviii) cash flow. The foregoing criteria may relate to the Company, one or more of its subsidiaries or one or more of its divisions or units, or any combination of the foregoing, and may be applied on an absolute basis and/or be relative to one or more peer group companies or indices, or any combination thereof, all as the Board shall

determine. In addition, to the degree consistent with the Code, the performance goals may be calculated without regard to extraordinary, unusual and/or non-recurring items.

(b) Determination of Satisfaction of Performance Goals. The Board shall determine whether, with respect to a performance period, the applicable performance goals have been met with respect to a given Grantee and, if they have, so certify and ascertain the amount of the applicable Performance-Based Award. No Performance-Based Awards will be paid for such performance period until such certification is made by the Board. The amount of the Performance-Based Award actually paid to a given Grantee may be less than the amount determined by the applicable performance goal formula, at the discretion of the Board. The amount of the Performance-Based Award determined by the Board for a performance period shall be paid to the Grantee at such time as determined by the Board in its sole discretion after the end of such performance period; provided, however, that a Grantee may, if and to the extent permitted by the Board and consistent with the provisions of Section 162(m) of the Code, elect to defer payment of a Performance-Based Award in a manner permitted by Section 409A of the Code. To the extent Section 162(m) of the Code (or any successor section thereto) provides terms different from the requirements of this Section 7, this Section 7 shall be deemed amended thereby

8. **Withholding of Taxes**

(a) Required Withholding. All Awards under the Plan shall be subject to applicable federal (including FICA), state, and local tax (or other governmental obligation) withholding requirements or other administration fees due. The Employer may require that the Grantee or other person receiving or exercising Awards pay to the Employer the amount of any federal, state, or local taxes (or other governmental obligations) that the Employer is required to withhold or any administration fees due with respect to such Awards, or the Employer may deduct from other wages paid by the Employer the amount of any withholding taxes, governmental obligations or administration fees due with respect to such Awards.

(b) Election to Withhold Shares. If the Board so permits, a Grantee may elect to satisfy the Employer's income tax (or other governmental obligation) withholding requirement and any administration fees due with respect to an Award by having shares withheld up to an amount that does not exceed the Grantee's minimum applicable withholding rate for federal (including FICA), state, and local tax (and other governmental obligation) liabilities plus any other administration fees due. The election must be in a form and manner prescribed by the Board and may be subject to the prior approval of the Board.

9. **Transferability of Awards**

(a) Nontransferability of Awards. Except as provided below, only the Grantee may exercise rights under an Award during the Grantee's lifetime. A Grantee may not transfer those rights except (i) by will or by the laws of descent and distribution or (ii) with respect to Awards other than Incentive Stock Options, if permitted in any specific case by the Board, pursuant to a domestic relations order or otherwise as permitted by the Board. When a Grantee dies, the personal representative or other person entitled to succeed to the rights of the Grantee may exercise such rights. Any such successor must furnish proof satisfactory to the Company of his

or her right to receive the Award under the Grantee's will or under the applicable laws of descent and distribution.

(b) Transfer of Nonqualified Stock Options. Notwithstanding the foregoing, the Board may provide, in an Award Agreement, that a Grantee may transfer Nonqualified Stock Options to family members, or one or more trusts or other entities for the benefit of or owned by family members, consistent with applicable securities laws, according to such terms as the Board may determine; provided that the Grantee receives no consideration for the transfer of an Option and the transferred Option shall continue to be subject to the same terms and conditions as were applicable to the Option immediately before the transfer.

10. **Right of First Refusal; Repurchase Right**

(a) Offer. Prior to a Public Offering, if at any time an individual desires to sell, encumber, or otherwise dispose of shares of Company Stock that were distributed to him or her under the Plan and that are transferable, the individual may do so only pursuant to a bona fide written offer, and the individual shall first offer the shares to the Company by giving the Company written notice disclosing: (i) the name of the proposed transferee of the Company Stock; (ii) the certificate number and number of shares of Company Stock proposed to be transferred or encumbered; (iii) the proposed price; (iv) all other terms of the proposed transfer; and (v) a written copy of the proposed offer. Within 60 days after receipt of such notice, the Company shall have the option to purchase all or part of such Company Stock at the price and on the terms described in the written notice; provided that the Company may pay such price in installments over a period not to exceed four years, at the discretion of the Board.

(b) Sale. In the event the Company (or a shareholder, as described below) does not exercise the option to purchase Company Stock, as provided above, the individual shall have the right to sell, encumber, or otherwise dispose of the shares of Company Stock described in subsection (a) at the price and on the terms of the transfer set forth in the written notice to the Company, provided such transfer is effected within 15 days after the expiration of the option period. If the transfer is not effected within such period, the Company must again be given an option to purchase, as provided above.

(c) Assignment of Rights. The Board, in its sole discretion, may waive the Company's right of first refusal and repurchase right under this Section 10. If the Company's right of first refusal or repurchase right is so waived, the Board may, in its sole discretion, assign such right to the remaining shareholders of the Company in the same proportion that each shareholder's stock ownership bears to the stock ownership of all the shareholders of the Company, as determined by the Board. To the extent that a shareholder has been given such right and does not purchase his or her allotment, the other shareholders shall have the right to purchase such allotment on the same basis.

(d) Purchase by the Company. Prior to a Public Offering, if a Grantee ceases to be employed by, or provide service to, the Employer, the Company shall have the right to purchase, within 60 days of the date that Grantee ceases to be employed by, or provide services to, the Employer, all or part of any Company Stock distributed to Grantee under the Plan at the Fair Market Value (as defined in Section 5(b)) on the date that Grantee ceases to be employed

by, or provide services to, the Employer (or at such other price as may be established in the Award Agreement); provided, however, that such repurchase shall be made in accordance with applicable accounting rules to avoid adverse accounting treatment.

(e) Public Offering. On and after a Public Offering, the Company shall have no further right to purchase shares of Company Stock under this Section 10.

(f) Shareholder's Agreement. Notwithstanding the provisions of this Section 10, if the Board requires that a Grantee execute a shareholder's agreement with respect to any Company Stock distributed pursuant to the Plan, which contains a right of first refusal or repurchase right, the provisions of this Section 10 shall not apply to such Company Stock.

11. **Change of Control of the Company**

As used herein, a "Change of Control" shall be deemed to have occurred if:

(a) Any "person" (as such term is used in sections 13(d) and 14(d) of the Exchange Act) (other than persons who are shareholders on the effective date of the Plan) becomes a "beneficial owner" (as defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of securities of the Company representing more than 50% of the voting power of the then outstanding securities of the Company; provided that a Change of Control shall not be deemed to occur as a result of a change of ownership resulting from the death of a shareholder, and a Change of Control shall not be deemed to occur as a result of a transaction in which the Company becomes a subsidiary of another corporation and in which the shareholders of the Company, immediately prior to the transaction, will beneficially own, immediately after the transaction, shares entitling such shareholders to more than 50% of all votes to which all shareholders of the parent corporation would be entitled in the election of directors (without consideration of the rights of any class of stock to elect directors by a separate class vote); or

(b) The consummation of (i) a merger or consolidation of the Company with another corporation where the shareholders of the Company, immediately prior to the merger or consolidation, will not beneficially own, immediately after the merger or consolidation, shares entitling such shareholders to more than 50% of all votes to which all shareholders of the surviving corporation would be entitled in the election of directors (without consideration of the rights of any class of stock to elect directors by a separate class vote); (ii) a sale or other disposition of all or substantially all of the assets of the Company; or (iii) a liquidation or dissolution of the Company.

(c) Notwithstanding the foregoing, the following acquisitions shall not constitute a Change of Control: (A) an acquisition by the Company or entity controlled by the Company, or (B) an acquisition by an employee benefit plan (or related trust) sponsored or maintained by the Company

12. **Consequences of a Change of Control**

(a) Assumption of Awards. Upon a Change of Control where the Company is not the surviving corporation (or survives only as a subsidiary of another corporation), unless the Board determines otherwise, all outstanding Awards shall be assumed by, or replaced with

comparable Awards by, the surviving corporation (or a parent or subsidiary of the surviving corporation).

(b) Termination of Awards. Upon a Change of Control where the Company is not the surviving corporation (or survives only as a subsidiary of another corporation), in the event the surviving corporation (or a parent or subsidiary of the surviving corporation) does not assume or replace the Awards with comparable Awards, (i) the Company shall provide each Grantee with outstanding Awards written notice of such Change of Control; (ii) all outstanding Options shall automatically accelerate and become fully vested and exercisable; (iii) all outstanding Stock Awards shall become vested and deliverable in accordance with Section 6(b); and (iv) all outstanding RSUs shall become vested and deliverable in accordance with Section 6(c).

(c) Other Alternatives. Notwithstanding the foregoing, in the event of a Change of Control, the Board may take one or both of the following actions: the Board may (i) require that Grantees surrender their outstanding Options in exchange for a payment by the Company, in cash or Company Stock as determined by the Board, in an amount equal to the amount by which the then Fair Market Value of the shares of Company Stock subject to the Grantee's unexercised Options exceeds the Exercise Price of the Options; or (ii) after giving Grantees an opportunity to exercise their outstanding Options, terminate any or all unexercised Options at such time as the Board deems appropriate. Such surrender or termination shall take place as of the date of the Change of Control or such other date as the Board may specify.

13. **Requirements for Issuance or Transfer of Shares**

(a) Shareholder's Agreement. The Board may require that a Grantee execute a shareholder's agreement, with such terms as the Board deems appropriate, with respect to any Company Stock issued or distributed pursuant to the Plan.

(b) Limitations on Issuance or Transfer of Shares. No Company Stock shall be issued or transferred in connection with any Award hereunder unless and until all legal requirements applicable to the issuance or transfer of such Company Stock have been complied with to the satisfaction of the Board. The Board shall have the right to condition any Award made to any Grantee hereunder on such Grantee's undertaking in writing to comply with such restrictions on his or her subsequent disposition of such shares of Company Stock as the Board shall deem necessary or advisable, and certificates representing such shares may be legended to reflect any such restrictions. Certificates representing shares of Company Stock issued or transferred under the Plan shall be subject to such stop-transfer orders and other restrictions as may be required by applicable laws, regulations, and interpretations, including any requirement that a legend be placed thereon.

(c) Lock-Up Period. If so requested by the Company or any representative of the underwriters (the "Managing Underwriter") in connection with any underwritten offering of securities of the Company under the Securities Act of 1933, as amended (the "Securities Act"), a Grantee (including any successor or assigns) shall not sell or otherwise transfer any shares or other securities of the Company during the 30-day period preceding and the 180-day period following the effective date of a registration statement of the Company filed under the

Securities Act for such underwriting (or such shorter period as may be requested by the Managing Underwriter and agreed to by the Company) (the "Market Standoff Period"). The Company may impose stop-transfer instructions with respect to securities subject to the foregoing restrictions until the end of such Market Standoff Period.

14. **Amendment and Termination of the Plan**

(a) Amendment. The Board may amend or terminate the Plan at any time; provided, however, that the Board shall not amend the Plan without shareholder approval if such approval is required in order to comply with the Code or other applicable laws or, after an Initial Public Offering, to comply with applicable stock exchange requirements.

(b) Termination of Plan. The Plan shall terminate on the day immediately preceding the tenth anniversary of its effective date, unless the Plan is terminated earlier by the Board or is extended by the Board with the approval of the shareholders.

(c) Termination and Amendment of Outstanding Awards . A termination or amendment of the Plan that occurs after an Award is made shall not materially impair the rights of a Grantee unless the Grantee consents or unless the Board acts under Section 20(b). The termination of the Plan shall not impair the power and authority of the Board with respect to an outstanding Award. Whether or not the Plan has terminated, an outstanding Award may be terminated or amended under Section 20(b) or may be amended by agreement of the Company and the Grantee consistent with the Plan.

(d) Governing Document. The Plan shall be the controlling document. No other statements, representations, explanatory materials or examples, oral or written, may amend the Plan in any manner. The Plan shall be binding upon and enforceable against the Company and its successors and assigns.

15. **Funding of the Plan**

The Plan shall be unfunded. The Company shall not be required to establish any special or separate fund or to make any other segregation of assets to assure the payment of any Awards under the Plan. In no event shall interest be paid or accrued on any Award, including unpaid installments of Awards.

16. **Rights of Participants**

Nothing in the Plan shall entitle any Employee, Key Advisor, Non-Employee Director, or other person to any claim or right to be granted an Award under the Plan. Neither the Plan nor any action taken hereunder shall be construed as giving any individual any rights to be retained by or in the employ of the Employer or any other employment rights.

17. **No Fractional Shares**

No fractional shares of Company Stock shall be issued or delivered pursuant to the Plan or any Award. The Board shall determine whether cash, other awards or other property shall be

issued or paid in lieu of such fractional shares or whether such fractional shares or any rights thereto shall be forfeited or otherwise eliminated.

18. **Headings**

Section headings are for reference only. In the event of a conflict between a title and the content of a Section, the content of the Section shall control.

19. **Effective Date of the Plan**

(a) Effective Date. The Plan shall be effective on September 3, 2015.

(b) Public Offering. The provisions of the Plan that refer to a Public Offering, or that refer to, or are applicable to persons subject to, section 16 of the Exchange Act or section 162(m) of the Code, shall be effective, if at all, upon the initial registration of the Company Stock under section 12(g) of the Exchange Act, and shall remain effective thereafter for so long as such stock is so registered.

20. **Miscellaneous**

(a) Awards in Connection with Corporate Transactions and Otherwise. Nothing contained in the Plan shall be construed to (i) limit the right of the Board to make Awards under the Plan in connection with the acquisition, by purchase, lease, merger, consolidation, or otherwise, of the business or assets of any corporation, firm or association, including Awards to employees thereof who become Employees, or for other proper corporate purposes; or (ii) limit the right of the Company to grant stock options or make other awards outside of the Plan. Without limiting the foregoing, the Board may make an Award to an employee of another corporation who becomes an Employee by reason of a corporate merger, consolidation, acquisition of stock or property, reorganization, or liquidation involving the Company, the Parent, or any of their subsidiaries in substitution for a stock option, stock award or other type of applicable equity grants made by such corporation. The terms and conditions of the substitute grants may vary from the terms and conditions required by the Plan and from those of the substituted stock incentives. The Board shall prescribe the provisions of the substitute grants.

(b) Compliance with Law. The Plan, exercise of Options, restrictions of Stock Awards and obligations of the Company to issue or transfer shares of Company Stock under Awards shall be subject to all applicable laws and to approvals by any governmental or regulatory agency as may be required. With respect to persons subject to section 16 of the Exchange Act, after a Public Offering, it is the intent of the Company that the Plan and all transactions under the Plan comply with all applicable provisions of Rule 16b-3 or its successors under the Exchange Act. In addition, it is the intent of the Company that the Plan and applicable Awards under the Plan comply with the applicable provisions of sections 162(m), 409A and 422 of the Code. To the extent that any legal requirement of section 16 of the Exchange Act or sections 162(m), 409A or 422 of the Code as set forth in the Plan ceases to be required under section 16 of the Exchange Act or sections 162(m), 409A or 422 of the Code, that Plan provision shall cease to apply. The Board may revoke any Award if it is contrary to law or modify an Award to bring it into compliance with any valid and mandatory government

regulation. The Board may also adopt rules regarding the withholding of taxes on payments to Grantees. The Board may, in its sole discretion, agree to limit its authority under this Section.

(c) Employees Subject to Taxation Outside the United States. With respect to Grantees who are subject to taxation in countries other than the United States, the Board may make Awards on such terms and conditions as the Board deems appropriate to comply with the laws of the applicable countries, and the Board may create such procedures, addenda, and subplans and make such modifications as may be necessary or advisable to comply with such laws.

(d) Governing Law. The validity, construction, interpretation, and effect of the Plan and Award Agreements issued under the Plan shall be governed and construed by and determined in accordance with the laws of the State of Delaware, without giving effect to the conflict of laws provisions thereof.

Exhibit 10.14

STRONGBRIDGE BIOPHARMA PLC
NON-EMPLOYEE DIRECTOR EQUITY COMPENSATION PLAN

The purpose of the Strongbridge Biopharma plc Non-Employee Director Equity Compensation Plan (the "Plan") is to provide non-employee members of the Board of Directors (the "Board") of Strongbridge Biopharma plc (the "Company") with the opportunity to receive grants of nonqualified stock options and stock awards. The Company believes that the Plan will encourage the participants to contribute materially to the growth of the Company, thereby benefitting the Company's shareholders, and will align the economic interests of the participants with those of the shareholders.

1. **Administration**

(a) Administrator. The Plan shall be administered and interpreted by the Board and all grants made hereunder shall be approved by the Board.

(b) Board Authority. The Board shall have the sole authority to (i) determine the individuals to whom grants shall be made under the Plan; (ii) determine the type, size, and terms of the grants to be made to each such individual; (iii) determine the time when the grants will be made and the duration of any applicable exercise or restriction period, including the criteria for exercisability and the acceleration of exercisability; (iv) amend the terms of any previously issued grant; (v) accelerate the vesting, exercisability, or lapse of any forfeiture condition with respect to an Award; and (vi) deal with any other matters arising under the Plan.

(c) Board Determinations. The Board shall have full power and authority to administer, construe and interpret the Plan, correct any defect, supply any omission, or reconcile any inconsistency in the Plan or any Award or Award Agreement, make factual determinations and adopt or amend such rules, regulations, agreements, and instruments for implementing the Plan and for the conduct of its business as it deems necessary or advisable, in its sole discretion. The Board's interpretations of the Plan and all determinations made by the Board pursuant to the powers vested in it hereunder shall be conclusive and binding on all persons having any interest in the Plan or in any awards granted hereunder. All powers of the Board shall be executed in its sole discretion, in the best interest of the Company, not as a fiduciary, and in keeping with the objectives of the Plan and need not be uniform as to similarly situated individuals.

(d) Limitation of Liability. To the maximum extent permitted by law, no member of the Board shall be liable for any action taken or decision made in good faith relating to the Plan or any Award thereunder. The Board may employ counsel, consultants, accountants, appraisers, brokers or other persons. The Board, the Company, and the officers and directors of the Company shall be entitled to rely upon the advice, opinions or valuations of any such persons.

2. **Awards**

Awards under the Plan may consist of grants of nonqualified stock options as described in Section 5 ("Options"), as stock awards as described in Section 6 ("Stock Awards"), and

restricted stock units as described in Section 6 ("RSUs") (hereinafter collectively referred to as "Awards"). All Awards shall be subject to the terms and conditions set forth herein and to such other terms and conditions consistent with the Plan as the Board deems appropriate and as are specified in writing by the Board to the individual in a grant instrument or an amendment to the grant instrument (the "Award Agreement"). The Board shall approve the form and provisions of each Award Agreement. Awards under a particular Section of the Plan need not be uniform as among the Grantees.

3. **Shares Subject to the Plan**

(a) Shares Authorized. Subject to adjustment as described below, the aggregate number of ordinary shares of par value US$0.01 each of the Company ("Company Stock") that may be issued or transferred under the Plan is 1,099,514 (the "Share Pool"). The shares may be authorized but unissued shares of Company Stock or reacquired shares of Company Stock, including shares purchased by the Company on the open market for purposes of the Plan.

(b) Automatic Share Pool Increase. The Share Pool shall be increased on the first day of each Fiscal Year beginning with the 2016 fiscal year, in an amount equal to one-half percent (0.5%) of the outstanding shares of Company Stock on the last day of the immediately preceding fiscal year.

(c) Adjustments to Share Pool. The Share Pool shall be reduced, on the date of grant, by one share for each Award granted under the Plan; provided that Awards that are valued by reference to shares of Company Stock but are required to be paid in cash pursuant to their terms shall not reduce the Share Pool. If and to the extent Options terminate, expire, or are canceled, forfeited, exchanged, or surrendered without having been exercised, or if any Stock Awards or RSUs (including restricted stock received upon the exercise of Options) are forfeited, the shares of Company Stock subject to such Awards shall again be available for Awards under the Share Pool. Notwithstanding the foregoing, shares tendered by Grantees, or withheld by the Company, as full or partial payment to the Company upon the exercise of Options granted under the Plan, shall not become available for issuance under the Plan.

(d) Adjustments. If there is any change in the number or kind of shares of Company Stock outstanding (i) by reason of a stock dividend, spinoff, recapitalization, stock split, or combination or exchange of shares; (ii) by reason of a merger, reorganization, or consolidation; (iii) by reason of a reclassification or change in par value; or (iv) by reason of any other extraordinary or unusual event affecting the outstanding Company Stock as a class without the Company's receipt of consideration, or if the value of outstanding shares of Company Stock is substantially reduced as a result of a spinoff or the Company's payment of an extraordinary dividend or distribution, the maximum number of shares of Company Stock available for Awards, the maximum number of shares of Company Stock that any individual participating in the Plan may be granted in any year, the number of shares covered by outstanding Awards, the kind of shares issued under the Plan, and the price per share of such Awards shall be adjusted by the Board to reflect any increase or decrease in the number of, or change in the kind or value of, issued shares of Company Stock to preclude the enlargement or dilution of rights and benefits under such Awards; provided, however, that any fractional shares resulting from such adjustment shall be eliminated. Any adjustments determined by the Board shall be final, binding, and conclusive.

4. **Eligibility for Participation**

(a) Eligible Persons. All members of the Board who are not employees ("Non-Employee Directors") shall be eligible to participate in the Plan.

(b) Selection of Grantees. The Board shall select the Non-Employee Directors to receive Awards and shall determine the number of shares of Company Stock subject to a particular Award in such manner as the Board determines. Non-Employee Directors who receive Awards under the Plan shall hereinafter be referred to as "Grantees."

5. **Granting of Options**

The following provisions are applicable to Options.

(a) Number of Shares. The Board shall determine the number of shares of Company Stock that shall be subject to each Award of Options.

(b) Type of Option and Price.

(i) The purchase price (the "Exercise Price") of Company Stock subject to an Option shall be determined by the Board and may be equal to or greater than the Fair Market Value (as defined below) of a share of Company Stock on the date the Option is granted.

(ii) If the Company Stock is publicly traded, the Fair Market Value per share shall be determined as follows: (x) if the principal trading market for the Company Stock is a national securities exchange or the Nasdaq National Market, the last reported sale price thereof on the relevant date or (if there were no trades on that date) the latest preceding date upon which a sale was reported, or (y) if the Company Stock is not principally traded on such exchange or market, the mean between the last reported "bid" and "asked" prices of Company Stock on the relevant date, as reported on Nasdaq or, if not so reported, as reported by the National Daily Quotation Bureau, Inc. or as reported in a customary financial reporting service, as applicable and as the Board determines.

(iii) If the Company Stock is not publicly traded or, if publicly traded, is not subject to reported transactions or "bid" or "asked" quotations as set forth above, the Fair Market Value per share shall be as determined by the Board. The Board shall determine the Fair Market Value based upon the application of a reasonable valuation method that considers all material information available to the Board. The Board may engage outside advisors, valuation experts and counsel to assist the Board in making a determination of Fair Market Value for purpose of the Plan.

(c) Option Term. The Board shall determine the term of each Option. The term of any Option shall not exceed ten years from the date of grant.

(d) Exercisability of Options. Options shall become exercisable in accordance with such terms and conditions, consistent with the Plan, as may be determined by the Board and specified in the Award Agreement. The Board may accelerate the exercisability of any or all outstanding Options at any time for any reason. The Board may provide in an Award Agreement

that the Grantee may elect to exercise part or all of an Option before it otherwise has become exercisable. Any shares so purchased shall be restricted shares and shall be subject to a repurchase right in favor of the Company during a specified restriction period, with the repurchase price equal to the lesser of (A) the Exercise Price or (B) the Fair Market Value of such shares at the time of repurchase, and (C) any other restrictions determined by the Company.

(e) Termination of Service, Disability, or Death.

(i) Except as provided below, an Option may only be exercised while the Grantee is providing service to the Company as a member of the Board. In the event that a Grantee ceases to provide service to the Company for any reason other than Disability, death, or termination for Cause, any Option which is otherwise exercisable by the Grantee shall terminate unless exercised within 90 days after the date on which the Grantee ceases to provide service to the Company (or within such other period of time as may be specified by the Board), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Board or in the Award Agreement, any of the Grantee's Options that are not otherwise exercisable as of the date on which the Grantee ceases to provide service to the Company shall terminate as of such date.

(ii) In the event the Grantee ceases to provide service to the Company on account of a removal from the Board for Cause by the Company, any Option held by the Grantee shall terminate as of the date the Grantee ceases to provide service to the Company. In addition, notwithstanding any other provisions of this Section 5, if the a majority of disinterested members of the Board determines that the Grantee has engaged in conduct that constitutes Cause at any time while the Grantee is providing service to the Company or after the Grantee's termination of service, any Option held by the Grantee shall immediately terminate, and the Grantee shall automatically forfeit all shares underlying any exercised portion of an Option for which the Company has not yet delivered the share certificates, upon refund by the Company of the Exercise Price paid by the Grantee for such shares. Upon any exercise of an Option, the Company may withhold delivery of share certificates pending resolution of an inquiry that could lead to a finding resulting in a forfeiture.

(iii) In the event the Grantee ceases to provide service to the Company because the Grantee is Disabled, any Option which is otherwise exercisable by the Grantee shall terminate unless exercised within one year after the date on which the Grantee ceases to provide service to the Company (or within such other period of time as may be specified by the Board), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Board, any of the Grantee's Options which are not otherwise exercisable as of the date on which the Grantee ceases to provide service to the Company shall terminate as of such date.

(iv) If the Grantee dies while providing service to the Company or within 90 days after the date on which the Grantee ceases to provide service on account of a termination specified in Section 5(f)(i) above (or within such other period of time as may be specified by the Board), any Option that is otherwise exercisable by the Grantee shall terminate unless exercised within one year after the date on which the Grantee ceases to provide service to the Company (or within such other period of time as may be specified by the Board), but in any event no later than

the date of expiration of the Option term. Except as otherwise provided by the Board, any of the Grantee's Options that are not otherwise exercisable as of the date on which the Grantee ceases to provide service to the Company shall terminate as of such date.

(v) For purposes of this Plan:

(A) "Provide service to the Company" shall mean service as a member of the Board (so that, for purposes of exercising Options and satisfying conditions with respect to Stock Awards or RSUs, a Grantee shall not be considered to have terminated service until the Grantee ceases to be a member of the Board), unless the Board determines otherwise.

(B) "Disability" shall mean a Grantee's becoming disabled within the meaning of section 22(e)(3) of the Internal Revenue Code of 1986, as amended (the "Code"), or as otherwise determined by the Board.

(C) "Cause" shall mean that the Grantee has been convicted of a felony or crime involving moral turpitude; or a determination by a majority of the disinterested members of the Board that the Grantee has engaged in any of the following: (i) malfeasance in office; (ii) gross misconduct or neglect; (iii) false or fraudulent misrepresentation inducing the Grantee's appointment to the Board; (iv) willful conversion of corporate funds; or (v) disclosure of trade secrets or confidential information of the Company to persons not entitled to receive such information.

(f) Exercise of Options. A Grantee may exercise an Option that has become vested and exercisable, in whole or in part, by delivering a notice of exercise to the Company. The Grantee shall pay the Exercise Price for an Option (i) in cash; (ii) by delivering shares of Company Stock owned by the Grantee (including Company Stock acquired in connection with the exercise of an Option, subject to such restrictions as the Board deems appropriate) and having a Fair Market Value on the date of exercise equal to the Exercise Price or by attestation (on a form prescribed by the Board) to ownership of shares of Company Stock having a Fair Market Value on the date of exercise equal to the Exercise Price; (iii) after an initial public offering of the Company's stock as described in Section 17(b) (a "Public Offering"), payment through a broker in accordance with procedures permitted by Regulation T of the Federal Reserve Board; or (iv) by such other method as the Board may approve. In addition, the Grantee may elect to settle the Option on a "net basis" by taking delivery of the number of Company Stock equal to Fair Market Value of the shares subject to any Option less the exercise price, any tax (or other governmental obligation) or other administration fees due. Shares of Company Stock used to exercise an Option shall have been held by the Grantee for the requisite period of time to avoid adverse accounting consequences to the Company with respect to the Option. The Grantee shall pay the Exercise Price as specified by the Board.

6. **Stock Awards and RSUs**

The following provisions are applicable to Stock Awards and RSUs:

(a) General Requirements. Shares of Company Stock issued or transferred pursuant to Stock Awards may be issued or transferred for consideration or for no consideration, and

subject to restrictions or no restrictions, as determined by the Board. The Board shall determine the number of shares of Company Stock subject to a Stock Award and the number of RSUs to be granted to a Grantee, the duration of the period during which, and the conditions, if any, under which, the Stock Award and RSUs may vest or may be forfeited to the Company and the other terms and conditions of such Awards. The Board may require different periods of service or different performance goals and objectives with respect to different Grantees holding different Stock Awards or RSUs or to separate, designated portions of shares constituting Stock Awards.

(b) Transfer Restrictions and Legend on Stock Certificate. Stock Awards and RSUs may not be sold, assigned, transferred, pledged or otherwise encumbered except as provided in the Plan or as may be provided in the applicable Award Agreement; provided, however, that the Board may determine that Stock Awards and RSUs may be transferred by the Grantee. Each certificate for Stock Awards shall contain a legend giving appropriate notice of the restrictions in the Award. The Grantee shall be entitled to have the legend removed from the stock certificate covering the shares subject to restrictions when all restrictions on such shares have lapsed. The Board may determine that the Company shall not issue certificates for Stock Awards until all restrictions on such shares have lapsed, or that the Company shall retain possession of certificates for Stock Awards until all restrictions on such shares have lapsed. Upon the lapse of the restrictions applicable to a Stock Award, the Company or other custodian, as applicable, shall deliver such certificates to the Grantee or the Grantee's legal representative.

(c) Payment/Lapse of Restrictions. Each RSU shall be granted with respect to one share of Company Stock or shall have a value equal to the Fair Market Value of one share of Company Stock. RSUs shall be paid in cash, shares of Company Stock, other securities, other Awards or other property, as determined in the sole discretion of the Board, upon the lapse of restrictions applicable thereto, or otherwise in accordance with the applicable Award Agreement. The amount payable as a result of the vesting of an RSU shall be distributed as soon as practicable following the vesting date and in no event later than the fifteenth date of the third calendar month of the year following the vesting date of the RSU (or as otherwise permitted under Section 409A of the Code); provided, however, that a Grantee may, if and to the extent permitted by the Board, elect to defer payment of RSUs in a manner permitted by Section 409A of the Code.

(d) Termination of Service. Except as otherwise set forth in the Award Agreement, if the Grantee ceases to provide service to the Company, any Stock Award or RSUs held by the Grantee that are subject to the transfer restrictions set forth in Section 6(b) above at such time shall be forfeited. The Board may, however, provide for complete or partial exceptions to this requirement as it deems appropriate.

(e) No Right to Vote and to Receive Dividends. Prior to the lapse of the transfer restrictions set forth in Section 6(b) above, the Grantee shall not have the right to vote shares subject to Stock Awards or to receive any dividends or other distributions paid on such shares, subject to any restrictions deemed appropriate by the Board.

7. **Transferability of Awards**

(a) Nontransferability of Awards. Except as provided below, only the Grantee may exercise rights under an Award during the Grantee's lifetime. A Grantee may not transfer those rights except (i) by will or by the laws of descent and distribution or (ii) if permitted in any specific case by the Board, pursuant to a domestic relations order or otherwise as permitted by the Board. When a Grantee dies, the personal representative or other person entitled to succeed to the rights of the Grantee may exercise such rights. Any such successor must furnish proof satisfactory to the Company of his or her right to receive the Award under the Grantee's will or under the applicable laws of descent and distribution.

(b) Transfer of Nonqualified Stock Options. Notwithstanding the foregoing, the Board may provide, in an Award Agreement, that a Grantee may transfer Options to family members, or one or more trusts or other entities for the benefit of or owned by family members, consistent with applicable securities laws, according to such terms as the Board may determine; provided that the Grantee receives no consideration for the transfer of an Option and the transferred Option shall continue to be subject to the same terms and conditions as were applicable to the Option immediately before the transfer.

8. **Right of First Refusal; Repurchase Right**

(a) Offer. Prior to a Public Offering, if at any time an individual desires to sell, encumber, or otherwise dispose of shares of Company Stock that were distributed to him or her under the Plan and that are transferable, the individual may do so only pursuant to a bona fide written offer, and the individual shall first offer the shares to the Company by giving the Company written notice disclosing: (i) the name of the proposed transferee of the Company Stock; (ii) the certificate number and number of shares of Company Stock proposed to be transferred or encumbered; (iii) the proposed price; (iv) all other terms of the proposed transfer; and (v) a written copy of the proposed offer. Within 60 days after receipt of such notice, the Company shall have the option to purchase all or part of such Company Stock at the price and on the terms described in the written notice; provided that the Company may pay such price in installments over a period not to exceed four years, at the discretion of the Board.

(b) Sale. In the event the Company (or a shareholder, as described below) does not exercise the option to purchase Company Stock, as provided above, the individual shall have the right to sell, encumber, or otherwise dispose of the shares of Company Stock described in subsection (a) at the price and on the terms of the transfer set forth in the written notice to the Company, provided such transfer is effected within 15 days after the expiration of the option period. If the transfer is not effected within such period, the Company must again be given an option to purchase, as provided above.

(c) Assignment of Rights. The Board, in its sole discretion, may waive the Company's right of first refusal and repurchase right under this Section 8. If the Company's right of first refusal or repurchase right is so waived, the Board may, in its sole discretion, assign such right to the remaining shareholders of the Company in the same proportion that each shareholder's stock ownership bears to the stock ownership of all the shareholders of the Company, as determined by the Board. To the extent that a shareholder has been given such

right and does not purchase his or her allotment, the other shareholders shall have the right to purchase such allotment on the same basis.

(d) Purchase by the Company. Prior to a Public Offering, if a Grantee ceases to provide service to the Company, the Company shall have the right to purchase, within 60 days of the date that Grantee ceases to provide services to the Company, all or part of any Company Stock distributed to Grantee under the Plan at the Fair Market Value (as defined in Section 5(b)) on the date that Grantee ceases to provide services to the Company (or at such other price as may be established in the Award Agreement); provided, however, that such repurchase shall be made in accordance with applicable accounting rules to avoid adverse accounting treatment.

(e) Public Offering. On and after a Public Offering, the Company shall have no further right to purchase shares of Company Stock under this Section 8.

(f) Shareholder's Agreement. Notwithstanding the provisions of this Section 8, if the Board requires that a Grantee execute a shareholder's agreement with respect to any Company Stock distributed pursuant to the Plan, which contains a right of first refusal or repurchase right, the provisions of this Section 8 shall not apply to such Company Stock.

9. **Change of Control of the Company**

As used herein, a "Change of Control" shall be deemed to have occurred if:

(a) Any "person" (as such term is used in sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act")) (other than persons who are shareholders on the effective date of the Plan) becomes a "beneficial owner" (as defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of securities of the Company representing more than 50% of the voting power of the then outstanding securities of the Company; provided that a Change of Control shall not be deemed to occur as a result of a change of ownership resulting from the death of a shareholder, and a Change of Control shall not be deemed to occur as a result of a transaction in which the Company becomes a subsidiary of another corporation and in which the shareholders of the Company, immediately prior to the transaction, will beneficially own, immediately after the transaction, shares entitling such shareholders to more than 50% of all votes to which all shareholders of the parent corporation would be entitled in the election of directors (without consideration of the rights of any class of stock to elect directors by a separate class vote); or

(b) The consummation of (i) a merger or consolidation of the Company with another corporation where the shareholders of the Company, immediately prior to the merger or consolidation, will not beneficially own, immediately after the merger or consolidation, shares entitling such shareholders to more than 50% of all votes to which all shareholders of the surviving corporation would be entitled in the election of directors (without consideration of the rights of any class of stock to elect directors by a separate class vote); (ii) a sale or other disposition of all or substantially all of the assets of the Company; or (iii) a liquidation or dissolution of the Company.

(c) Notwithstanding the foregoing, the following acquisitions shall not constitute a Change of Control: (A) an acquisition by the Company or entity controlled by the Company, or

(B) an acquisition by an employee benefit plan (or related trust) sponsored or maintained by the Company

10. **Consequences of a Change of Control**

(a) Assumption of Awards. Upon a Change of Control where the Company is not the surviving corporation (or survives only as a subsidiary of another corporation), unless the Board determines otherwise, all outstanding Awards shall be assumed by, or replaced with comparable Awards by, the surviving corporation (or a parent or subsidiary of the surviving corporation).

(b) Termination of Awards. Upon a Change of Control where the Company is not the surviving corporation (or survives only as a subsidiary of another corporation), in the event the surviving corporation (or a parent or subsidiary of the surviving corporation) does not assume or replace the Awards with comparable Awards, (i) the Company shall provide each Grantee with outstanding Awards written notice of such Change of Control; (ii) all outstanding Options shall automatically accelerate and become fully vested and exercisable; (iii) all outstanding Stock Awards shall become vested and deliverable in accordance with Section 6(b); and (iv) all outstanding RSUs shall become vested and deliverable in accordance with Section 6(c).

(c) Other Alternatives. Notwithstanding the foregoing, in the event of a Change of Control, the Board may take one or both of the following actions: the Board may (i) require that Grantees surrender their outstanding Options in exchange for a payment by the Company, in cash or Company Stock as determined by the Board, in an amount equal to the amount by which the then Fair Market Value of the shares of Company Stock subject to the Grantee's unexercised Options exceeds the Exercise Price of the Options; or (ii) after giving Grantees an opportunity to exercise their outstanding Options, terminate any or all unexercised Options at such time as the Board deems appropriate. Such surrender or termination shall take place as of the date of the Change of Control or such other date as the Board may specify.

11. **Requirements for Issuance or Transfer of Shares**

(a) Shareholder's Agreement. The Board may require that a Grantee execute a shareholder's agreement, with such terms as the Board deems appropriate, with respect to any Company Stock issued or distributed pursuant to the Plan.

(b) Limitations on Issuance or Transfer of Shares. No Company Stock shall be issued or transferred in connection with any Award hereunder unless and until all legal requirements applicable to the issuance or transfer of such Company Stock have been complied with to the satisfaction of the Board. The Board shall have the right to condition any Award made to any Grantee hereunder on such Grantee's undertaking in writing to comply with such restrictions on his or her subsequent disposition of such shares of Company Stock as the Board shall deem necessary or advisable, and certificates representing such shares may be legended to reflect any such restrictions. Certificates representing shares of Company Stock issued or transferred under the Plan shall be subject to such stop-transfer orders and other restrictions as

may be required by applicable laws, regulations, and interpretations, including any requirement that a legend be placed thereon.

(c) Lock-Up Period. If so requested by the Company or any representative of the underwriters (the "Managing Underwriter") in connection with any underwritten offering of securities of the Company under the Securities Act of 1933, as amended (the "Securities Act"), a Grantee (including any successor or assigns) shall not sell or otherwise transfer any shares or other securities of the Company during the 30-day period preceding and the 180-day period following the effective date of a registration statement of the Company filed under the Securities Act for such underwriting (or such shorter period as may be requested by the Managing Underwriter and agreed to by the Company) (the "Market Standoff Period"). The Company may impose stop-transfer instructions with respect to securities subject to the foregoing restrictions until the end of such Market Standoff Period.

12. **Amendment and Termination of the Plan**

(a) Amendment. The Board may amend or terminate the Plan at any time; provided, however, that the Board shall not amend the Plan without shareholder approval if such approval is required in order to comply with the Code or other applicable laws or, after an Initial Public Offering, to comply with applicable stock exchange requirements.

(b) Termination of Plan. The Plan shall terminate on the day immediately preceding the tenth anniversary of its effective date, unless the Plan is terminated earlier by the Board or is extended by the Board with the approval of the shareholders.

(c) Termination and Amendment of Outstanding Awards . A termination or amendment of the Plan that occurs after an Award is made shall not materially impair the rights of a Grantee unless the Grantee consents or unless the Board acts under Section 18(b). The termination of the Plan shall not impair the power and authority of the Board with respect to an outstanding Award. Whether or not the Plan has terminated, an outstanding Award may be terminated or amended under Section 18(b) or may be amended by agreement of the Company and the Grantee consistent with the Plan.

(d) Governing Document. The Plan shall be the controlling document. No other statements, representations, explanatory materials or examples, oral or written, may amend the Plan in any manner. The Plan shall be binding upon and enforceable against the Company and its successors and assigns.

13. **Funding of the Plan**

The Plan shall be unfunded. The Company shall not be required to establish any special or separate fund or to make any other segregation of assets to assure the payment of any Awards under the Plan. In no event shall interest be paid or accrued on any Award, including unpaid installments of Awards.

14. **Rights of Participants**

Nothing in the Plan shall entitle any Non-Employee Director or other person to any claim or right to be granted an Award under the Plan. Neither the Plan nor any action taken hereunder shall be construed as giving any individual any rights to be retained by the Company or any other employment rights.

15. **No Fractional Shares**

No fractional shares of Company Stock shall be issued or delivered pursuant to the Plan or any Award. The Board shall determine whether cash, other awards or other property shall be issued or paid in lieu of such fractional shares or whether such fractional shares or any rights thereto shall be forfeited or otherwise eliminated.

16. **Headings**

Section headings are for reference only. In the event of a conflict between a title and the content of a Section, the content of the Section shall control.

17. **Effective Date of the Plan**

(a) Effective Date. The Plan shall be effective on September 3, 2015.

(b) Public Offering. The provisions of the Plan that refer to a Public Offering, or that refer to, or are applicable to persons subject to, section 16 of the Exchange Act, shall be effective, if at all, upon the initial registration of the Company Stock under section 12(g) of the Exchange Act, and shall remain effective thereafter for so long as such stock is so registered.

18. **Miscellaneous**

(a) Withholding. To the extent required by applicable Federal, state or local law, a Grantee must make arrangements satisfactory to the Company for the payment of any withholding or similar tax obligations that arise in connection with the Plan.

(b) Compliance with Law. The Plan, exercise of Options, restrictions of Stock Awards and obligations of the Company to issue or transfer shares of Company Stock under Awards shall be subject to all applicable laws and to approvals by any governmental or regulatory agency as may be required. With respect to persons subject to section 16 of the Exchange Act, after a Public Offering, it is the intent of the Company that the Plan and all transactions under the Plan comply with all applicable provisions of Rule 16b-3 or its successors under the Exchange Act. In addition, it is the intent of the Company that the Plan and applicable Awards under the Plan comply with the applicable provisions of section 409A of the Code. To the extent that any legal requirement of section 16 of the Exchange Act or section 409A of the Code as set forth in the Plan ceases to be required under section 16 of the Exchange Act or section 409A of the Code, that Plan provision shall cease to apply. The Board may revoke any Award if it is contrary to law or modify an Award to bring it into compliance with any valid and mandatory government regulation. The Board may also adopt rules regarding the

withholding of taxes on payments to Grantees. The Board may, in its sole discretion, agree to limit its authority under this Section.

(c) Grantees Subject to Taxation Outside the United States. With respect to Grantees who are subject to taxation in countries other than the United States, the Board may make Awards on such terms and conditions as the Board deems appropriate to comply with the laws of the applicable countries, and the Board may create such procedures, addenda, and subplans and make such modifications as may be necessary or advisable to comply with such laws.

(d) Governing Law. The validity, construction, interpretation, and effect of the Plan and Award Agreements issued under the Plan shall be governed and construed by and determined in accordance with the laws of the State of Delaware, without giving effect to the conflict of laws provisions thereof.

Exhibit 10.15

STRONGBRIDGE BIOPHARMA PLC
2017 INDUCEMENT PLAN

The purpose of the Strongbridge Biopharma plc 2017 Inducement Plan is to assist Strongbridge Biopharma plc and its affiliates and subsidiaries in attracting valued employees by offering them a greater stake in the Company's success and a closer identity with it, and to encourage ownership of the Company's stock by such employees.

1. **Definitions**

As used herein, the following definitions shall apply:

(a) "Award" means a grant of Options, Stock Awards or Restricted Stock Units under the Plan.

(b) "Award Agreement" means the written agreement, instrument or document evidencing an Award.

(c) "Board" means the Board of Directors of the Company.

(d) "Change of Control" means, after the Effective Date, any of the following events:

(i) Any "person" (as such term is used in sections 13(d) and 14(d) of the Exchange Act) (other than persons who are shareholders on the Effective Date) becomes a "beneficial owner" (as defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of securities of the Company representing more than 50% of the voting power of the then outstanding securities of the Company; provided that a Change of Control shall not be deemed to occur as a result of a change of ownership resulting from the death of a shareholder, and a Change of Control shall not be deemed to occur as a result of a transaction in which the Company becomes a subsidiary of another corporation and in which the shareholders of the Company, immediately prior to the transaction, will beneficially own, immediately after the transaction, shares entitling such shareholders to more than 50% of all votes to which all shareholders of the parent corporation would be entitled in the election of directors (without consideration of the rights of any class of stock to elect directors by a separate class vote); or

(ii) The consummation of (i) a merger or consolidation of the Company with another corporation where the shareholders of the Company, immediately prior to the merger or consolidation, will not beneficially own, immediately after the merger or consolidation, shares entitling such shareholders to more than 50% of all votes to which all shareholders of the surviving corporation would be entitled in the election of directors (without consideration of the rights of any class of stock to elect directors by a separate class vote); (ii) a sale or other disposition of all

or substantially all of the assets of the Company; or (iii) a liquidation or dissolution of the Company.

(iii) Notwithstanding the foregoing, the following acquisitions shall not constitute a Change of Control: (A) an acquisition by the Company or entity controlled by the Company, or (B) an acquisition by an employee benefit plan (or related trust) sponsored or maintained by the Company.

(e) "Code" means the Internal Revenue Code of 1986, as amended, and the Treasury regulations promulgated thereunder. A reference to any provision of the Code or the Treasury regulations promulgated thereunder shall include reference to any successor provision of the Code or the Treasury regulations.

(f) "Committee" means the committee designated by the Board to administer the Plan under Section 2. The Committee shall consist of at least two members and each member shall be a Non-Employee Director and an "independent director" within the meaning of Rule 5605(a)(3) of the Nasdaq Stock Market Equity Rules.

(g) "Company" means Strongbridge BioPharma plc.

(h) "Company Stock" means the ordinary shares of the Company, par value US$0.01 per share each.

(i) "Effective Date" has the meaning set forth in Section 17.

(j) "Eligible Individual" means any individual who was not previously an employee or a Non-Employee Director of the Company or any of its subsidiaries (or who had a bona fide period of non-employment with the Company and its subsidiaries) who is hired by the Company or a subsidiary.

(k) "Exchange Act" means the Securities Exchange Act of 1934, as amended, and the rules promulgated thereunder. A reference to any provision of the Exchange Act or rule promulgated under the Exchange Act shall include reference to any successor provision or rule.

(l) "Fair Market Value" means: (x) if the principal trading market for the Company Stock is a national securities exchange or the Nasdaq National Market, the last reported sale price thereof on the relevant date or (if there were no trades on that date) the latest preceding date upon which a sale was reported, or (y) if the Company Stock is not principally traded on such exchange or market, the mean between the last reported "bid" and "asked" prices of Company Stock on the relevant date, as reported on Nasdaq or, if not so reported, as reported by the National Daily

Quotation Bureau, Inc. or as reported in a customary financial reporting service, as applicable and as the Committee determines.

(m) "Grantee" means an Eligible Individual who receives an Award under the Plan.

(n) "Non-Employee Director" means a member of the Board who meets the definition of a "non-employee director" under Rule 16b-3(b)(4) promulgated by the Exchange Act.

(o) "Option" means a right to purchase a specified number of Company Stock at a specified price awarded by the Committee as described in Section 6 of the Plan.

(p) "Plan" means the Strongbridge BioPharma plc 2017 Inducement Plan.

(q) "Restricted Stock Unit" means the right to a payment in Company Stock or in cash, or in a combination thereof, awarded by the Committee under Section 7 of the Plan.

(r) "Stock Award" means the right to payment in Company Stock awarded by the Committee under Section 7 of the Plan.

2. **Administration**

(a) Administration and Authority. The Plan shall be administered by the Compensation Committee. The Committee shall have the sole authority to (i) determine the Eligible Individuals to whom Awards shall be made under the Plan; (ii) determine the type, size, and terms of the Award to be made to each such Eligible Individual; (iii) determine the time when the Awards will be made and the duration of any applicable exercise or restriction period, including the criteria for exercisability and the acceleration of exercisability; (iv) amend the terms of any previously issued Award; (v) accelerate the vesting, exercisability, or lapse of any forfeiture condition with respect to an Award; and (vi) deal with any other matters arising under the Plan.

(b) Committee Determinations. The Committee shall have full power and authority to administer, construe and interpret the Plan, correct any defect, supply any omission, or reconcile any inconsistency in the Plan or any Award or Award Agreement, make factual determinations and adopt or amend such rules, regulations, agreements, and instruments for implementing the Plan and for the conduct of its business as it deems necessary or advisable, in its sole discretion. The Committee's interpretations of the Plan and all determinations made by the Committee pursuant to the powers vested in it hereunder shall be conclusive and binding on all persons having any interest in the Plan or in any Awards granted hereunder. All powers of the Committee shall be executed in its sole discretion, in the best interest of the Company, not as a fiduciary, and in keeping with the objectives of the Plan and need not be uniform as to similarly situated individuals.

(c) Limitation of Liability. To the maximum extent permitted by law, no member of the Committee shall be liable for any action taken or decision made in good faith relating to the Plan or any Award thereunder. The Committee may employ counsel, consultants, accountants, appraisers, brokers or other persons. The Committee, the Company, and the officers and directors

of the Company shall be entitled to rely upon the advice, opinions or valuations of any such persons.

3. **Awards**

Awards under the Plan may consist of grants of Options as described in Section 6, as Stock Awards as described in Section 7, and Restricted Stock Units as described in Section 7. All Awards shall be subject to the terms and conditions set forth herein and to such other terms and conditions consistent with the Plan as the Committee deems appropriate and as are specified in the Award Agreement. The Committee shall approve the form and provisions of each Award Agreement. Awards under a particular Section of the Plan need not be uniform as among the Grantees.

4. **Shares Subject to the Plan**

(a) Shares Authorized. Subject to adjustment as described below, the Company Stock available for Awards under the Plan is 2,750,000 (the "Share Pool"). The shares may be authorized but unissued shares of Company Stock or reacquired shares of Company Stock, including shares purchased by the Company on the open market for purposes of the Plan.

(b) Adjustments to Share Pool. The Share Pool shall be reduced, on the date of grant, by one share for each Award granted under the Plan; provided that Awards that are valued by reference to shares of Company Stock but are required to be paid in cash pursuant to their terms shall not reduce the Share Pool. If and to the extent Options terminate, expire, or are canceled, forfeited, exchanged, or surrendered without having been exercised, or if any Stock Awards or Restricted Stock Units (including restricted stock received upon the exercise of Options) are forfeited, the shares of Company Stock subject to such Awards shall again be available for Awards under the Share Pool. Notwithstanding the foregoing, the following shares of Company Stock shall not become available for issuance under the Plan: (A) shares tendered by Grantees, or withheld by the Company, as full or partial payment to the Company upon the exercise of stock options granted under the Plan; and (B) shares withheld by, or otherwise remitted to, the Company to satisfy a Grantee's tax withholding obligations upon the lapse of restrictions on Stock Awards or the exercise of Options granted under the Plan.

(c) Adjustments. If there is any change in the number or kind of shares of Company Stock outstanding (i) by reason of a stock dividend, spinoff, recapitalization, stock split, or combination or exchange of shares; (ii) by reason of a merger, reorganization, or consolidation; (iii) by reason of a reclassification or change in par value; or (iv) by reason of any other extraordinary or unusual event affecting the outstanding Company Stock as a class without the Company's receipt of consideration, or if the value of outstanding shares of Company Stock is substantially reduced as a result of a spinoff or the Company's payment of an extraordinary dividend or distribution, the maximum number of shares of Company Stock available for Awards, the maximum number of shares of Company Stock that any individual participating in the Plan may be granted in any year, the number of shares covered by outstanding Awards, the kind of shares issued under the Plan, and the price per share of such Awards shall be adjusted by the Committee to reflect any increase or decrease in the number of, or change in the kind or value of, issued shares of Company Stock to preclude the enlargement or dilution of rights and benefits under such Awards; provided, however, that any fractional shares resulting from such adjustment

shall be eliminated. Any adjustments determined by the Committee shall be final, binding, and conclusive.

5. **Eligibility for Participation**

Any Eligible Individual shall be eligible to participate in the Plan. The Committee shall select the Eligible Individuals to receive Awards and shall determine the number of shares of Company Stock subject to a particular Award in such manner as the Committee determines.

6. **Granting of Options**

The Company may grant Options to purchase shares of Company Stock to Eligible Individuals. The following provisions are applicable to Options.

(a) Number of Shares. The Committee shall determine the number of shares of Company Stock that shall be subject to each Award of Options.

(b) Price. The purchase price (the "Exercise Price") of Company Stock subject to an Option shall be determined by the Board and shall be equal to or greater than the Fair Market Value of a share of Company Stock on the date the Option is granted.

(c) Option Term. The Committee shall determine the term of each Option. The term of any Option shall not exceed ten years from the date of grant.

(d) Exercisability of Options. Options shall become exercisable in accordance with such terms and conditions, consistent with the Plan, as may be determined by the Committee and specified in the Award Agreement. The Committee may accelerate the exercisability of any or all outstanding Options at any time for any reason. The Committee may provide in an Award Agreement that the Grantee may elect to exercise part or all of an Option before it otherwise has become exercisable. Any shares so purchased shall be restricted shares and shall be subject to a repurchase right in favor of the Company during a specified restriction period, with the repurchase price equal to the lesser of (A) the Exercise Price, or (B) the Fair Market Value of such shares at the time of repurchase, and (C) any other restrictions determined by the Company.

(e) Termination of Employment, Disability, or Death.

(i) Except as provided below, an Option may only be exercised while the Grantee is employed by, or providing service to, the Employer (as defined below) as an Eligible Individual. In the event that a Grantee ceases to be employed by, or provide service to, the Employer for any reason other than Disability, death, or termination for Cause, any Option which is otherwise exercisable by the Grantee shall terminate unless exercised within 90 days after the date on which the Grantee ceases to be employed by, or provide service to, the Employer (or within such other period of time as may be specified by the Committee), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Committee or in the Award Agreement, any of the Grantee's Options that are not otherwise exercisable as of the date on which the Grantee ceases to be employed by, or provide service to, the Employer shall terminate as of such date.

(ii) In the event the Grantee ceases to be employed by, or provide service to, the Employer on account of a termination for Cause by the Employer, any Option held by the Grantee shall terminate as of the date the Grantee ceases to be employed by, or provide service to, the Employer. In addition, notwithstanding any other provisions of this Section 6, if the Committee determines that the Grantee has engaged in conduct that constitutes Cause at any time while the Grantee is employed by, or providing service to, the Employer or after the Grantee's termination of employment or service, any Option held by the Grantee shall immediately terminate, and the Grantee shall automatically forfeit all shares underlying any exercised portion of an Option for which the Company has not yet delivered the share certificates, upon refund by the Company of the Exercise Price paid by the Grantee for such shares. Upon any exercise of an Option, the Company may withhold delivery of share certificates pending resolution of an inquiry that could lead to a finding resulting in a forfeiture.

(iii) In the event the Grantee ceases to be employed by, or provide service to, the Employer because the Grantee is Disabled (as defined below), any Option which is otherwise exercisable by the Grantee shall terminate unless exercised within one year after the date on which the Grantee ceases to be employed by, or provide service to, the Employer (or within such other period of time as may be specified by the Committee), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Committee, any of the Grantee's Options which are not otherwise exercisable as of the date on which the Grantee ceases to be employed by, or provide service to, the Employer shall terminate as of such date.

(iv) If the Grantee dies while employed by, or providing service to, the Employer or within 90 days after the date on which the Grantee ceases to be employed or provide service on account of a termination specified in Section 6(e)(i) above (or within such other period of time as may be specified by the Committee), any Option that is otherwise exercisable by the Grantee shall terminate unless exercised within one year after the date on which the Grantee ceases to be employed by, or provide service to, the Employer (or within such other period of time as may be specified by the Committee), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Committee, any of the Grantee's Options that are not otherwise exercisable as of the date on which the Grantee ceases to be employed by, or provide service to, the Employer shall terminate as of such date.

(v) For purposes of this Plan:

(A) The term "Employer" shall mean the Company and its parent and subsidiary corporations or other entities, as determined by the Committee.

(B) "Employed by, or provide service to, the Employer" shall mean employment or service as an Eligible Individual (so that, for purposes of exercising Options and satisfying conditions with respect to Stock Awards or Restricted Stock Units, a Grantee shall not be considered to have terminated employment or service until the Grantee ceases to be an Eligible Individual, unless the Committee determines otherwise.

(C) "Disability" shall mean a Grantee's becoming disabled within the meaning of section 22(e)(3) of the Code, within the meaning of the Employer's long-

term disability plan applicable to the Grantee, or as otherwise determined by the Committee.

(D) "Cause" shall mean, except to the extent specified otherwise by the Committee or as defined in any other agreement between the Grantee and the Company, a finding by the Committee that the Grantee has (i) been convicted of a felony or crime involving moral turpitude; (ii) disclosed trade secrets or confidential information of the Employer to persons not entitled to receive such information; (iii) breached any written noncompetition or nonsolicitation agreement between the Grantee and the Employer; or (iv) engaged in willful and continued negligence in the performance of the duties assigned to the Grantee by the Employer, after the Grantee has received notice of and failed to cure such negligence.

(f) Exercise of Options. A Grantee may exercise an Option that has become vested and exercisable, in whole or in part, by delivering a notice of exercise to the Company. The Grantee shall pay the Exercise Price for an Option by the Committee (i) in cash; (ii) by delivering shares of Company Stock owned by the Grantee (including Company Stock acquired in connection with the exercise of an Option, subject to such restrictions as the Committee deems appropriate) and having a Fair Market Value on the date of exercise equal to the Exercise Price or by attestation (on a form prescribed by the Committee) to ownership of shares of Company Stock having a Fair Market Value on the date of exercise equal to the Exercise Price; (iii) payment through a broker in accordance with procedures permitted by Regulation T of the Federal Reserve Board; or (iv) by such other method as the Committee may approve. In addition, the Grantee may elect to settle the Option on a "net basis" by taking delivery of the number of Company Stock equal to Fair Market Value of the shares subject to any Option less the exercise price, any tax (or other governmental obligation) or other administration fees due. The Grantee shall pay the Exercise Price and the amount of any withholding tax due (pursuant to Section 8) as specified by the Committee.

7. **Stock Awards and Restricted Stock Units**

The Company may issue or transfer shares of Company Stock to an Eligible Individual under a Stock Award or Restricted Stock Unit, upon such terms as the Committee deems appropriate. The following provisions are applicable to Stock Awards and Restricted Stock Units:

(a) General Requirements. Shares of Company Stock issued or transferred pursuant to Stock Awards may be issued or transferred for consideration or for no consideration, and subject to restrictions or no restrictions, as determined by the Committee. The Committee shall determine the number of shares of Company Stock subject to a Stock Award and the number of Restricted Stock Units to be granted to a Grantee, the duration of the period during which, and the conditions, if any, under which, the Stock Award and Restricted Stock Units may vest or may be forfeited to the Company and the other terms and conditions of such Awards. The Committee may require different periods of service wiith respect to different Grantees holding different Stock Awards or Restricted Stock Units or to separate, designated portions of shares constituting Stock Awards.

(b) Transfer Restrictions and Legend on Stock Certificate. Stock Awards and Restricted Stock Units may not be sold, assigned, transferred, pledged or otherwise encumbered

except as provided in the Plan or as may be provided in the applicable Award Agreement; provided, however, that the Committee may determine that Stock Awards and Restricted Stock Units may be transferred by the Grantee. Each certificate for Stock Awards shall contain a legend giving appropriate notice of the restrictions in the Award. The Grantee shall be entitled to have the legend removed from the stock certificate covering the shares subject to restrictions when all restrictions on such shares have lapsed. The Committee may determine that the Company shall not issue certificates for Stock Awards until all restrictions on such shares have lapsed, or that the Company shall retain possession of certificates for Stock Awards until all restrictions on such shares have lapsed. Upon the lapse of the restrictions applicable to a Stock Award, the Company or other custodian, as applicable, shall deliver such certificates to the Grantee or the Grantee's legal representative.

(c) Payment/Lapse of Restrictions. Each Restricted Stock Unit shall be granted with respect to one share of Company Stock or shall have a value equal to the Fair Market Value of one share of Company Stock. Restricted Stock Units shall be paid in cash, shares of Company Stock, other securities, other Awards or other property, as determined in the sole discretion of the Committee, upon the lapse of restrictions applicable thereto, or otherwise in accordance with the applicable Award Agreement. The amount payable as a result of the vesting of an Restricted Stock Unit shall be distributed as soon as practicable following the vesting date and in no event later than the fifteenth date of the third calendar month of the year following the vesting date of the Restricted Stock Unit (or as otherwise permitted under Section 409A of the Code); provided, however, that a Grantee may, if and to the extent permitted by the Committee, elect to defer payment of Restricted Stock Units in a manner permitted by Section 409A of the Code.

(d) Termination of Employment or Service. Except as otherwise set forth in the Award Agreement, if the Grantee ceases to be employed by, or provide service to, the Employer (as defined in Section 6(e)), any Stock Award or Restricted Stock Units held by the Grantee that are subject to the transfer restrictions set forth in Section 7(b) above at such time shall be forfeited. The Committee may, however, provide for complete or partial exceptions to this requirement as it deems appropriate.

(e) No Right to Vote and to Receive Dividends. Prior to the lapse of the transfer restrictions set forth in Section 7(b) above, the Grantee shall not have the right to vote shares subject to Stock Awards or to receive any dividends or other distributions paid on such shares, subject to any restrictions deemed appropriate by the Committee.

8. **Withholding of Taxes**

(a) Required Withholding. All Awards under the Plan shall be subject to applicable federal (including FICA), state, and local tax (or other governmental obligation) withholding requirements or other administration fees due. The Employer may require that the Grantee or other person receiving or exercising Awards pay to the Employer the amount of any federal, state, or local taxes (or other governmental obligations) that the Employer is required to withhold or any administration fees due with respect to such Awards, or the Employer may deduct from other wages paid by the Employer the amount of any withholding taxes, governmental obligations or administration fees due with respect to such Awards.

(b) Election to Withhold Shares. If the Board so permits, a Grantee may elect to satisfy the Employer's income tax (or other governmental obligation) withholding requirement and any administration fees due with respect to an Award by having shares withheld up to an amount that does not exceed the Grantee's minimum applicable withholding rate for federal (including FICA), state, and local tax (and other governmental obligation) liabilities plus any other administration fees due. The election must be in a form and manner prescribed by the Committee and may be subject to the prior approval of the Committee.

9. **Transferability of Awards**

(a) Nontransferability of Awards. Except as provided below, only the Grantee may exercise rights under an Award during the Grantee's lifetime. A Grantee may not transfer those rights except by will or by the laws of descent and distribution. When a Grantee dies, the personal representative or other person entitled to succeed to the rights of the Grantee may exercise such rights. Any such successor must furnish proof satisfactory to the Company of his or her right to receive the Award under the Grantee's will or under the applicable laws of descent and distribution.

(b) Transfer of Stock Options. Notwithstanding the foregoing, the Committee may provide, in an Award Agreement, that a Grantee may transfer Options to family members, or one or more trusts or other entities for the benefit of or owned by family members, consistent with applicable securities laws, according to such terms as the Committee may determine; provided that the Grantee receives no consideration for the transfer of an Option and the transferred Option shall continue to be subject to the same terms and conditions as were applicable to the Option immediately before the transfer.

10. **Consequences of a Change of Control**

(a) Assumption of Awards. Upon a Change of Control where the Company is not the surviving corporation (or survives only as a subsidiary of another corporation), unless the Committee determines otherwise, all outstanding Awards shall be assumed by, or replaced with comparable Awards by, the surviving corporation (or a parent or subsidiary of the surviving corporation).

(b) Termination of Awards. Upon a Change of Control where the Company is not the surviving corporation (or survives only as a subsidiary of another corporation), in the event the surviving corporation (or a parent or subsidiary of the surviving corporation) does not assume or replace the Awards with comparable Awards, (i) the Company shall provide each Grantee with outstanding Awards written notice of such Change of Control; (ii) all outstanding Options shall automatically accelerate and become fully vested and exercisable; (iii) all outstanding Stock Awards shall become vested and deliverable in accordance with Section 7(b); and (iv) all outstanding Restricted Stock Units shall become vested and deliverable in accordance with Section 7(c).

(c) Other Alternatives. Notwithstanding the foregoing, in the event of a Change of Control, the Committee may take one or both of the following actions: the Committee may (i) require that Grantees surrender their outstanding Options in exchange for a payment by the

Company, in cash or Company Stock as determined by the Committee, in an amount equal to the amount by which the then Fair Market Value of the shares of Company Stock subject to the Grantee's unexercised Options exceeds the Exercise Price of the Options; or (ii) after giving Grantees an opportunity to exercise their outstanding Options, terminate any or all unexercised Options at such time as the Committee deems appropriate. Such surrender or termination shall take place as of the date of the Change of Control or such other date as the Committee may specify.

11. **Requirements for Issuance or Transfer of Shares**

(a) Shareholder's Agreement. The Committee may require that a Grantee execute a shareholder's agreement, with such terms as the Committee deems appropriate, with respect to any Company Stock issued or distributed pursuant to the Plan.

(b) Limitations on Issuance or Transfer of Shares. No Company Stock shall be issued or transferred in connection with any Award hereunder unless and until all legal requirements applicable to the issuance or transfer of such Company Stock have been complied with to the satisfaction of the Committee. The Committee shall have the right to condition any Award made to any Grantee hereunder on such Grantee's undertaking in writing to comply with such restrictions on his or her subsequent disposition of such shares of Company Stock as the Committee shall deem necessary or advisable, and certificates representing such shares may be legended to reflect any such restrictions. Certificates representing shares of Company Stock issued or transferred under the Plan shall be subject to such stop-transfer orders and other restrictions as may be required by applicable laws, regulations, and interpretations, including any requirement that a legend be placed thereon.

(c) Lock-Up Period. If so requested by the Company or any representative of the underwriters (the "Managing Underwriter") in connection with any underwritten offering of securities of the Company under the Securities Act of 1933, as amended (the "Securities Act"), a Grantee (including any successor or assigns) shall not sell or otherwise transfer any shares or other securities of the Company during the 30-day period preceding and the 180-day period following the effective date of a registration statement of the Company filed under the Securities Act for such underwriting (or such shorter period as may be requested by the Managing Underwriter and agreed to by the Company) (the "Market Standoff Period"). The Company may impose stop-transfer instructions with respect to securities subject to the foregoing restrictions until the end of such Market Standoff Period.

12. **Amendment and Termination of the Plan**

(a) Amendment. The Board may amend or terminate the Plan at any time; provided, however, that the Board shall not amend the Plan without shareholder approval if such approval is required in order to comply with the Code or other applicable laws or to comply with applicable stock exchange requirements.

(b) Termination of Plan. The Plan shall terminate on the day immediately preceding the tenth anniversary of its effective date, unless the Plan is terminated earlier by the Board or is extended by the Board.

(c) Termination and Amendment of Outstanding Awards . A termination or amendment of the Plan that occurs after an Award is made shall not materially impair the rights of a Grantee unless the Grantee consents or unless the Board acts under Section 20(b). The termination of the Plan shall not impair the power and authority of the Committee with respect to an outstanding Award. Whether or not the Plan has terminated, an outstanding Award may be terminated or amended under Section 20(b) or may be amended by agreement of the Company and the Grantee consistent with the Plan. Notwithstanding the foregoing, any such amendment or termination shall be subject to the approval of the Company's stockholders if such stockholder approval is required by any federal or state law or regulation or the rules of any stock exchange or automated quotation system on which the Company Stock may then be listed or quoted, in each case.

(d) Governing Document. The Plan shall be the controlling document. No other statements, representations, explanatory materials or examples, oral or written, may amend the Plan in any manner. The Plan shall be binding upon and enforceable against the Company and its successors and assigns.

13. **Funding of the Plan**

The Plan shall be unfunded. The Company shall not be required to establish any special or separate fund or to make any other segregation of assets to assure the payment of any Awards under the Plan. In no event shall interest be paid or accrued on any Award, including unpaid installments of Awards.

14. **Rights of Participants**

Nothing in the Plan shall entitle any Eligible Individual or other person to any claim or right to be granted an Award under the Plan. Neither the Plan nor any action taken hereunder shall be construed as giving any individual any rights to be retained by or in the employ of the Employer or any other employment rights.

15. **No Fractional Shares**

No fractional shares of Company Stock shall be issued or delivered pursuant to the Plan or any Award. The Committee shall determine whether cash, other awards or other property shall be issued or paid in lieu of such fractional shares or whether such fractional shares or any rights thereto shall be forfeited or otherwise eliminated.

16. **Headings**

Section headings are for reference only. In the event of a conflict between a title and the content of a Section, the content of the Section shall control.

17. **Effective Date of the Plan**

The Plan shall be effective on February 23, 2017.

18. **Miscellaneous**

(a) Awards in Connection with Corporate Transactions and Otherwise. Nothing contained in the Plan shall be construed to (i) limit the right of the Committee to make Awards under the Plan in connection with the acquisition, by purchase, lease, merger, consolidation, or otherwise, of the business or assets of any corporation, firm or association; or (ii) limit the right of the Company to grant stock options or make other awards outside of the Plan.

(b) Compliance with Law. The Plan, exercise of Options, restrictions of Stock Awards and obligations of the Company to issue or transfer shares of Company Stock under Awards shall be subject to all applicable laws and to approvals by any governmental or regulatory agency as may be required. With respect to persons subject to section 16 of the Exchange Act, it is the intent of the Company that the Plan and all transactions under the Plan comply with all applicable provisions of Rule 16b-3 or its successors under the Exchange Act. In addition, it is the intent of the Company that the Plan and applicable Awards under the Plan comply with the applicable provisions of section 409A of the Code. To the extent that any legal requirement of section 16 of the Exchange Act or section 409A of the Code as set forth in the Plan ceases to be required under section 16 of the Exchange Act or section 409A of the Code, that Plan provision shall cease to apply. The Committee may revoke any Award if it is contrary to law or modify an Award to bring it into compliance with any valid and mandatory government regulation. The Committee may also adopt rules regarding the withholding of taxes on payments to Grantees. The Committee may, in its sole discretion, agree to limit its authority under this Section.

(c) Employees Subject to Taxation Outside the United States. With respect to Grantees who are subject to taxation in countries other than the United States, the Committee may make Awards on such terms and conditions as the Committee deems appropriate to comply with the laws of the applicable countries, and the Committee may create such procedures, addenda, and subplans and make such modifications as may be necessary or advisable to comply with such laws.

(d) Governing Law. The validity, construction, interpretation, and effect of the Plan and Award Agreements issued under the Plan shall be governed and construed by and determined in accordance with the laws of the State of Delaware, without giving effect to the conflict of laws provisions thereof.

Exhibit 21.1

Subsidiaries of the Company

Strongbridge U.S. Inc. (a Delaware corporation)

Strongbridge Dublin Limited (a private limited company incorporated under the laws of Ireland)

Cortendo AB (publ) (a public limited liability company incorporated under the laws of Sweden)

Cortendo Cayman Ltd. (an exempted company incorporated in the Cayman Islands)

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements: (Form S-3 Nos. 333-223575 and 333-223576) of Strongbridge Biopharma plc, (Form S-8 No. 333-225319) pertaining to the 2017 Inducement Plan of Strongbridge Biopharma plc, (Form S-8 No. 333-222818) pertaining to the 2015 Equity Compensation Plan, Non-Employee Director Equity Compensation Plan and 2017 Inducement Plan of Strongbridge Biopharma plc; and (Form S-8 No. 333-215532) pertaining to the 2015 Equity Compensation Plan, Non-Employee Director Equity Compensation Plan and Individual Stock Option Agreements of Strongbridge Biopharma plc; of our report dated February 27, 2019, with respect to the consolidated financial statements of Strongbridge Biopharma plc included in this Annual Report (Form 10-K) for the year ended December 31, 2018.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania
February 27, 2019

Exhibit 31.1

CERTIFICATIONS

I, Matthew Pauls, certify that:

1. I have reviewed this Annual Report on Form 10-K of Strongbridge Biopharma plc;

2. Based on my knowledge, this Annual Report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this Annual Report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2019

By:/s/ Matthew Pauls

Matthew Pauls
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, A. Brian Davis, certify that:

1. I have reviewed this Annual Report on Form 10-K of Strongbridge Biopharma plc;

2. Based on my knowledge, this Annual Report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this Annual Report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2019

By:/s/ A. Brian Davis

A. Brian Davis
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATIONS PURSUANT TO 18 U.S.C. 1350

Pursuant to the requirement set forth in Rule 13a-14(b) or Rule 15d-14(b) of the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. § 1350), as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Matthew Pauls, the Chief Executive Officer (principal executive officer) of Strongbridge Biopharma plc (the "Company"), and A. Brian Davis, the Chief Financial Officer (principal financial officer) of the Company, each hereby certifies that, to his knowledge on the date hereof:

(a) The Annual Report on Form 10-K of the Company for the period ended December 31, 2018 filed on the date hereof with the Securities and Exchange Commission (the "Annual Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(b) The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the period covered by the Annual Report.

These certifications accompanying the Annual Report to which they relate, are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Annual Report), irrespective of any general incorporation language contained in such filing. A signed original of this written statement required by Section 906 has been provided to the Company and will be retained and furnished to the Securities and Exchange Commission or its staff upon request.

By:/s/ Matthew Pauls
Matthew Pauls
Chief Executive Officer
(Principal Executive Officer)
February 27, 2019

By:/s/ A. Brian Davis
A. Brian Davis
Chief Financial Officer
(Principal Financial Officer)
February 27, 2019